ウゴーヒ皮下注 0.25mg SD
ウゴーヒ皮下注 0.5mg SD
ウゴーヒ皮下注 1.0mg SD
ウゴーヒ皮下注 1.7mg SD
ウゴーヒ皮下注 2.4mg SD

2.7.4 臨床的安全性

ノボ ノルディスク ファーマ株式会社

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略語一覧

ADA	:	American Diabetes Association（米国糖尿病学会）
ADR	:	adverse drug reaction（副作用）
AE	:	adverse event（有害事象）
ALP	:	alkaline phosphatase（アルカリホスファターゼ）
ALT	:	alanine aminotransferase（アラニンアミノトランスフェラーゼ）
AST	:	aspartate aminotransferase（アスパラギン酸アミノトランスフェラーゼ）
BMI	:	body mass index（体容量指数）
CI	:	confidence interval（信頼区間）
CK	:	creatine kinase（クレアチンキナーゼ）
CKD-EPI	:	Chronic Kidney Disease Epidemiology Collaboration formula（慢性腎臓病疫学共同研究）
C_{max}	:	maximum plasma drug concentration（最高血漿中濃度）
COVID-19	:	Coronavirus disease SARS-CoV-2 2019（新型コロナウイルス感染症）
CRF	:	case report form（症例報告書）
C-SSRS	:	Columbia-Suicide Severity Rating Scale（コロンビア自殺評価スケール）
CV	:	coefficient of variation（変動係数）
CVOT	:	cardiovascular outcomes trial（心血管アウトカム試験）
CYP450	:	cytochrome P450（チトクロム P450）
DPP-4	:	dipeptidyl peptidase 4（ジペプチジルペプチダーゼ-4）
EAC	:	event adjudication committee（イベント判定委員会）
EASD	:	European Association for the Study of Diabetes（欧州糖尿病学会）
eGFR	:	estimated glomerular filtration rate（推算糸球体濾過量）
FAS	:	full analysis set（最大の解析対象集団）
FU	:	follow-up（事後調査）
GGT	:	gamma glutamyl transferase（γ-グルタミルトランスフェラーゼ）
GLP-1	:	glucagon-like peptide-1（グルカゴン様ペプチド-1）
HbA1c	:	glycated haemoglobin
IBT	:	Intensive Behavioural Therapy（集中的行動療法）
ICH	:	International Conference on Harmonisation（日米 EU 医薬品規制調和国際会議）
IHSG	:	International Hypoglycaemia Study Group
JASSO	:	Japan Society for the Study of Obesity（日本肥満学会）
LCD	:	low calorie diet（低カロリー食）
MedDRA	:	Medical Dictionary for Regulatory Activities（国際医薬用語集）
MTC	:	medullary thyroid carcinoma（甲状腺髄様癌）
OAD	:	oral antidiabetic drug（経口糖尿病薬）
PHQ-9	:	Patient Health Questionaire-9（患者さんの健康に関する質問票-9）
PT	:	preferred term（基本語）
PYE	:	patient-years of exposure（被験者の曝露人年）
PYO	:	patient-years of observation（被験者の観察人年）
QTc	:	corrected QT interval（補正した QTc 間隔）
QTcF	:	Fridericia heart rate corrected QT interval（Fridericia 法で補正した QT 間隔）
SAS	:	safety analysis set（安全性解析対象集団）
SAE	:	serious adverse event（重篤な有害事象）
SD	:	standard deviation（標準偏差）
SGLT2	:	sodium glucose cotransporter 2（ナトリウム・グルコース共輸送体 2）
SOC	:	system organ class（器官別大分類）
STEP 1	:	NN9536-4373
STEP 2	:	NN9536-4374
STEP 3	:	NN9536-4375

STEP 4	:	NN9536-4376
STEP 6	:	NN9536-4382
SU	:	sulfonylurea（スルホニルウレア薬）
SUSAR	:	suspected unexpected serious adverse reaction（予測できない重篤な有害事象の疑い）
T2D	:	type 2 diabetes（2 型糖尿病）
TBL	:	total bilirubin（総ビリルビン）
TSH	:	thyroid stimulating hormone（甲状腺刺激ホルモン）
UACR	:	urinary albumin to creatinine ratio（尿アルブミン/クレアチニン比）
ULN	:	upper limit of the normal（基準範囲上限）

臨床試験の表記：

肥満症のための皮下投与用セマグルチドの開発プログラムに含まれる臨床試験は、プロジェクト番号 NN9536 と 4 桁の固有の番号（例：NN9536-4373）にて特定する。本概要では、臨床試験は 4 桁の固有の番号を用いて「XXXX 試験」と表記する。図表では第 3 相試験プログラムの 5 試験を STEP 1～4 及び STEP 6 と表記する場合がある。他の皮下投与用セマグルチドの開発プログラムの臨床試験は、プロジェクト番号と 4 桁の固有の番号（例：NN9535-3744）で表記する。

特記する場合を除き、「セマグルチド 2.4 mg 週 1 回皮下投与」は「セマグルチド 2.4 mg」と表記する。

2.7.4.1　医薬品への曝露

2.7.4.1.1　総括的安全性評価計画及び安全性試験の記述

2.7.4.1.1.1　セマグルチドの適応症及び背景

セマグルチド（遺伝子組換え）（以下、セマグルチド）は長時間作用型のグルカゴン様ペプチド-1（GLP-1）アナログであり、ヒト GLP-1 に対して高い相同性を有する。

セマグルチド 0.5 mg 及び 1.0 mg の週 1 回皮下投与は、オゼンピックの販売名で、2 型糖尿病の治療薬として世界各国で承認を取得しているほか、米国及びロシアでは、心血管疾患を有する 2 型糖尿病患者の心血管系リスク低減の適応でも承認を取得している。経口投与用のセマグルチド（リベルサス）は、2 型糖尿病の治療薬として米国、カナダ、欧州及び日本で承認を取得している。

本概要には、カロリーを制限した食事及び身体活動量の増加に対する補助療法としての肥満症治療のための、セマグルチド 2.4 mg 週 1 回皮下投与（以降、セマグルチド 2.4 mg）を支持するノボ ノルディスク社（治験依頼者、申請者）が収集したデータを提示する。

2.7.4.1.1.2　非臨床の安全性

2 型糖尿病のための皮下投与用セマグルチドの承認申請の一部として提出した非臨床に関する資料を、セマグルチドの非臨床での適切な評価の主な根拠とする。詳細は Module 2.4 を参照のこと。

2.7.4.1.1.3　肥満症に対するセマグルチドの臨床開発プログラム

2.7.4.1.1.3.1　臨床開発プログラムの概観

肥満症のためのセマグルチド 2.4 mg の臨床開発プログラムは、計 9 つの完了した試験から構成される：5 つの第 3 相試験（1 つの東アジア試験、2 つの国際共同試験及び 2 つの海外試験）、1 つの海外第 2 相用量設定試験及び 3 つの臨床薬理試験（このうち 2 つは生物学的同等性試験）（表 2.7.4.1-1）。これらの試験のうち、3 つの第 3 相試験（4373、4374 及び 4382 試験）に日本人被験者が組み入れられた。

表 2.7.4.1-1　肥満症のためのセマグルチドの臨床開発プログラムに含まれる完了した臨床試験

試験番号	被験者数	概要
第 3 相試験		
4373 試験（STEP 1） 国際共同試験	N=1961 （JP: N=100）	成人の過体重又は肥満被験者を対象とした、生活習慣への介入に対する補助療法としてのセマグルチド 2.4 mg（週 1 回皮下投与）の有効性及び安全性をプラセボと比較検討する、68 週間、無作為割り付け、二重盲検試験
4374 試験（STEP 2） 国際共同試験	N=1210 （JP: N=125）	成人の 2 型糖尿病を有する過体重又は肥満被験者を対象とした、生活習慣への介入に対する補助療法としてのセマグルチド 2.4 mg（週 1 回皮下投与）の有効性及び安全性をプラセボ及びセマグルチド 1.0 mg（週 1 回皮下投与）と比較検討する、68 週間、無作為割り付け、二重盲検試験
4375 試験（STEP 3） 海外試験	N=611	成人の過体重又は肥満被験者を対象とした、集中的行動療法の補助療法としてのセマグルチド 2.4 mg（週 1 回皮下投与）の有効性及び安全性をプラセボと比較検討する、68 週間、無作為割り付け、二重盲検試験
4376 試験（STEP 4） 海外試験	N=902	導入期間である最初の 20 週間で目標とする維持用量（セマグルチド 2.4 mg）に到達した、成人の過体重又は肥満被験者を対象として、セマグルチド 2.4 mg（週 1 回皮下投与）の有効性及び安全性をプラセボと比較検討する、68 週間、無作為割り付け、二重盲検試験
4382 試験（STEP 6） 東アジア試験	N=401 （JP: N=360）	成人の 2 型糖尿病を有する又は有さない過体重又は肥満被験者を対象とした、生活習慣への介入に対する補助療法としてのセマグルチド 1.7 mg 及び 2.4 mg（週 1 回皮下投与）の有効性及び安全性をプラセボと比較検討する、68 週間、無作為割り付け、二重盲検試験
第 2 相試験		
4153 試験 海外用量設定試験	N=957	成人の肥満被験者を対象とした、セマグルチド 1 日 1 回投与（2 つの用量漸増を用いた 0.05 mg/日～0.4 mg/日）の安全性及び有効性をプラセボ及び実薬（リラグルチド 3.0 mg）と比較検討する、52 週間、無作為割り付け、二重盲検、プラセボ対照、16 群並行群間比較試験
臨床薬理試験		
4455 試験 薬力学的作用	N=72	成人の肥満被験者を対象とした、胃内容排出に対するセマグルチド 2.4 mg 週 1 回投与の影響を検討する、21 週間、無作為割り付け、二重盲検、プラセボ対照試験
4590 試験 1.0 mg 及び 2.4 mg に対応する製剤の生物学的同等性	N=68	成人の過体重又は肥満被験者を対象とした、単回使用のペン型注入器（DV3396）の製剤（セマグルチド処方 D）と PDS290 ペン型注入器の製剤（セマグルチド処方 B）の生物学的同等性を評価する、21 週間、無作為割り付け、非盲検試験
NN9535-4588 試験 [a] 0.25 mg に対応する製剤の生物学的同等性	N=68	成人の過体重又は肥満被験者を対象とした、単回使用のペン型注入器（DV3396）の製剤（セマグルチド処方 D）と PDS290 ペン型注入器の製剤（セマグルチド処方 B）の生物学的同等性を評価する、7 週間、無作為割り付け、非盲検試験

[a]：NN9535-4588 試験（オゼンピック皮下注の開発プログラムで実施）は、0.25 mg 及び 1.0 mg に対する製剤について生物学的同等性を評価したが、肥満症の開発プログラムにおいては、0.25 mg のための製剤に関する結果のみ関連する。本試験の対照薬はオゼンピック皮下注の 1.34 mg/mL 濃度製剤である。
N：無作為割り付け被験者数。JP（N）は日本人被験者数。

5 つの 68 週間、無作為割り付け、二重盲検、プラセボ対照の第 3 相試験では、カロリーを制限した食事及び身体活動量の増加（4373、4374、4376 及び 4382 試験）又は集中的行動療法（4375 試験）に対する補助療法としての肥満症治療のためのセマグルチド 2.4 mg の有効性及び安全性を評価した。

これら 5 試験のデザインの主な特徴を 2.7.4.1.1.3.2 項に要約する。本概要では、主に日本人被験者が参加した 3 つの第 3 相試験（4373、4374 及び 4382 試験）に基づく安全性の評価を提示する。これらの試験の安全性データは試験別に示す。

第 2 相用量設定試験の安全性データは用量反応の評価に用いる。臨床薬理試験も安全性データの一部であることから、簡潔に概要を記載する。これらの試験デザインの主な特徴は Module 2.7.2.1.3 に示す。

2.7.4.1.1.3.2　試験対象被験者及び試験デザインの主な特徴

肥満症のためのセマグルチド 2.4 mg の第 3 相試験プログラムでは、セマグルチド 2.4 mg の有効性及び安全性をプラセボと比較して評価した。プログラムを構成する 5 つの第 3 相試験の試験デザインの主な特徴を図 2.7.4.1-1 に、日本人被験者が参加した 3 試験の主な適格性基準を Module 2.7.3.1.4.1.1 に示す。以下に概要を記載する。

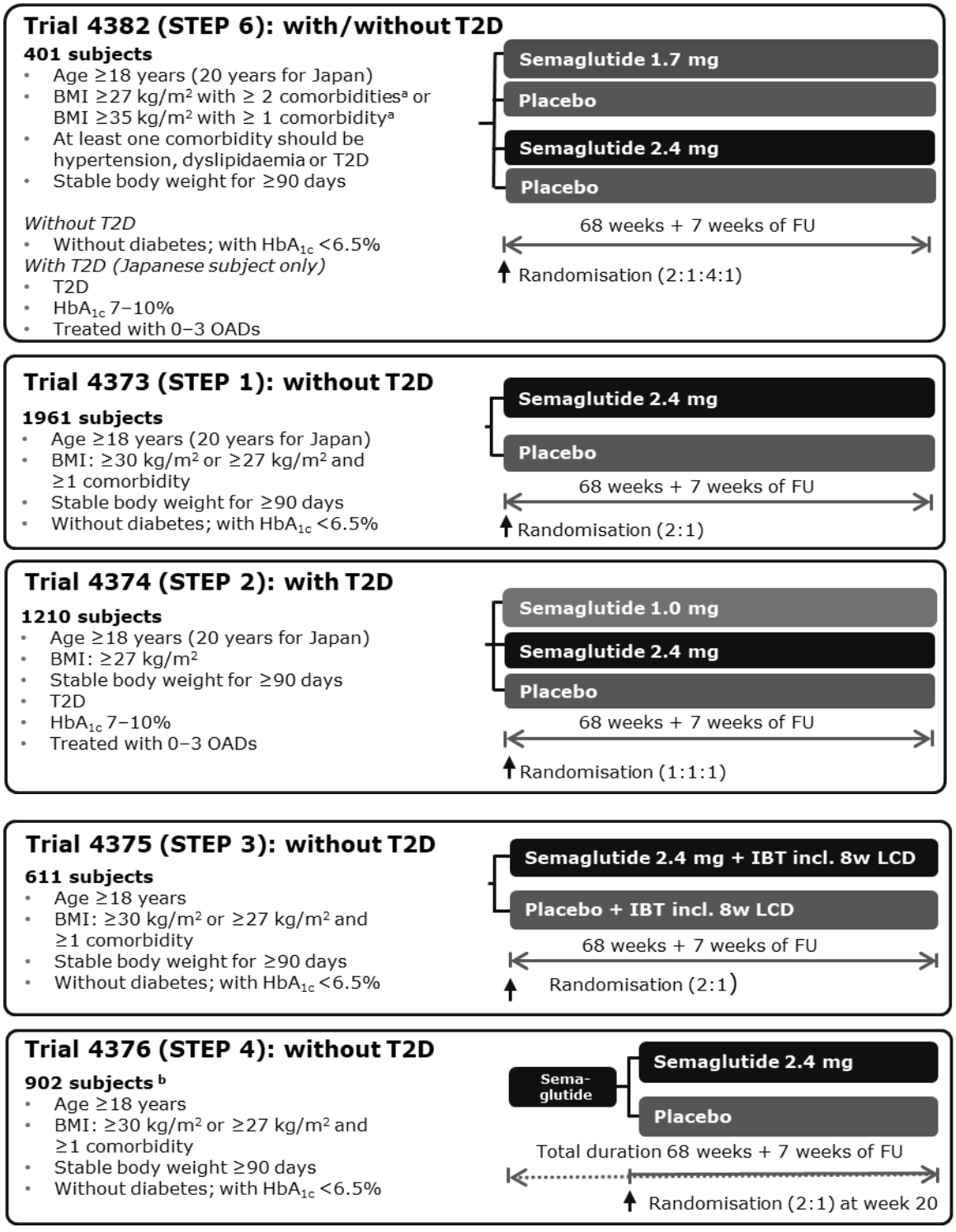
東アジア試験（4382 試験）は日本及び韓国で実施し、体容量指数（BMI）が 27.0 kg/m^2 以上かつ 2 つ以上の肥満に関連する合併症を有する被験者又は BMI が 35.0 kg/m^2 以上かつ 1 つ以上の肥満に関連する合併症を有する被験者を組み入れた〔日本肥満学会（JASSO）発行の肥満症診療ガイドライン[1]（以降、JASSO ガイドライン）に準ずる〕。4382 試験では、2 型糖尿病を有する被験者及び有さない被験者のいずれも組み入れた。4382 試験では、カロリーを制限した食事及び身体活動量の増加に対する補助療法としての肥満症治療のためのセマグルチド（2 用量：2.4 及び 1.7 mg）を評価した。

4 つの国際共同又は海外の第 3 相試験（4373、4374、4375 及び 4376 試験）には、いずれも肥満（BMI が 30 kg/m^2 以上）、又は過体重（BMI が 27 kg/m^2 以上 30 kg/m^2 未満）かつ 1 つ以上の肥満に関連する合併症を有する被験者を組み入れた（国際的なガイドライン[2, 3]に準ずる）。なお、4374 試験に組み入れられた被験者は 2 型糖尿病（HbA1c が 7～10%）を有する過体重又は肥満被験者であった。

4373、4375 及び 4376 試験では、肥満被験者又は過体重かつ 1 つ以上の肥満に関連する合併症を有する被験者における、カロリーを制限した食事及び身体活動量の増加に対する補助療法としての体重管理のためのセマグルチド 2.4 mg を評価した。4373 試験は体重減少効果を検討した標準的な試験であった。4375 試験では、体重減少効果を最大化するため、集中的行動療法（試験開始後 8 週間の低カロリー食を含む）を実施した。4376 試験は、達成された体重減少の維持を評価するため、治療中止デザインとし、20 週間の導入期間にセマグルチド 2.4 mg を投与後、セマグルチド 2.4 mg の継続投与群又はプラセボへの切り替え群に無作為に割り付けた。

4374 試験ではセマグルチド 2.4 及び 1.0 mg の 2 用量を検討した。

図 2.7.4.1-1　　肥満症のためのセマグルチド 2.4 mg の開発プログラムに含まれる 5 つの第 3 相試験の概要



[a] Comorbidities according to the JASSO guideline: (1) Impaired glucose tolerance, (2) Dyslipidaemia, (3) Hypertension, (4) Hyper-uricemia /Gout, (5) Coronary artery disease, (6) Cerebral infarction, (7) Non-alcoholic fatty liver disease, (8) Menstrual disorder/infertility, (9) Obstructive sleep apnoea syndrome /obesity-hypoventilation syndrome, (10) Locomotory disease or (11) Obesity-related kidney disease.

[b] In trial 4376, 803 subjects continued after the run-in into the randomised, controlled period.

8w: 8 weeks; BMI: body mass index; FU: follow-up; IBT: Intensive Behavioural Therapy; LCD: low calorie diet - 1000-1200 kcal/day diet; OAD: oral anti-diabetic drug; T2D: type 2 diabetes.

5 つの第 3 相試験は、いずれも投与期間が 68 週間であり、投与期間終了後に 7 週間の事後調査期間を設けた。4376 試験では、68 週間の投与期間を 2 つに分け、無作為割り付け前 20 週間の導入期間にはすべての被験者がセマグルチド 2.4 mg による治療を受け、その後の 48 週間の無作為割り付け群間比較期間では、セマグルチド 2.4 mg の継続又はプラセボへの切り替えのいずれかによる治療を受けた。

5 つの第 3 相試験のいずれにおいても、被験者をセマグルチド又はプラセボの投与に無作為に割り付けた。4373、4375 及び 4376 試験では、1 用量（セマグルチド 2.4 mg）の週 1 回投与を評価し、4374 試験及び 4382 試験では、2 用量（4374 試験：セマグルチド 1.0 mg 及び 2.4 mg、4382 試験：セマグルチド 1.7 mg 及び 2.4 mg）の週 1 回投与を評価した。5 つのすべての試験で、偏りのない試験の実施と結果の解釈を可能にするため、治験薬への割り付けを盲検化した。

胃腸障害の有害事象のリスクを軽減するため、2 型糖尿病のための皮下投与用セマグルチドの開発プログラム、第 2 相用量設定試験（4153 試験）及び GLP-1 受容体作動薬クラス全般で得られている知見に基づき、用量漸増法を採用した。開始用量はセマグルチド 0.25 mg 週 1 回投与とし、その後、固定の用量漸増法に従い維持用量に達するまで 4 週ごとに段階的に増量した（0.5、1.0、1.7 及び 2.4 mg）。各投与群の維持用量である 1.0 mg（4374 試験のみ）、1.7 mg（4382 試験のみ）及び 2.4 mg には、それぞれ 8 週、12 週及び 16 週後に到達した。

すべての被験者は推奨の維持用量であるセマグルチド 2.4 mg（又は 1.0 mg/1.7 mg）又は相当する液量のプラセボの投与を目指すこととした。推奨の維持用量に忍容性を示さなかった被験者は、より低い用量で投与を継続することを可能とした。ただし、そうしなければ被験者が治験薬投与を中止しなければならない場合で、かつ治験薬投与の継続が安全性上問題ないと治験責任医師が判断した場合にのみ、この措置が許容された。この場合でも、治験責任医師の判断で、維持用量への再増量を少なくとも 1 回は試みることが推奨された。

統計解析のためにデータベースリリース（データベースロック時）まで、無作為に割り付けられた治療について、試験の実施、データの取扱い、解析及び報告に携わるスタッフの盲検性が維持された。以下については、厳格な盲検化の例外とした：

- ノボ ノルディスク社のグローバル安全性部門のスタッフは、予測できない重篤な有害事象の疑い（suspected unexpected serious adverse reaction：SUSAR）に対して盲検化されなかった（標準的な安全性監視手順に従った報告目的のため）。
- セマグルチド濃度及び抗セマグルチド抗体測定用の血液検体の分析に携わる臨床検査スタッフは盲検化されなかった（この分析はセマグルチドを投与された被験者の血液検体に限られるため）。

2.7.4.1.1.3.3　本概要に含まれる試験に対する COVID-19 の影響

COVID-19 の世界的なパンデミック及び疫学的制限措置による、試験実施に対する重大な影響はなく、試験結果へ対する影響もないと判断された。日本人が参加した第 3 相試験に関する詳細は各試験の治験総括報告書に記載する〔4373 試験（Module 5.3.5.1）Section 7.3、4374 試験（Module 5.3.5.1）Section 7.3、4382 試験（Module 5.3.5.1）Section 7.3〕。

第 2 相試験（4153 試験）及び薬力学試験（4455 試験）は、COVID-19 のパンデミックの発生前に完了していた。生物学的同等性試験（4590 試験及び NN9535-4588 試験）に対する COVID-19 の影響は非

常に小さい。詳細は各試験の治験総括報告書に記載する〔4590 試験（Module 5.3.1.2）Section 7.3、NN9535-4588 試験（Module 5.3.1.2）Section 7.3〕。

2.7.4.1.1.4　試験とデータの分類及び併合

2.7.4.1.1.4.1　国際共同第 3 相試験データの併合及び分類

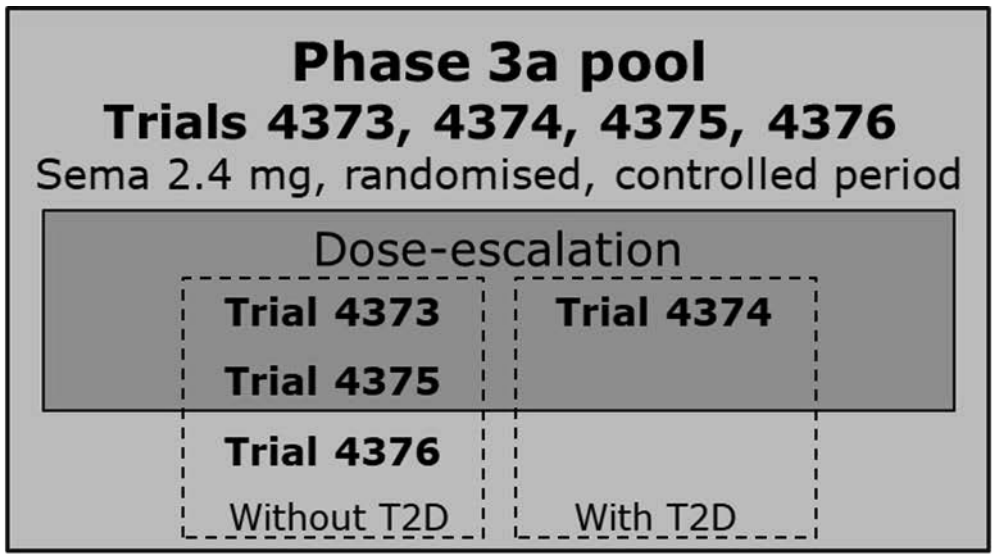
セマグルチドの安全性評価は、試験の併合データにより補足される。データの併合によりセマグルチド 2.4 mg の安全性を集約的に評価し、潜在的な安全性上の懸念を検出する可能性を高めることが可能となる。特定の安全性項目について、国際共同第 3 相試験の併合データを、患者集団の関連性や特定の試験デザインの特徴に応じた様々なグループに分けて評価した。併合する試験のデータの一貫性の評価も行うことにより、併合の適切性を確認し、試験の併合により見過ごされた安全性上の問題がないことを確認した。国際共同第 3 相試験の併合データの cut-off date は 2020 年 10 月 28 日とした。

データの併合及び併合データ内のグループ化（評価する安全性項目による）は、以下のように規定した：

- 4 つの第 3 相試験（4373、4374、4375 及び 4376 試験）を含む**第 3 相試験併合データ**
  無作為割り付け群間比較期間におけるセマグルチド 2.4 mg とプラセボの比較。
  - **用量漸増を含む第 3 相試験併合データ**（4373、4374 及び 4375 試験）
    無作為割り付け群間比較期間に用量漸増期間が含まれた試験におけるセマグルチド 2.4 mg とプラセボの比較。
  - **2 型糖尿病を有する被験者を含む第 3 相試験**（4374 試験）
    2 型糖尿病を有する過体重及び又は肥満被験者における特定の安全性項目についてのセマグルチド 2.4 mg の評価（本概要には含めない）。
  - **2 型糖尿病を有さない被験者を含む第 3 相試験併合データ**（4373、4375 及び 4376 試験）
    2 型糖尿病を有さない過体重及び又は肥満被験者における特定の安全性項目についてのセマグルチド 2.4 mg の評価。

第 3 相試験の併合及びグループ化の概要を図 2.7.4.1-2 に示す。各安全性項目の評価には、最も適した併合データ、グループ及び試験を用いた。

図 2.7.4.1-2　　各安全性項目又は異なる集団における評価に用いた併合、グループ化及び試験の概要



Trial 4374: Safety evaluations of retinal disorders and hypoglycaemic episodes that are specific to this trial includes assessments of both the 2.4 mg dose and the 1.0 mg dose. T2D: type 2 diabetes.

第 3 相試験併合データ

第 3 相試験併合データには、4373、4374、4375 及び 4376 試験における無作為割り付け群間比較期間のセマグルチド 2.4 mg のデータを含めた。4376 試験における無作為割り付け前 20 週間の導入期間は、プラセボ対照が設定されていないため除外した。第 3 相試験併合データに基づく安全性評価（2.7.4.2.3 項）には、有害事象（すべての有害事象、死亡及び重篤な有害事象）及び注目すべき安全性領域（胃腸障害の有害事象、低血糖及び網膜障害を除く）の概要を含めた。さらに、発現件数の少ない領域における潜在的な安全性シグナルを特定するために、第 3 相試験併合の安全性データに基づき離脱症状及び反跳現象を評価した（2.7.4.5.9 項）。

第 3 相試験併合データではセマグルチド 2.4 mg 群を併合した。投与群間の潜在的な違いを見えにくくすることのないよう、4374 試験のセマグルチド 1.0 mg 群は除外した。セマグルチド 1.0 mg の安全性は、2 型糖尿病のための皮下投与用のセマグルチド（オゼンピック）開発プログラムで十分に評価されている。第 3 相試験併合データでは、事象を発現した被験者の割合及び単位時間あたりの発現件数については、Cochran-Mantel-Haenszel の重み付け法により調整した（2.7.4.1.1.9 項）。

用量漸増を含む第 3 相試験併合データ

用量漸増を含む第 3 相試験併合データには、無作為割り付け群間比較期間に用量漸増期間が含まれた 4373、4374 及び 4375 試験を含めた。これらの試験のグループ化により、用量漸増期間中に認められる頻度が高くなることが知られている（あるいは可能性がある）安全性所見（胃腸障害の有害事象など、2.7.4.2.3 項）を評価することが可能となった。

4376 試験は、無作為割り付け前の 20 週間の導入期間及び用量漸増期間にすべての被験者がセマグルチドの投与を受けており、プラセボ対照ではなかったため、本併合データからは除外した。これは、事象（胃腸障害の有害事象など）の単位時間あたりの発現件数が少なく算出されることを避けるためである。

2 型糖尿病を有さない被験者を含む第 3 相試験併合データ

2 型糖尿病を有さない被験者で注目すべき安全性項目については、4373、4375 及び 4376 試験の併合データに基づいて評価した。これには低血糖（事前に定義した MedDRA 検索）の評価が含まれる（2.7.4.2.3 項）。

2.7.4.1.1.4.2　第 2 相試験

肥満症のためのセマグルチド 2.4 mg の臨床開発プログラム（表 2.7.4.1-1）には、1 つの第 2 相用量設定試験（4153 試験）が含まれた。4153 試験の安全性データは用量反応の評価に含めた（2.7.4.2.1.5 項）。4153 試験では、52 週間のセマグルチド 0.05、0.1、0.2、0.3 及び 0.4 mg の 1 日 1 回投与を検討しており、これは、第 3 相試験プログラムで選択したセマグルチド 2.4 mg の週 1 回投与とは異なる投与方法及び用量であった。母集団薬物動態モデルに基づき、セマグルチド週 1 回投与時の維持用量を 2.4 mg とすることで、定常状態における C_{max} が 4153 試験のセマグルチド 0.4 mg の 1 日 1 回投与時と同程度となると推定された〔Phase 2 modelling report（Module 5.3.3.5）Section 4.3.1〕。

2.7.4.1.1.4.3　第 1 相試験／臨床薬理試験

肥満症のためのセマグルチドの臨床開発プログラムには 3 つの臨床薬理試験、すなわち 1 つの薬力学試験、及び市販予定製剤（セマグルチド処方 D／単回使用ペン型注入器）と第 3 相試験で用いた製剤（セマグルチド処方 B／PDS290 ペン型注入器）の生物学的同等性を評価するための 2 つの生物学的同等性試験が含まれた（表 2.7.4.1-1）。薬力学試験には肥満被験者、生物学的同等性試験には過体重又は肥満被験者を組み入れた。選択及び除外基準の詳細は、各試験の治験総括報告書に記載する。3 つの臨床薬理試験は、試験期間が短く（7～21 週間）、試験に組み入れられた被験者数が比較的少なかったことから、その安全性評価については本概要では簡潔に記載するのみとする。有害事象の要約表は各試験の治験総括報告書に提示する。

2.7.4.1.1.5　本臨床概要の構成

肥満症のためのセマグルチド週 1 回皮下投与の安全性は、主に、日本人被験者が参加した 3 つの第 3 相試験（4373、4374 及び 4382 試験）の結果を比較することにより評価した。

安全性は以下のデータに基づき評価した：

- 曝露
- 被験者背景及びベースラインの疾患特性（既往歴及び併用薬を含む）
- 安全性評価
    - 有害事象（特定の事象に関する追加データ収集、MedDRA 検索及び特定の事象に関するイベント判定を含む）
    - 低血糖（4374 及び 4382 試験の 2 型糖尿病を有する被験者）
    - 臨床検査項目評価
        - 臨床検査値
        - 血漿中セマグルチド濃度
        - 抗セマグルチド抗体

- バイタルサイン
- 眼科的検査（4374 及び 4382 試験の 2 型糖尿病を有する被験者）
- 心電図
- 身体所見
- メンタルヘルスに関する質問票〔患者さんの健康に関する質問票-9（PHQ-9）及びコロンビア自殺評価スケール（C-SSRS）〕
- 妊娠
- 有害事象に関連するテクニカルな苦情

本概要で評価したすべての領域及び評価基準の概要を、用いた観察期間とあわせて表 2.7.4.1-2 に示す。観察期間の定義は 2.7.4.1.1.9.1 項に示す。個々の安全性領域の評価は、各領域に応じた適切な方法及びデータソースに基づいて行った。MedDRA 検索及びイベント判定の両方に基づいて評価される注目すべき安全性領域については、治験責任医師の報告に基づく事象とイベント判定委員会（EAC）の判定結果に基づく事象をそれぞれ要約し、2 つの評価方法に基づき総合的に評価した。

表 2.7.4.1-2　　評価した安全性領域及び評価項目の概要

General safety, analysis of adverse events (Section 2.7.4.2.1)			
Areas	**Section**	**Basis for the evaluation**	**Observation period**
AEs	2.7.4.2.1.1	All AEs, and AEs in: ≥5% of subjects	On-treatment
Deaths	2.7.4.2.1.2	Deaths AEs with fatal outcome Adjudication outcome	In-trial
SAEs	2.7.4.2.1.3	AEs reported as serious	On-treatment
Other significant adverse events leading to treatment intervention	2.7.4.2.1.4	AEs leading to permanent treatment discontinuation	On-treatment
Safety focus areas (Section 2.7.4.2.2)			
Areas	**Section**	**Basis for the evaluation**	**Observation period**
Gastrointestinal disorders	2.7.4.2.2.2	Predefined MedDRA search (phase 3a dose escalation group)	On-treatment
Gallbladder-related disorders	2.7.4.2.2.3	Predefined MedDRA search	On-treatment
Acute pancreatitis	2.7.4.2.2.4	Predefined MedDRA search Adjudication outcome Laboratory assessments of amylase and lipase	On-treatment In-trial On-treatment
Cardiovascular disorders	2.7.4.2.2.5	Predefined MedDRA search Adjudication outcome Pulse measurements Electrocardiogram	In-trial On-treatment
Neoplasms	2.7.4.2.2.6	Predefined MedDRA searches: Overall neoplasms Malignant neoplasms Laboratory assessment of calcitonin	In-trial On-treatment
Hepatic disorders	2.7.4.2.2.7	Predefined MedDRA search Laboratory assessment of ALT, AST, total bilirubin and alkaline phosphatase Concurrent elevations in ALT/AST >3xULN and total bilirubin >2xULN, and post-baseline ALT >5xULN	On-treatment In-trial
Acute renal failure	2.7.4.2.2.8	Predefined MedDRA search Laboratory assessments: eGFR and creatinine UACR (trial 4374)	On-treatment
Hypoglycaemia	2.7.4.2.2.9	Predefined MedDRA search (trial 4373 and subjects without T2D in trial 4382) Hypoglycaemic episodes form (trial 4374 and subjects with T2D in trial 4382)	On-treatment

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Areas	Section	Basis for the evaluation	Observation period
Retinal disorders	2.7.4.2.2.10	Predefined MedDRA search (trial 4374 and subjects with T2D in trial 4382) Eye examination results (trial 4374 and subjects with T2D in trial 4382)	In-trial
Immunogenicity	2.7.4.2.2.11	Predefined MedDRA searches: allergic reactions injection site reactions Anti-semaglutide antibodies	On-treatment In-trial
Psychiatric disorders	2.7.4.2.2.12	Predefined MedDRA search C-SSRS PHQ-9	On-treatment In-trial
Rare events	2.7.4.2.2.13	Predefined MedDRA search	On-treatment

Analysis of adverse events in the global phase 3a pool (Section 2.7.4.2.3)

Areas	Section	Basis for the evaluation	Observation period
Safety in the global phase 3a pool	2.7.4.2.3	All AEs, deaths, SAEs (evaluation based on phase 3a pool) Overview of results from safety focus areas - Safety focus area except for gastrointestinal disorders, hypoglycaemia and retinal disorders: evaluation based on phase 3a pool - Gastrointestinal disorders: evaluation based on phase 3a dose escalation group - Hypoglycaemia: evaluation based on phase 3a without T2D group	On-treatment / in-trial

Clinical laboratory evaluation (Section 2.7.4.3) and Vital signs, physical findings and other evaluations related to safety (Section 2.7.4.4)

Areas	Section	Basis for the evaluation	Observation period
Clinical laboratory evaluations	2.7.4.3	Laboratory measurements of haematology and biochemistry parameters not covered under a safety focus area	On-treatment
Vital signs, physical findings and other evaluations related to safety	2.7.4.4	Physical examination. Note: Blood pressure is addressed in the Module 2.7.3.3.4.1 and Module 2.7.3.3.4.2. Pulse and electrocardiogram covered under safety focus area Cardiovascular disorders	On-treatment

Safety in special groups and situations (Section 2.7.4.5)

Areas	Section	Basis for the evaluation	Observation period
Consistency between entire trial population and Japanese sub-population	2.7.4.5.1	All AEs, GI AEs, SAEs, AEs leading to premature discontinuation, AEs possibly or probably related to trial product	On-treatment

Continues on next page

Areas	Section	Basis for the evaluation	Observation period
Intrinsic factors	2.7.4.5.2	AEs by: - Sex, baseline age, baseline body weight, BMI and baseline renal function - Baseline glycaemic status (trials 4374 and 4382) - Baseline Dyslipidaemia status and baseline hypertension status	On-treatment
Extrinsic factors	2.7.4.5.3	AEs by: Background anti-diabetic medication (trial 4374 and subjects with T2D in trial 4382)	On-treatment
Weight loss	2.7.4.5.4	AEs by weight loss	On-treatment
Drug interactions	2.7.4.5.5	Trial 4455 and results from drug-drug interaction trials for semaglutide s.c. for T2D	NA
Use in pregnancy and lactation	2.7.4.5.6	Cases reported on pregnancy forms Pre-defined MedDRA searches (lactation and fertility)	In-trial On-treatment
Areas	**Section**	**Basis for the evaluation**	**Observation period**
Medication errors, abuse and misuse, and overdose	2.7.4.5.7	Pre-defined MedDRA searches and listings of events co-reported within 2 weeks after resolution of event of medication errors/abuse and misuse/overdose	On-treatment
Suspected transmission of an infectious agent	2.7.4.5.8	Predefined MedDRA search	On-treatment
Withdrawal and rebound	2.7.4.5.9	AEs after trial product permanently discontinued Note: evaluation based on data from the phase 3a pool	On-treatment
Effects on ability to drive and operate machinery	2.7.4.5.10	ADRs assessed as relevant for the ability to drive and operate machinery	On-treatment
Technical complaints	2.7.4.5.11	AEs reported in relation to a technical complaint	On-treatment

If not stated otherwise, the evaluation is based on the three phase 3a trials with Japanese subjects included (trials 4373, 4374 and 4382).

Adjudication is done for: deaths, acute pancreatitis and cardiovascular disorders

Additional data collection is performed for: acute renal failure and retinal disorders (trials 4374 and 4382), and for gallbladder-related disorders, acute pancreatitis, malignant neoplasms, hepatic disorders, overdose, medication error, abuse and misuse (all phase 3a trials).

ADR: adverse drug reaction, AE: adverse event, BMI: body mass index, C-SSRS: Columbia-Suicide Severity Rating Scale, EAC: event adjudication committee, eGFR: estimated glomerular filtration rate, MedDRA: Medical Dictionary for Regulatory Activities, NA: not applicable, PHQ-9: Patient Health Questionaire-9, s.c.: subcutaneous; SAE: serious adverse event, T2D: type 2 diabetes; UACR: urinary albumin-to-creatinine ratio.

2.7.4.1.1.6　本臨床概要に含まれるデータの cut-off date

本概要には、4382 試験の治験総括報告書の完成までに完了した 9 つの臨床試験のデータを含める。肥満症のためのセマグルチド 2.4 mg 開発プログラムにおいて完了した 9 つの臨床試験は、5 つの第 3 相試験、1 つの第 2 相試験及び 3 つの臨床薬理試験である（表 2.7.4.1-1）。

2.7.4.1.1.7　安全性データソース

本概要では、各試験の治験総括報告書のデータ及び本概要の関連資料（別添等）を適宜参照する。

完了した試験の安全性データは、ノボ ノルディスク社の臨床試験データベース内（データベースロック後）の試験データに基づく。臨床試験データベースは、臨床試験で収集されたデータの処理及び保管のために用いられ、各試験の治験総括報告書及び本概要に提示するデータの一次資料となる。

ただし、本概要に含めた死亡に至った有害事象、重篤な有害事象及び妊娠に関する叙述は、ノボ ノルディスク社の安全性データベースのデータに基づく。安全性データベースは臨床試験及び市販製品の進行中の安全性モニタリングに用いられる。安全性データベース内の臨床試験データは試験完了時に固定されることはない。したがって、完了した試験のデータベースロック後は、データベースロック前に報告された死亡に至った有害事象、重篤な有害事象及び妊娠の更新情報、又はデータベースロック後に報告された新たな事象に関する情報（新たな死亡に至った有害事象、重篤な有害事象及び妊娠を含む）は安全性データベースには入力されるが、臨床試験データベースには入力されない。

2.7.4.1.1.8　安全性データの収集

2.7.4.1.1.8.1　既往歴及び併発疾患

スクリーニング時（又は遅くとも無作為割り付け前）に既往歴及び併発疾患に関する情報を収集した。特定の疾患のためのフォームを用いて、以下の疾患に関する情報を体系的に収集した：

- 胆嚢系疾患の既往歴
- 乳癌の既往歴
- 大腸新生物の既往歴
- 皮膚癌の既往歴
- 精神障害の既往歴
- 糖尿病の既往歴及び合併症（4374 及び 4382 試験の 2 型糖尿病を有する被験者）

これらの特定の疾患のためのフォームに含まれない、その他の関連する既往歴及び併発疾患に関する情報は、一般的な既往歴及び併発疾患のためのフォームを用いて収集し、既往歴（スクリーニング時には既に存在しない疾患）又は併発疾患（スクリーニング時に認められるか、スクリーニング手順又は治験薬投与前に実施されたその他の手順の結果として発見された疾患）として要約した。

乳癌及び大腸新生物については、投与終了時及び試験終了時にすべての被験者（乳癌についてはすべての女性被験者）から検査及び検査理由（スクリーニングのためか症状を有するためか）に関する情報を収集した（違いが認められる場合に検討するため）。

2.7.4.1.1.8.2　有害事象及びイベント判定

2.7.4.1.1.8.2.1　有害事象

すべての試験で有害事象は治験責任医師の報告から収集された。有害事象の定義は、完了した第 3 相試験のいずれの試験でも同様であり、医薬品の使用と時間的に関連のある、被験者に生じたあらゆる好ましくない医療上の出来事であり、当該医薬品との因果関係の有無は問わないこととした。有害事象とは、医薬品（治験薬を含む）の使用と時間的に関連のある、あらゆる好ましくない、意図しない徴候（臨床検査値の異常を含む）、症状又は疾病（新たな発現又は悪化）のことである。

すべての第 3 相試験において、有害事象は MedDRA の最新バージョンを用いてコーディングした。MedDRA のバージョンは、4382 試験では MedDRA Ver. 23.1 を、他の第 3 相試験では MedDRA Ver. 22.1 を用いた。

治験責任医師は、有害事象に関して以下を評価することとした：

- 重篤性〔非重篤又は重篤（重篤の基準に合致するものを含む）〕
- 重症度（軽度、中等度又は重度）
- 治験薬との因果関係（あり、可能性あり又はなし）
- 転帰（回復、軽快、回復したが後遺症あり、未回復、死亡又は不明）

各有害事象について、治験責任医師は治験薬に対する措置を以下のカテゴリーに従って報告することとした：投与の中断、投与の中止、投与量の減量、投与量の増量、投与量の変更なし、不明又は該当なし。治験薬に対する措置は、治験薬の投与中止、一時的な投与中断又は投与量の減量の 3 つカテゴリーで要約した。

詳細な定義は、Module 5 の各試験の治験総括報告書の別添に含まれる治験実施計画書に提示する（治験総括報告書の Appendix 16.1.1）。

有害事象の定義に合致するすべての事象を症例報告書の「AE form」を用いて報告することとした。

重篤な有害事象については、「AE form」に加え「Safety information form」を作成することにより、補足的な臨床情報を収集し、これを重篤な有害事象に関する叙述に含めることとした。「Safety information form」に収集される補足情報は、重篤な有害事象に関する叙述（本申請資料に含める）の作成に用いられた。

有害事象又は重篤な有害事象の性質及び／又は因果関係を可能な限り完全に解明するため、治験責任医師には、医学的に妥当な場合あるいはノボ ノルディスク社が要請した場合には、追加の検査及び／又は評価を実施又は手配することにより、有害事象／重篤な有害事象の追跡調査を行うこととした。この追跡調査には、追加の臨床検査又は他の検査、組織病理学的検査、又は他の医療従事者への相談などが含まれた。

試験参加中又は確認されている事後調査期間中に被験者が死亡した場合は、治験責任医師はノボ ノルディスク社に組織病理学検査を含む剖検報告書（実施した場合）の写し 1 部を提出することが求められた。

2.7.4.1.1.8.2.2　追加データ収集及びイベント判定

特定の種類の事象については、特に注目すべき事象、追加のデータ収集を要する事象、及び／又はイベント判定対象の事象として治験実施計画書に規定した。これらの事象の概要を表 2.7.4.1-3 に示す。追加データ収集用のフォームへの入力及びイベント判定が必要な事象の症状及び種類の詳細は 2.7.4.2.2 項「注目すべき安全性領域」に示す。

表 2.7.4.1-3　追加のデータ収集（特定のイベントフォームを使用）が必要な事象及び／又はイベント判定対象の事象

Event type	Event with specific event form	Event for adjudication
Death		X
Cardiovascular events		
Acute Coronary Syndrome		X
Cerebrovascular event		X
Heart failure		X
Coronary artery revascularisation		X
Acute pancreatitis	X	X
Acute gallbladder disease	X	
Malignant neoplasms	X	
Hepatic event	X	
Medication error Misuse or abuse of trial product[a]	X	
Acute renal failure[b]	X	
Diabetic retinopathy[b]	X	

[a] Additional data for Misuse or abuse of trial product is reported on the medication error event form.
[b] For Acute renal failure and Diabetic retinopathy, additional data collection was only done for the subjects with T2D in trials 4374 and 4382.

治験責任医師は、有害事象が重篤か否か、特定のイベントフォームを用いた追加データ収集が必要か否か、及びイベント判定対象となるか否かを評価することとした。

追加情報は、治験実施計画書の Appendix 4 に従った事象の種類に関する治験責任医師の評価に基づいて収集されるが、これは MedDRA 検索により特定された事象とは異なる可能性がある。

追加データ収集が必要な有害事象は、「AE form」（重篤な有害事象は「Safety information form」）と特定のイベントフォーム（該当する事象に関する特定の情報を収集するためのフォーム）の両方を用いて報告することとした。イベント判定対象の有害事象については、イベント判定のためのフォームにも記入することとし、実施医療機関から提供される臨床データを特定した。したがって、有害事象の性質により、治験責任医師はフォームを 1 つから 4 つまで記入することとした。

追加データ収集用のフォームを用いて得られた情報は、各有害事象の評価に用い、各試験の治験総括報告書の叙述及び／又はデータ一覧に含めた。

追加データ収集には、診断（画像診断など）、リスク因子及び事象の治療に関する情報（重症度を示している場合がある）が含まれる。追加データ収集用のフォームの情報は個々の有害事象の評価に用い、被験者及び受けた治療に関する情報、有害事象の情報、及び追加データ収集用のフォームで得られた情報を合わせて試験ごとに一覧に示した。収集された情報は、個々の症例の評価と叙述の作成に用いた。重篤な有害事象の叙述は、症例が試験を完了するまで更新を続けるのに対し、症例報告書（CRF）（「AE form」及び／又は追加データ収集用のフォーム）に収集された有害事象情報は事象の発現時に記入されているため、重篤な有害事象の叙述に含まれている情報と一覧に提示されている情報には不一致が生じる場合がある。

イベント判定

イベント判定のために送付される有害事象は、事前に規定された、死亡、急性膵炎ならびに以下の心血管系イベントであった：急性冠症候群、脳血管発作、冠動脈血行再建術及び心不全（各イベント種類及び判定結果の概要は、それぞれの安全性領域の情報を参照）。

特定のイベントの判定は、独立した外部のイベント判定委員会（EAC）が実施した。判定は、EACチャーター（憲章）において事前に規定された基準及びガイドラインを用いて、特定のイベントに関連する臨床データ（盲検下）に基づき、各分野（心臓病学、神経学又は消化器病学）の専門家が実施した。外部の判定機関（ICON IDEA）が、外注業者であるAG Mednetと共にイベント判定システムの設定を含むプロセスを管理し、すべての関連する原資料が治験実施医療機関から収集され、イベント判定委員会に提供されるようにした。各イベントに用いられた基準の詳細は、各安全性領域の背景及び評価方法の項に記載する。事前に規定した判定基準は、各試験の治験総括報告書（Module 5.3.5.1）Appendix 16.1.13（4153試験はSection 4、第3相試験はAppendix A）に記載する。

無作為割り付けされた被験者について、スクリーニング来院時からデータベースロックまでの間に収集されたすべてのイベント判定対象の事象（スクリーニング期間中に発現した事象も含む）の判定を実施した。スクリーニング不適格例の有害事象は判定しなかった〔各試験の治験総括報告書（Module 5.3.5.1）Appendix 16.1.13〕。イベント判定プロセスで重複が生じた事象に対処するために、ノボ ノルディスク社は、いくつかの統計的取り扱いのルールを事前に設定し、イベント判定委員会により確定された事象のうち、発生時点が近い同じ種類の事象、又は発現日が同じで同定されたソースが異なる同じ種類の事象に適用した。したがって、イベント判定委員会により、連続した3暦日以内の事象発現日に1例の患者で2件以上の同じ種類の事象が確定された場合、最初に発現した事象を統計データセットに含めることとした。また、1例の患者に発現日が同じでソースの異なる同じ種類の事象が特定された場合、優先順位（治験責任医師＞有害事象検索＞判定者）を適用することにより、1つの事象のみを選択した。

治験総括報告書には、判定された事象の種類ごとに以下の2つの一覧を示す：

- 被験者（年齢、性別及びBMI）及び治療群に関する情報、有害事象に関する情報〔有害事象番号（AE number）、観察期間、治験責任医師の報告に基づく有害事象については；各有害事象の器官別大分類（SOC）、基本語（PT）及びReported term、ただし、死亡の一覧には含めなかった〕、イベント判定委員会により判定された発現日（イベントが確定された場合）、イベントの判定結果及び合致した基準を含めた一覧
- 判定者のコメント（被験者と治療、事象のソース、及び判定結果に関する情報を含む）の一覧

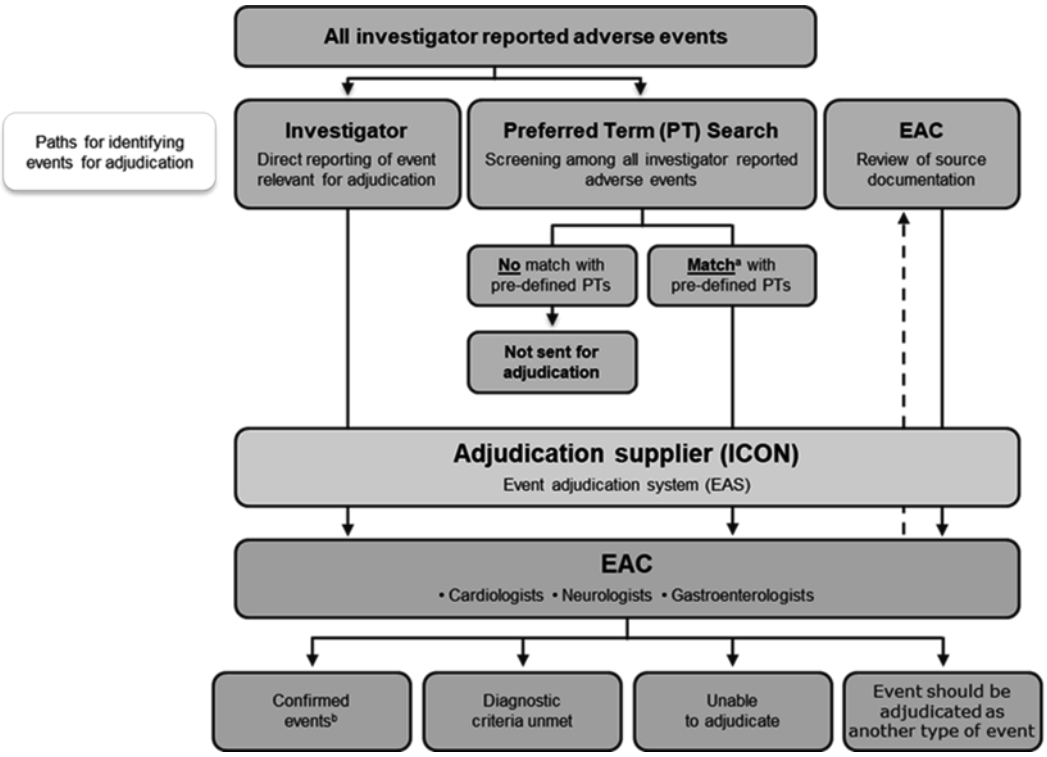
上記の一覧には、判定されたすべての事象（確定、不確定、判定不能）について判定者のコメントが記載されている。急性膵炎では、判定者は、確定された事象及び確定されなかった事象のいずれについても、アトランタ分類のいずれかの定義に合致しているか否かを追加フォームに記入することとした。本フォームで、判定者は、重度の急性上腹部痛、血液中膵酵素（リパーゼ／アミラーゼ）の基準範囲上限の3倍以上への上昇、及び／又は特徴的な画像所見、の選択肢の中から1つ以上を選択した。アトランタ分類のいずれの定義にも合致しない場合、判定者はいずれも選択せずにコメントを記

載することとした。急性膵炎として確定されなかった事象に対するコメントは、各試験の治験総括報告書の一覧に提示した。

判定のために送付される事象は、以下の 3 つの経路のいずれかにより特定された（図 2.7.4.1-3）：

- 治験責任医師：
  治験責任医師は、有害事象が判定の対象になると治験実施計画書に規定した有害事象の種類の 1 つに合致するか否かを評価し（表 2.7.4.1-3）、該当する場合、CRF の「AE form」で関連する事象の種類を選択することとした。その後、選択した事象に特有のイベント判定のためのフォームが表示され、収集してイベント判定システムにアップロードする原データが示される。死亡に至った有害事象が選択された際には、必ず死亡に関するイベント判定のためのフォームが表示されることとした。
- 基本語検索：
  すべての報告された有害事象（治験責任医師により判定対象のイベントとして特定されなかった事象）について、事前に定義した基本語検索を用いてノボ ノルディスク社のイベント判定部門がスクリーニングを行い、判定に関連する可能性がある有害事象を特定した〔検索用語は Global summary of safety（Module 5.3.5.3）Appendix 7.9 に示す〕。判定対象として特定された場合、CRF 内のイベント判定のためのフォームが表示され、治験責任医師に対し、イベント判定システムに関連する原資料の収集及びアップロードを依頼した。
- イベント判定委員会（原資料のレビュー）：
  判定のために送付された他の事象の原資料のレビューに基づき、イベント判定委員会は、当初治験責任医師から報告されなかったが、判定対象として適切な追加事象を特定することが可能であった。このような場合、イベント判定委員会はイベント判定システムを通じて ICON に通知することとした。必要な場合は、当該事象の裏付け原資料を治験責任医師に照会し、イベント判定システムを通じてイベント判定委員会に提供するよう依頼した。治験責任医師は、当該事象の所見について通知を受け、そのイベントを有害事象として報告することが可能であった。イベント判定委員会により特定された追加事象の判定は、治験責任医師が当該事象を報告するかにかかわらず実施された。

図 2.7.4.1-3　　イベント判定プロセスの概要



[a] Coded term (PT) for the reported adverse event was on the pre-defined preferred term list for screening of events relevant for adjudication. b Events were confirmed using the adjudication outcome terms listed in 表 2.7.4.1-3.
EAC = event adjudication committee.

2.7.4.1.1.8.3　　叙述及び症例報告書

第 3 相試験では、以下について叙述を作成した：

- 死亡に至った有害事象
- 重篤な有害事象
- 妊娠
- 稀な事象
- 事前に規定した MedDRA 検索により特定された、治験薬投与の中止に至った、重篤でない注目すべき安全性領域の有害事象（胃腸障害の有害事象を除く）
- 中央検査機関の測定値（予定及び予定外の測定及び再検査）に基づく臨床検査の外れ値（以下に規定）：
  - アラニンアミノトランスフェラーゼ（ALT）又はアスパラギン酸アミノトランスフェラーゼ（AST）が基準範囲上限の 3 倍を超え、かつ総ビリルビンが基準範囲上限の 2 倍を超える
  - ALT が基準範囲上限の 5 倍を超える
  - AST が基準範囲上限の 5 倍を超える
  - 総ビリルビンが基準範囲上限の 10 倍を超える
  - アルカリホスファターゼが基準範囲上限の 20 倍を超える
  - クレアチンキナーゼが基準範囲上限の 10 倍を超える
  - 血清クレアチニンが基準範囲上限の 6 倍を超える
  - カリウムが 2.50 mmol/L 未満又は 7.0 mmol/L を超える

- ナトリウムが 120 mmol/L 未満又は 160 mmol/L を超える
- アルブミン補正血清カルシウムが 1.50 mmol/L 未満又は 3.4 mmol/L を超える
- 白血球が 1 × 10^9/L 未満である
- 血小板が 25 × 10^9/L 未満である
- リンパ球が 0.2 × 10^9/L 未満である

- 重大な低血糖

第 2 相試験及び臨床薬理試験では、以下について叙述を作成した：

- 死亡に至った有害事象
- 重篤な有害事象
- 治験薬投与の中止又は試験の中止に至った、重篤でない有害事象
- 妊娠

叙述は各試験の治験総括報告書 Section 14.3.3 に提示する。
CRF の複製は要求に応じて提供可能である。

2.7.4.1.1.8.4　低血糖

2.7.4.1.1.8.4.1　第 3 相試験における 2 型糖尿病を有さない被験者

4373 及び 4382 試験の 2 型糖尿病を有さない被験者では、低血糖の報告には専用の「Hypoglycaemic episode form」は使用せず、すべて有害事象として報告することとした。

2.7.4.1.1.8.4.2　第 3 相試験における 2 型糖尿病を有する被験者

4374 及び 4382 試験の 2 型糖尿病を有する被験者では、低血糖を専用の「Hypoglycaemic episode form」を用いて報告することとした。
以下の基準に合致する事象はすべて低血糖として報告することとした：

- 血糖値が 3.9 mmol/L（70 mg/dL）以下
- 血糖値が 3.9 mmol/L（70 mg/dL）超えていても、低血糖症状がみられた場合

その後の血糖値が 3.9 mmol/L（70 mg/dL）を超え、かつ／又は症状が消失した場合、低血糖は回復したと判断した（再測定及び／又は再発症状も 1 つの「Hypoglycaemic episode form」に記載）。

併用薬剤

4374 及び 4382 試験においてスルホニルウレア薬の投与（単独又は他の経口糖尿病薬との併用）を受けていた被験者は、治験責任医師の判断により、無作為割り付け時にスルホニルウレア薬の用量を約半分に減量することとした。
治験責任医師は、米国糖尿病学会（ADA）／欧州糖尿病学会（EASD）のガイドライン[4]等に従い、被験者の治療を強化することが可能であった〔GLP-1 受容体作動薬、ジペプチジルペプチダーゼ-4（DPP-4）阻害薬及びアミリンアナログは除外し、体重に影響しない薬剤を用いることが望ましい〕。インスリンの使用はレスキュー薬としてのみ許容された。

レスキュー治療

4374 及び 4382 試験の 2 型糖尿病を有する被験者において高血糖〔空腹時血漿グルコース濃度 >15 mmol/L（270 mg/dL）〕が持続する場合は、治験責任医師はレスキュー治療を開始する、すなわち、基礎治療としての経口糖尿病薬の強化又は新たな経口糖尿病薬の追加を開始することとした。レスキュー治療薬は、体重に影響しない薬剤が望ましく、ADA／EASD のガイドライン[4]等に従うこととした（GLP-1 受容体作動薬、DPP-4 阻害薬及びアミリンアナログは除外）。インスリンの使用は可能な限り短期間とすることとした。

2.7.4.1.1.8.5 臨床検査

日本人被験者が参加した 3 つの第 3 相試験の臨床検査項目の一覧を表 2.7.4.1-4 に示す。すべての第 3 相試験で同じ中央検査機関及び測定方法が用いられ、検体採取の頻度も同じであった。治験総括報告書及び／又は本概要では、すべての臨床検査項目の評価を平均値のプロット、箱ひげ図、及びカテゴリカル値の記述統計量に基づき行った。事前に定義した基準に合致する臨床検査の外れ値については叙述を作成した（2.7.4.1.1.8.3 項）。

表 2.7.4.1-4　　4373、4374 及び 4382 試験における臨床検査項目

Biochemistry (measured in serum)	**Haematology (measured in whole blood)**
Amylase and lipase	Erythrocytes
ALT, AST, ALP, TBL	Haemoglobin
CK	Haematocrit
Creatinine	Leucocytes
Albumin	Thrombocytes
Urea	Differential cell count (eosinophils, neutrophils,
Albumin corrected calcium	basophils, monocytes and lymphocytes)
Potassium	
Sodium	**Urine analysis**
Bicarbonate[a]	UACR[c]
GGT[b]	
Calcitonin	**Other tests**
TSH	eGFR (CKD-EPI)
	Tryptase, in case of severe hypersensitivity

[a] only collected in trial 4374 and subjects with T2D in trial 4382, [b] only collected in trials 4373 and 4374, [c] only collected in trial 4374.
ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; CK: creatine kinase; eGFR (CKD-EPI): estimated glomerular filtration rate (eGFR) as per the Chronic Kidney Disease Epidemiology Collaboration formula (CKD-EPI); GGT: gamma glutamyl transferase; TBL: total bilirubin; TSH: thyroid stimulating hormone; UACR: urinary albumin to creatinine ratio.

試験実施中、中央検査機関は、治験責任医師に臨床検査結果を継続的に提供することとした。すべての中央検査機関の測定による測定値は臨床試験データベースに含めた（データセットに転送される）。また、治験実施計画書に規定されている cut-off 値を上回る値又は下回る値はすべて臨床検査の外れ値と判定され、治験責任医師はこれを「Laboratory outlier form」に記入して報告することとし、追加情報の収集を可能にした。肝臓パラメータである ALT、AST、アルカリホスファターゼ及び総ビリルビンについては、事前に規定した cut-off 値を超える値はすべて肝臓の臨床検査の外れ値として「Hepatic event form」に記入し、報告することとした（表 2.7.4.1-3）。他に原因が認められず、ALT 又は AST が基準範囲上限の 3 倍を超え、かつ総ビリルビンが基準範囲上限の 2 倍を超える場合は、重篤

な有害事象として報告することとした。基準範囲外の値について、治験責任医師はその値が臨床的に問題のある値か否かを特定し、臨床的に問題のある検査値異常はいずれも有害事象として報告することとした。臨床検査所見が治験責任医師により臨床的に問題のある所見（すなわち疾患及び／又は臓器毒性を示唆し、治験責任医師による処置を必要とする重症度の異常所見）であると評価された場合、当該所見は有害事象として報告しなければならず（2.7.4.1.1.8.2 項）、スクリーニング時の臨床検査で認められた所見であれば併発疾患／既往歴として報告することとした（2.7.4.1.1.8.1 項）。

すべての治験実施医療機関及び実施国で標準化された測定法及び基準範囲が用いられるようにするため、すべての臨床検査値の解析は中央検査機関で実施された。治験責任医師は、被験者の通常診療に関連する検査（有害事象の診断や治療など）では治験実施医療機関の臨床検査設備を用いることが可能であった。このように治験実施医療機関で解析された臨床検査パラメータは、通常は臨床試験データベースに入力されず、図表や一覧に提示されない（あるいはデータセットに含まれない）。治験実施医療機関の臨床検査室は中央検査機関とは別の測定法や基準範囲を用いている可能性があるため、治験実施医療機関の臨床検査室と中央検査機関で得られた評価結果の比較は難しい。治験実施医療機関の臨床検査室で測定され、治験責任医師が専用の追加データ収集用のフォーム又は「Laboratory outlier form」を用いて報告した臨床検査パラメータは、臨床試験データベースに入力され（データセットに転送され）、適宜、追加データの一覧及び叙述に含まれる。治験実施医療機関の臨床検査室で測定され、「Safety information form」（重篤な有害事象）に報告された臨床検査パラメータは、重篤な有害事象の叙述に含まれるが、これらの値は臨床試験データベースには入力されず、一覧、要約表及び図にも含まれない。

2.7.4.1.1.8.6　　血漿中セマグルチド濃度

日本人被験者が参加した 3 つの第 3 相試験では、すべての被験者において事前に規定した来院時に血漿中セマグルチド濃度を測定した。これらの来院では、被験者は採血が完了するまで、来院日の朝の治験薬投与を控えるよう指示された。セマグルチドの投与に割り付けられた被験者の血漿中セマグルチド濃度は、共変量解析、曝露反応解析、及び抗セマグルチド抗体の解析に干渉する治験薬の濃度の評価に用いた。

2.7.4.1.1.8.7　　抗セマグルチド抗体

日本人被験者が参加した 3 つの第 3 相試験では、事前に規定した来院時に抗セマグルチド抗体を測定した。これらの来院では、被験者は採血が完了するまで、来院日の朝の治験薬投与を控えるよう指示された。

抗セマグルチド抗体及び血漿中セマグルチド濃度の測定は、専門の臨床検査機関で実施された。抗セマグルチド抗体は段階的（スクリーニング、抗体価の確定、交叉反応性評価、*in vitro* での中和作用の評価を含む）に測定した。抗体反応のレベルは、総放射能に対する結合率（%B/T）を力価として測定した。検証的な分析で抗セマグルチド抗体陽性であった検体は、内因性 GLP-1 に対する交叉反応及びセマグルチドに対する *in vitro* での中和作用についてさらに評価した。また、検体が内因性 GLP-1 に対する交叉反応を有する抗セマグルチド抗体陽性であった場合は、内因性 GLP-1 に対する *in vitro* での中和作用についても検討した。抗体の測定方法の詳細は、Module 2.7.1.1.4.2 に記載する。

抗体に関する結果は本概要の 2.7.4.2.2.11.4 項に要約する。

2.7.4.1.1.8.8　バイタルサイン

すべての第 3 相試験において、規定の来院時に収縮期及び拡張期血圧、及び脈拍数を測定した。測定は、完全自動測定器を用いて、5 分以上安静にした後に座位で行った。手動の測定方法は、自動測定器が利用不能である場合にのみ使用した。試験を通して同じ測定器を用いることとした。

2.7.4.1.1.8.9　眼科的検査

2 型糖尿病を有する過体重又は肥満被験者を対象とした 4374 試験及び 2 型糖尿病患者を組み入れた 4382 試験では、コントロール不良で病態が不安定となる可能性のある糖尿病網膜症又は黄斑症を有する被験者は、除外基準として設定することにより試験への組み入れを不可とした。

4374 及び 4382 試験の 2 型糖尿病を有する被験者に対して、以下の時点で眼科的検査を実施することとした：

- スクリーニング来院（又は、適格性評価のため無作為割り付け前 90 日以内に得られた検査結果を用いる）
- 52 週来院
- 68 週の投与終了来院

直近の検査後に視覚機能の悪化を認めた被験者については、無作為割り付け前に再度眼科的検査を行うこととした。眼科的検査は、眼科医又はその他の適切な資格を有する医療従事者により、眼底写真（例：2 象限で画角 60 度以上、カラー又は red-free）又は細隙灯顕微鏡検査（例：前角膜レンズ又は角膜接触レンズを用いた検査方法）により実施した。眼科的検査は薬剤による散瞳下で実施した。

無作為割り付け前に認められた問題となる所見は、併発疾患／糖尿病歴及び合併症として記録することとした。無作為割り付け後に認められた糖尿病網膜症の新たな発現又は悪化は、治験責任医師が有害事象として報告し、追加データを収集することとした（2.7.4.1.1.8.2.2 項）。

各眼（左／右）について結果を評価し、正常又は異常に分類した。異常の場合は、さらに当該所見が臨床的に問題となる所見か否かを判断した。

2.7.4.1.1.8.10　心電図

すべての第 3 相試験において、以下の時点で 12 誘導心電図を測定した：

- 無作為割り付け来院
- 20 週来院
- 投与終了来院

心電図は、治験責任医師が評価し、正常又は異常に分類した。異常である場合は、さらに当該所見が臨床的に問題となる所見か否かを判断した。

ベースライン時における臨床的に問題となる心電図の異常所見は、併発疾患／既往歴として報告することとした（2.7.4.1.1.8.1 項）。無作為割り付け後に実施した心電図検査の結果として、以前から存

在していた疾患の臨床的に問題となる悪化ならびに臨床的に問題となる新たな徴候、症状又は疾患が認められた場合は、有害事象として報告することとした（2.7.4.1.1.8.2 項）。

治験責任医師の判断により、追加の心電図検査を実施することが可能であった。追加検査を実施した場合、理由を記録し、該当する場合は有害事象として報告した。

また、4382 試験において、事前に定義したすべての来院（無作為割り付け来院、20 週来院及び投与終了来院）で、自動で心拍数を計算し、PR、QRS、QT 及び QTc 間隔を計測する心電計を用いて 12 誘導心電図を記録した。QTc 間隔は中央測定機関が推定した。

2.7.4.1.1.8.11　身体所見

すべての第 3 相試験において、以下の時点で身体所見を確認した：

- スクリーニング来院
- 投与終了来院

4376 試験では、無作為割り付け来院（20 週）時にも実施した。

治験実施医療機関の手順に従って、少なくとも、一般状態、甲状腺、乳房（女性）及び腹部ならびに心血管系及び呼吸器系の評価を実施した。

各評価項目について、治験責任医師は結果を正常又は異常に分類し、異常である場合は、当該所見が臨床的に問題となるか否かを示すこととした。

スクリーニング時に実施した検査で認められた関連所見は、併発疾患／既往歴として報告することとした（2.7.4.1.1.8.1 項）。投与終了時（4376 試験では投与終了時に加えて 20 週の無作為割り付け来院時）に実施した検査に基づき特定された臨床的に問題となる新たな異常は、有害事象基準に合致する場合、有害事象として報告することとした（2.7.4.1.1.8.2 項）。

2.7.4.1.1.8.12　メンタルヘルスに関する質問票

スクリーニング時、ベースライン時、及び試験期間中に定期的に PHQ-9[5]及び C-SSRS[6]の質問票を用いてメンタルヘルスを評価した：

- PHQ-9 は、健康に関する質問票の 9 項目のうつ病モジュールであり、精神障害の評価に使用される自己記入式の診断ツールである。質問票は、言語的妥当性を担保した翻訳版が利用可能であった。
- C-SSRS は、自殺行動及び自殺念慮の両方を評価する詳細な質問票である。質問票への回答は、治験責任医師又は資格を有する代理人との面談として実施した。質問票（C-SSRS -ベースライン評価-及び C-SSRS -前回の評価以来-）は言語的妥当性を担保した翻訳版が利用可能であった。
    - C-SSRS 質問票による評価を実施する前に、治験責任医師又は資格を有する代理人は十分なトレーニングを完了した。

PHQ-9 スコアが 10～14 点であった場合には、被験者をメンタルヘルス専門家に紹介することとした。ただし、治験責任医師が適切ではないと判断し、その理由を被験者の診療録に記載した場合は除いた。

以下のいずれかに該当する被験者は、メンタルヘルス専門家に紹介しなければならなかった：

- PHQ-9 スコアが 15 以上
- 自殺行為があった被験者
- C-SSRS 評価で 4 型又 5 型の自殺念慮があった被験者
- 治験責任医師が被験者の安全上の理由で必要であると判断した被験者

被験者がメンタルヘルス専門家への紹介を拒否した場合は、被験者の決定を被験者の診療録に記録し、治験責任医師は、被験者の治験継続が安全であるか、又は被験者は治験薬投与を中止すべきかを判断することとした。

被験者の精神障害が心理療法及び／又は薬物治療で適切に治療可能であった場合は、治験責任医師の判断で（及びメンタルヘルス専門家の合意の下）、被験者は治験の継続を可能とした。それ以外の場合は、被験者は治験責任医師の判断による安全性上の懸念により、治験薬投与を中止しなければならなかった。

2.7.4.1.1.8.13　過量投与

治験薬に関連する過量投与（偶発的又は意図した）は、有害事象として報告することとし、追加情報は「Medication error form」を用いて記録することとした。過量投与があった場合、治験責任医師は過量投与に関連する有害事象／重篤な有害事象及び臨床検査値異常がないか被験者を注意深く観察した。すべての過量投与の症例についてレビューを行い、治験薬と関連する可能性がある事象（精神障害に関連する事象及び低血糖を含む）があるか判定した。

2.7.4.1.1.8.14　テクニカルな苦情

治験実施医療機関で治験薬投与を受けた時点から最後に使用した時点までの間に生じたテクニカルな苦情はすべて、「Technical complaint form」を用いて報告することとした。テクニカルな苦情とは、製品（薬剤又は医療機器）の不具合に関する、文書、電子又は口頭による連絡による申し立てである。治験責任医師は、テクニカルな苦情が有害事象に関連するか否か（はい／いいえ）を評価した。関連する場合は、「AE form」を用いて有害事象を報告した（2.7.4.1.1.8.2 項）。

2.7.4.1.1.8.15　妊娠

第 3 相試験では、妊娠可能な女性は妊娠を避けるようにし、被験者が妊娠した場合に措置を取るために、治験実施計画書に複数の規定を設けた。これらの一つとして、除外基準に「妊娠中、授乳中、妊娠を希望している女性被験者、あるいは妊娠可能で有効性の高い避妊法を受け入れられない女性被験者」を規定した。妊娠可能な女性は、有効性の高い避妊法を一貫して正しく使用することに同意する場合には本試験への参加が適格とされた。有効性が高いと考えられる避妊法についての詳細な指示は、治験実施計画書の中で治験責任医師に対して示された。また、女性被験者は、本試験の参加が適格と判定される前に妊娠検査で陰性でなければならず、試験期間を通して妊娠検査を定期的（4 又は 8 週間ごと）に実施した。月経が遅れているか、妊娠が疑われる場合は、追加の妊娠検査の実施を必要とした。被験者が妊娠した場合は、治験薬投与を中止しなければならなかった。

避妊に関するガイダンス及び妊娠情報収集の詳細は、各第 3 相試験の治験実施計画書の Appendix 5 に示す。

セマグルチド曝露後に報告された妊娠及び出産に関連した安全性情報は 2.7.4.5.6 項に記載する。

2.7.4.1.1.9　統計手法及びデータの提示

2.7.4.1.1.9.1　解析対象集団及び観察期間

日米 EU 医薬品規制調和国際会議（ICH）E9[7]に従い、盲検解除の前に、治験実施計画書及び統計解析計画書において以下の解析対象集団を定義した：

最大の解析対象集団（FAS）には、intention-to-treat（ITT）の原則に従い無作為割り付けされたすべての被験者を含めた。最大の解析対象集団の被験者は「as randomised」の評価に寄与した。

安全性解析対象集団（SAS）には、無作為割り付けされ、割り付けられた治療を少なくとも 1 回受けたすべての被験者を含めた。安全性解析対象集団の被験者は「as treated」の評価に寄与した。

各試験及び第 3 相試験併合データの安全性評価には安全性解析対象集団を用いた。なお、4376 試験については、20 週から試験終了までの無作為割り付け群間比較期間のみが第 3 相試験併合データに含まれた。

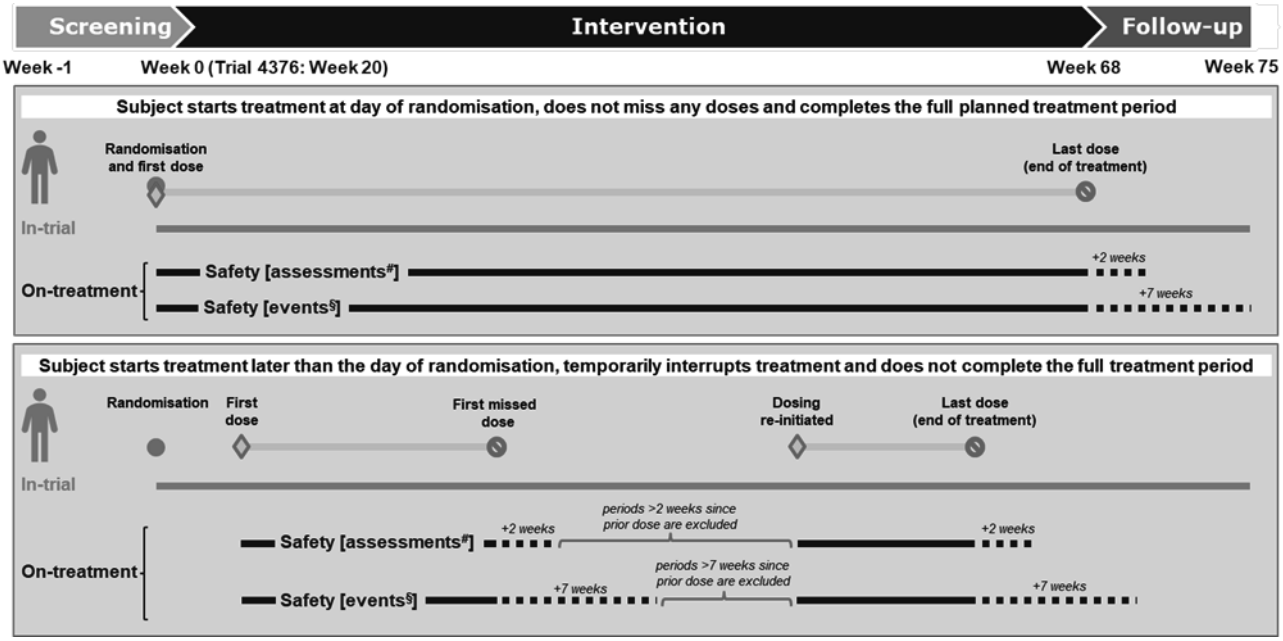
安全性評価のために、以下の 2 つの観察期間を設定した：

- **In-trial 観察期間**：無作為割り付けの日から治験実施医療機関と最後のコンタクトを取った日までの連続した期間と定義され、以下の評価に用いられた：
  - 死亡、及び潜伏期間が長く診断に至るまでに時間を要する可能性がある事象
- **On-treatment 観察期間**：治験薬の初回投与日から治験薬の最終投与日までの期間に最終投与後の追跡期間を加え、一時的に治療を中断した期間を除外した期間と定義した。最終投与後及び一時的な投与中断後の追跡期間の長さは以下のとおりとした：
  - 心電図、臨床検査、身体所見及び脈拍数の評価：2 週間
  - 有害事象、イベント判定委員会に確定された事象及び低血糖の評価：7 週間

In-trial 観察期間及び on-treatment 観察期間それぞれの合計時間が、被験者の観察人年（PYO）及び被験者の曝露人年（PYE）の期間として定義された。

これらの観察期間の定義の含意について、異なるシナリオを有する 2 種類の代表例を図 2.7.4.1-4 に図示する。

図 2.7.4.1-4　　すべての第 3 相試験における安全性評価の観察期間



ECG, laboratory assessments, physical examination and pulse; § AEs, adjudicated events and hypoglycaemic episodes.

ある被験者がベースライン後のどのデータ収集時点での評価に寄与するかは、この観察期間に基づいた。ベースライン値はすべての観察期間に含めた。

それぞれの安全性評価において、図表の見出しにデータが得られた観察期間を提示する。

2.7.4.1.1.9.2　　有害事象及びイベント判定委員会により確定された事象

有害事象及びイベント判定委員会により確定された事象は、少なくとも 1 件の事象を発現した被験者数（N）、少なくとも 1 件の事象を発現した被験者の割合（%）、事象の発現件数（E）及び単位時間あたりの発現件数（R）〔曝露期間 100 人年（PYE）あたり又は観察期間 100 人年（PYO）あたりの発現件数〕を用いて要約した。単位時間あたりの発現件数の算出には、事象発現数及び総曝露期間／観察期間が考慮されており、これによって治療間及び／又は試験間での曝露期間／観察期間の違いが勘案されている。

日本人被験者が参加した 3 つの第 3 相試験において、有害事象の要約表に追加して、試験及び投与群ごとの有害事象を発現した被験者の割合を提示した、Bar plot（有害事象の概要）及び器官別大分類別の Dot plot（%）を作成した。

有害事象の累積件数の経時変化を示すために、特定の基本語及び有害事象カテゴリー（すべての有害事象、重篤な有害事象、治験薬投与の中止に至った有害事象及び胃腸障害の有害事象）について、最初の事象発現までの時間の Kaplan-Meier plot を提示した。繰り返し発現する有害事象の評価には平均累積関数を用いた。

胃腸障害の有害事象については、on-treatment 観察期間中に事象を報告した被験者の割合の詳細な評価を行うために prevalence plot も提示した。日本人被験者が参加した 3 つの第 3 相試験では、これらの有害事象の経時変化を示す図は on-treatment 観察期間に基づく。

「悪心」、「下痢」、「便秘」及び「嘔吐」については、Kaplan-Meier 推定法を用いて事象の持続期間を算出した。消失日がない事象は治験終了時に打ち切りとした。

第 3 相試験の併合における調整方法

肥満症のためのセマグルチドの臨床開発プログラムに含まれる第 3 相試験は、試験デザイン、試験対象集団、安全性データ収集の方法及び時期が十分に類似しており、安全性データの意味のある併合が可能であった。しかしながら、試験対象集団や無作為割り付け比率の違いによって生じる試験による交絡（Simpson's Paradox）の潜在的なリスクを最小限にするために、第 3 相試験の併合にあたり、発現した被験者の割合及び単位時間あたりの発現件数の調整を行った。有害事象及びイベント判定委員会により確定された事象の要約について同じ調整を行った。第 3 相試験の併合にあたり、少なくとも 1 件の事象を発現した被験者の割合及び単位時間あたりの発現件数は、Cochran-Mantel-Haenszel[8]の重み付け法を用いた直接標準化法により調整した。

2.7.4.1.1.9.3　注目すべき安全性領域の評価

MedDRA 検索及びイベント判定の両方に基づいて評価される注目すべき安全性領域については、治験責任医師の報告に基づく事象とイベント判定委員会の判定結果に基づく事象をそれぞれ要約することにより、2 つの評価方法を用いて総合的に評価した。2 つの評価方法により評価される個々の事象は同一の事象であることが多いため、これらの結果を共に提示する場合がある。

以下の理由により、2 つの評価方法の間で事象が完全に重複（1：1 対応）することはない：

- MedDRA 検索は対象となる事象の範囲が広く、イベント判定委員会により確定されなかった事象や事前に規定されたイベント判定委員会で判定される事象に該当しない事象が含まれる可能性がある。
- MedDRA 検索には、イベント判定委員会の判定で複数の事象カテゴリーに分類され，別々に判定を受けそれぞれ要約された事象が含まれる可能性がある。
- イベント判定委員会では、ある事象の判定中に、原資料に含まれた情報から他の事象が追加で判定の対象として特定される可能性がある。そうした事象は、イベント判定者のデータベースに直接入力されるため、MedDRA 検索には含まれない。
- 一部の有害事象は、治験責任医師によりイベント判定委員会の判定対象とされて判定のために送付されるが、MedDRA 検索の検索語（基本語）に含まれない可能性がある。
- MedDRA 検索による事象は治験責任医師から報告された有害事象の発現日に基づき要約されるが、イベント判定委員会により確定された事象はイベント判定委員会が確認した事象発現日に基づき要約される。

2.7.4.1.1.9.4　サブグループにおける安全性データの評価

表 2.7.4.1-5 に示すサブグループ別のセマグルチドの安全性を評価した。サブグループは、関連する被験者背景及びベースラインの疾患特性（ベースライン時の内因性及び外因性民族的要因）に基づいて規定した。すべての有害事象、重篤な有害事象、及び胃腸障害の有害事象についてサブグループ別の評価を行った。サブグループ別の評価は、日本人被験者が参加した 3 つの第 3 相試験について行った。

表 2.7.4.1-5　　安全性データの評価に用いたサブグループ

Subgroup	**Trial 4373**	**Trial 4374**	**Trial 4382**
Sex	Male Female		
Age (years)	< 65 65 ≤		
Baseline body weight (kg)	<90 90 ≤ to < 100 100 ≤ to < 115 115 ≤		<80 80 ≤ to < 90 90 ≤ to < 100 100 ≤
Baseline BMI (kg/m^2)	<30 30≤ to < 35 35≤ to < 40 ≥40		
Baseline renal function (eGFR, mL/min/1.73 m^2)	Normal (≥90) Mild RI (60 ≤ to < 90) Moderate RI (≥30 to <60) Severe RI (≥15 to <30)		
Glycaemic status	Normo-glycaemic Pre-diabetes	Not applicable	Normo-glycaemic Pre-diabetes T2D
Dyslipidaemia	Yes No		
Hypertension	Yes No		
Anti-diabetic background medication	Not applicable	Group 1: Diet and physical activity only or 1 OAD (metformin or SGLT2i) Group 2: 1 OAD (SU or glitazone) or 2–3 OADs (metformin, SU, SGLT2i or glitazone)	Subjects with T2D only Group 1: Diet and physical activity only or 1 OAD (metformin or SGLT2i) Group 2: 1 OAD (SU or glitazone) or 2–3 OADs (metformin, SU, SGLT2i or glitazone)

eGFR: estimated glomerular filtration rate (CKD-EPI); T2D: type 2 diabetes; RI: renal impairment. OAD: oral anti-diabetic agent; SGLT2i: sodium-glucose co-transporter 2 inhibitor; SU: sulfonylurea.

上記に加え、日本人被験者が参加した 2 つの国際共同試験及び 1 つの東アジア試験（4373、4374 及び 4382 試験）では、日本人集団と全集団における安全性の結果の一貫性を検討した（2.7.4.5.1 項）。この検討は、全集団の結果を日本人集団に適切に外挿するため、「国際共同治験に関する基本的考え方について」[9]及び ICH-E5 ガイドライン[10]に基づき行った。

2.7.4.1.1.9.5　　低血糖

4374 及び 4382 試験における 2 型糖尿病を有する被験者では、低血糖を専用の「Hypoglycaemic episode form」を用いて報告した。低血糖の評価は on-treatment 観察期間に基づき行った。低血糖は 2018 年 ADA/2017 年 International Hypoglycaemia Study Group（IHSG）分類[11, 12]を用いて要約したが、過去に実施した試験のデータとの比較を可能にするため、ノボ ノルディスク社の分類及び ADA 2013 分類[13]に基づく要約も行った。

4373 及び 4382 試験における 2 型糖尿病を有さない被験者では、低血糖は有害事象データに基づき評価した。

2.7.4.1.1.9.6　心電図

心電図は心血管障害とあわせて評価した。試験別及び投与群別に、20 週及び 68 週（投与終了）に心電図結果の全体的な解釈のカテゴリー（「正常」、「異常／臨床的に問題なし」、「異常／臨床的に問題あり」）が変化した被験者の数及び割合を示すシフトテーブルを作成した。

上記に加え、4382 試験では、記述統計量とカテゴリー別〔絶対値（>450 msec、>480 msec 及び >500 msec）及びベースラインからの変化量（>30 msec 及び>60 msec）の要約〕を用いて QTc 間隔を評価した。

2.7.4.1.1.9.7　眼科的検査所見

4374 及び 4382 試験における 2 型糖尿病を有する被験者では、スクリーニング及び投与終了時の眼科的検査の結果を、左眼及び右眼でカテゴリー別（「正常」、「異常／臨床的に問題なし」、「異常／臨床的に問題あり」）に要約し、試験別及び投与群別に提示した。さらに、左眼及び右眼別のシフトテーブルにより、投与開始から 1 年及び投与終了時にカテゴリーが変化した被験者を提示した。

2.7.4.1.1.9.8　臨床検査、バイタルサイン及び身体所見

臨床検査

本概要における臨床検査データの評価は、主に表 2.7.4.1-4 に示すパラメータについて、日本人被験者が参加した 3 つの第 3 相試験の on-treatment 観察期間に基づき行った。試験間の比較及び／又はデータの併合を可能にするため、すべての第 3 相試験で同じ中央検査機関及び測定方法を用いた。採血頻度は試験間で同一であった。中央検査機関の測定値（予定及び予定外の測定及び再検査）に基づく臨床検査の外れ値を治験実施計画書で規定し（2.7.4.1.1.8.3 項）、専用の「Laboratory outlier form」を用いて報告した。

急性膵炎の症状とあわせてリパーゼ及びアミラーゼ、悪性新生物とあわせてカルシトニン、肝障害の評価の一環として肝臓パラメータ〔ALT、AST、アルカリホスファターゼ、γ-グルタミルトランスフェラーゼ（GGT）及び総ビリルビン〕、及び腎障害の評価の一環として推算糸球体濾過量（eGFR）、クレアチニン及び尿アルブミン／クレアチニン比（UACR）をそれぞれ評価した。

日本人被験者が参加した 3 つの第 3 相試験では、臨床検査パラメータを試験別及び投与群別に以下のとおり提示した：

- ベースライン及び 68 週（投与終了）における記述統計量〔平均又は幾何平均、中央値、ばらつき（標準偏差：SD 又は変動係数：CV）及び範囲を含む〕
- 68 週（投与終了）におけるベースラインからの変化量又はベースラインに対する比〔平均又は幾何平均、中央値、ばらつき（標準偏差：SD 又は変動係数：CV）及び範囲を含む〕
- 特定の臨床検査パラメータについて、ベースライン及び 68 週（投与終了）における、治験実施計画書に規定した臨床的に問題となる異常値の cut-off 値に基づくカテゴリー別〔低値（基準範囲下限未満）、正常値（基準範囲下限以上及び基準範囲上限以下）、高値（基準範囲上限を超え

る）〕の要約、ならびに各パラメータに関して治験実施計画書に規定した臨床的に問題となる異常値の cut-off 値に基づく要約

肝臓パラメータの詳細な評価には、第 3 相試験の in-trial 観察期間全体を含む 2 つの一覧を作成した。1）ベースライン後のいずれかの時点で基準範囲上限の 5 倍を超える ALT が認められた被験者、2）ベースライン後のいずれかの時点で基準範囲上限の 3 倍を超える AST／ALT 及び基準範囲上限の 2 倍を超える総ビリルビンが認められた被験者。

バイタルサイン

バイタルサインには血圧及び脈拍数が含まれる。脈拍数は心血管障害とあわせて評価した。バイタルサインを来院別及び投与群別に記述的に要約し、平均値、中央値、ばらつき及び範囲を示した。脈拍数のベースラインからの最大の変化量について、ベースラインの脈拍数によるカテゴリー別に要約した。

身体所見

身体所見については、68 週（投与終了）に結果の全般的な解釈のカテゴリー（「正常」、「異常／臨床的に問題なし」、「異常／臨床的に問題あり」）が変化した被験者の数及び割合のシフトテーブルを試験別及び投与群別に提示した。

2.7.4.1.1.9.9　安全性データに貢献した試験の叙述

肥満症のためのセマグルチドの開発プログラムに含まれるすべての臨床試験は、安全性データに加え有効性又は臨床薬理学のデータに寄与した。臨床薬理試験の詳細は Module 2.7.1、付録 2.7.1.4.1 又は Module 2.7.2.2、第 3 相試験の詳細は Module 2.7.3.2 に示す。各試験の詳細は Module 2.7.6 に提示する。

2.7.4.1.2　全般的な曝露状況

2.7.4.1.2.1　被験者の内訳

評価方法

日本人被験者が参加した第 3 相試験（4373、4374 及び 4382 試験）における被験者の内訳は Module 2.7.3.3.1.1 に詳述する。本項では、第 3 相試験併合データにおける被験者の内訳の概要（治験薬の投与を完了した被験者、試験を完了した被験者及び治験薬の投与を中止した被験者の数）について説明する。

治験薬の投与を完了した被験者とは、無作為割り付けされた被験者のうち治験薬の投与を完了した被験者、すなわち治験薬投与を中止しなかった被験者と定義した。試験を完了した被験者は、無作為割り付けされた被験者のうち、電話又は来院により試験終了来院を完了した被験者と定義した。

すべての選択及び除外基準ならびに治験薬投与の中止基準は、各試験の治験総括報告書（Module 5）に記載する。主な選択基準及び除外基準の概要は、Module 2.7.3、表 2.7.3.1-5 及び表 2.7.3.1-6 に提示する。

結果

日本人被験者が参加した第 3 相試験（4373、4374 及び 4382 試験）における被験者の内訳は、Module 2.7.3.3.1.1 に示す。

第 3 相試験併合データでは、セマグルチド 2.4 mg の投与を受けた被験者は 2650 例及びプラセボの投与を受けた被験者は 1529 例であった（表 2.7.4.1-6）。セマグルチド 2.4 mg の投与を受けた被験者のうち、試験を完了した被験者及び投与を完了した被験者の割合はいずれも高かったことから（それぞれ 95.6%及び 86.2%）、試験が適切に実施されたことが示され、試験結果の安定性が裏付けられた〔Global summary of safety（Module 5.3.5.3）Appendix 7.1、Table 7.1.1〕。

表 2.7.4.1-6　　被験者の内訳（第 3 相試験併合データ、併合グループ別）

Trial		Semaglutide		Placebo	
	Dose	Number of subjects randomised/ exposed	Number of treatment completers/ trial completers	Number of subjects randomised/ exposed	Number of treatment completers/ trial completers
Phase 3a pool	2.4 mg	2652 / 2650	2283 / 2533	1530 / 1529	1258 / 1442
Phase 3a dose escalation group	2.4 mg	2117 / 2116	1779 / 2007	1262 / 1261	1021 / 1182
Phase 3a without T2D group	2.4 mg	2248 / 2247	1926 / 2143	1127 / 1127	911 / 1060

Treatment completers: randomised subjects who completed treatment without permanent discontinuation of trial product. Permanent discontinuation is when a subject stopped taking trial product and did not resume treatment and is therefore not considered as 'on-treatment' at end of treatment period (week 68). A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.

第 3 相試験併合データ及び用量漸増を含む第 3 相試験併合データのいずれでも、治験薬投与を中止した被験者の割合は、プラセボ併合群と比較してセマグルチド 2.4 mg 併合群で低かった〔Global summary of safety （Module 5.3.5.3）Appendix 7.1、Table 7.1.1、7.1.2〕。セマグルチド 2.4 mg 併合群において、投与を完了しなかった主な理由は有害事象（主に胃腸障害の有害事象）であった。有害事象の発現状況は、日本人被験者が参加した 3 つの第 3 相試験（4373、4374 及び 4382 試験）で認められた結果（詳細は Module 2.7.3）と同様であった。

各試験の被験者の内訳の詳細は、各試験の治験総括報告書（Module 5.3.5.1）Section 10 に示す。

2.7.4.1.2.2　総曝露

曝露期間は、治験薬投与の一時中断又は治験薬投与終了の 7 週間までを含む on-treatment 観察期間全体と定義した。観察期間の定義は 2.7.4.1.1.9.1 項に示す。

本項は、主に、日本人被験者が参加した 3 つの第 3 相試験の曝露について記載する。第 3 相試験併合データの総曝露については簡潔に説明する。

日本人被験者が参加した第 3 相試験、第 3 相試験併合データ及び併合グループ別の曝露を表 2.7.4.1-7 に要約する（安全性解析のためのデータ併合の方法は 2.7.4.1.1.4 項に示す）。4382 及び 4373 試験では、総曝露は無作為割り付けの比率である 4：1：2：1（4382 試験、セマグルチド 2.4 mg：プラセボ：セマグルチド 1.7 mg：プラセボ）及び 2：1（4373 試験、セマグルチド 2.4 mg：プラセボ）を反映して

おり、プラセボ群及びセマグルチド 1.7 mg 群（4382 試験のみ）と比較してセマグルチド 2.4 mg 群で高かった。4374 試験の総曝露はすべての投与群で同様であった。

第 3 相試験の併合データでは、on-treatment 観察期間におけるセマグルチドの総曝露（セマグルチド 2.4 mg 併合群）は、第 3 相試験併合データでは 3309 PYE、用量漸増を含む第 3 相試験併合データでは 2765 PYE、2 型糖尿病を有さない被験者を含む第 3 相試験併合データでは 2776 PYE であった。4373、4375 及び 4376 試験は無作為割り付けの比率が不均等であったため、総曝露はプラセボ併合群と比較してセマグルチド 2.4 mg 併合群で高かった。

表 2.7.4.1-7　　総曝露－on-treatment 観察期間－安全性解析対象集団（第 3 相試験及び第 3 相試験の併合データ）

	Sema 1.0 mg		Sema 1.7 mg		Sema 2.4 mg		Placebo	
	N	PYE	N	PYE	N	PYE	N	PYE
4373					1306	1706	655	830
4374	402	530			403	533	402	528
4382			100	136	199	275	101	142
Phase 3a pool					2650	3309	1529	1885
Phase 3a without T2D group					2247	2776	1127	1357
Phase 3a dose escalation group					2116	2765	1261	1619

Phase 3a pool: trials 4373, 4374, 4375 and 4376 data from subjects randomised to Sema 2.4 mg or Placebo during the controlled periods of the trials.
Phase 3a without T2D group: trials 4373, 4375 and 4376 data from subjects randomised to Sema 2.4 mg or Placebo during the controlled periods of the trials.
Phase 3a dose escalation group: trials 4373, 4374 and 4375 data from subjects randomised to Sema 2.4 mg or Placebo during the controlled periods of the trials.
N: Number of subjects, PYE: Patient years of exposure, T2D: Type 2 diabetes,
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days. Only subjects from trial 4376 that have been exposed to trial product after randomisation are included.

2.7.4.1.2.3　治験期間別の曝露

日本人被験者が参加した 3 つの第 3 相試験における各観察期間の平均値、中央値及び総観察期間は各試験の治験総括報告書〔4382 試験（Module 5.3.5.1）Section 10.5.1、EOT Table 14.1.26、14.1.27、4373 試験（Module 5.3.5.1）Section 10.4.1、EOT Table 14.1.23、14.1.24、4374 試験（Module 5.3.5.1）Section 10.3.1, EOT Table 14.1.23、14.1.24〕に示す。

日本人被験者が参加した 3 つの第 3 相試験において、期間別（ヵ月）の治験薬の投与を受けた被験者の割合を表 2.7.4.1-8 に示す。これらの 3 試験における 16～17 ヵ月及び 17～18 ヵ月にかけての曝露人数の減少は、投与終了時期を反映している。

表 2.7.4.1-8　　期間別の曝露状況－on-treatment 観察期間－安全性解析対象集団（4382、4373 及び 4374 試験）

	Sema 1.7 mg N (%)	Sema 2.4 mg N (%)	Placebo N (%)	Total N (%)
Trial 4382				
Number of subjects	100	199	101	400
On-treatment duration (months)				
>=0	100 (100)	199 (100)	101 (100)	400 (100)
>=1	100 (100)	199 (100)	101 (100)	400 (100)
>=2	100 (100)	199 (100)	101 (100)	400 (100)
>=3	99 (99.0)	197 (99.0)	101 (100)	397 (99.3)
>=4	98 (98.0)	197 (99.0)	101 (100)	396 (99.0)
>=5	98 (98.0)	196 (98.5)	101 (100)	395 (98.8)
>=6	98 (98.0)	196 (98.5)	100 (99.0)	394 (98.5)
>=7	98 (98.0)	195 (98.0)	100 (99.0)	393 (98.3)
>=8	98 (98.0)	195 (98.0)	100 (99.0)	393 (98.3)
>=9	96 (96.0)	195 (98.0)	99 (98.0)	390 (97.5)
>=10	94 (94.0)	194 (97.5)	99 (98.0)	387 (96.8)
>=11	94 (94.0)	193 (97.0)	99 (98.0)	386 (96.5)
>=12	93 (93.0)	192 (96.5)	99 (98.0)	384 (96.0)
>=13	93 (93.0)	191 (96.0)	99 (98.0)	383 (95.8)
>=14	92 (92.0)	188 (94.5)	98 (97.0)	378 (94.5)
>=15	91 (91.0)	185 (93.0)	98 (97.0)	374 (93.5)
>=16	91 (91.0)	183 (92.0)	98 (97.0)	372 (93.0)
>=17	86 (86.0)	179 (89.9)	95 (94.1)	360 (90.0)

	Sema 2.4 mg N (%)	Placebo N (%)	Total N (%)
Trial 4373			
Number of subjects	1306	655	1961
On-treatment duration (months)			
>=0	1306 (100)	655 (100)	1961 (100)
>=1	1305 (99.9)	654 (99.8)	1959 (99.9)
>=2	1294 (99.1)	650 (99.2)	1944 (99.1)
>=3	1273 (97.5)	644 (98.3)	1917 (97.8)
>=4	1251 (95.8)	632 (96.5)	1883 (96.0)
>=5	1241 (95.0)	624 (95.3)	1865 (95.1)
>=6	1225 (93.8)	616 (94.0)	1841 (93.9)
>=7	1209 (92.6)	604 (92.2)	1813 (92.5)
>=8	1196 (91.6)	587 (89.6)	1783 (90.9)
>=9	1190 (91.1)	579 (88.4)	1769 (90.2)
>=10	1172 (89.7)	564 (86.1)	1736 (88.5)
>=11	1164 (89.1)	556 (84.9)	1720 (87.7)
>=12	1153 (88.3)	541 (82.6)	1694 (86.4)
>=13	1144 (87.6)	529 (80.8)	1673 (85.3)
>=14	1129 (86.4)	520 (79.4)	1649 (84.1)
>=15	1118 (85.6)	512 (78.2)	1630 (83.1)
>=16	1081 (82.8)	501 (76.5)	1582 (80.7)
>=17	998 (76.4)	472 (72.1)	1470 (75.0)
>=18	0	1 (0.2)	1 (<0.1)

	Sema 1.0 mg N (%)	Sema 2.4 mg N (%)	Placebo N (%)	Total N (%)
Trial 4374				
Number of subjects	402	403	402	1207
On-treatment duration (months)				
>=0	402 (100)	403 (100)	402 (100)	1207 (100)
>=1	400 (99.5)	403 (100)	401 (99.8)	1204 (99.8)
>=2	395 (98.3)	398 (98.8)	395 (98.3)	1188 (98.4)
>=3	389 (96.8)	391 (97.0)	391 (97.3)	1171 (97.0)

(continues)

	Sema 1.0 mg N (%)	Sema 2.4 mg N (%)	Placebo N (%)	Total N (%)
Trial 4374				
Number of subjects	402	403	402	1207
On-treatment duration (months)				
>=4	381 (94.8)	384 (95.3)	388 (96.5)	1153 (95.5)
>=5	376 (93.5)	381 (94.5)	382 (95.0)	1139 (94.4)
>=6	373 (92.8)	376 (93.3)	377 (93.8)	1126 (93.3)
>=7	371 (92.3)	375 (93.1)	371 (92.3)	1117 (92.5)
>=8	370 (92.0)	372 (92.3)	370 (92.0)	1112 (92.1)
>=9	369 (91.8)	369 (91.6)	367 (91.3)	1105 (91.5)
>=10	366 (91.0)	368 (91.3)	364 (90.5)	1098 (91.0)
>=11	364 (90.5)	367 (91.1)	361 (89.8)	1092 (90.5)
>=12	361 (89.8)	366 (90.8)	356 (88.6)	1083 (89.7)
>=13	359 (89.3)	364 (90.3)	354 (88.1)	1077 (89.2)
>=14	355 (88.3)	358 (88.8)	351 (87.3)	1064 (88.2)
>=15	355 (88.3)	353 (87.6)	348 (86.6)	1056 (87.5)
>=16	353 (87.8)	350 (86.8)	343 (85.3)	1046 (86.7)
>=17	331 (82.3)	331 (82.1)	322 (80.1)	984 (81.5)
>=18	0	1 (0.2)	0	1 (<0.1)

N: Number of subjects, %: Percentages are based on number of subjects.
A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.

第 3 相試験併合データでは、12～13 ヵ月にかけての曝露人数の低下は 4376 試験の投与終了時期を、また 16～17 ヵ月／17～18 ヵ月にかけての曝露人数の低下は 4373、4374 及び 4375 試験の投与終了時期を反映している（表 2.7.4.1-9）。

表 2.7.4.1-9　　期間別の曝露状況－on-treatment 観察期間（第 3 相試験併合データ）

	Sema 2.4 mg N (%)	Placebo N (%)	Total N (%)
Number of subjects	2650	1529	4179
Duration of exposure (months)			
>=0	2650 (100)	1529 (100)	4179 (100)
>=1	2646 (99.8)	1524 (99.7)	4170 (99.8)
>=2	2623 (99.0)	1513 (99.0)	4136 (99.0)
>=3	2586 (97.6)	1499 (98.0)	4085 (97.8)
>=4	2548 (96.2)	1479 (96.7)	4027 (96.4)
>=5	2533 (95.6)	1456 (95.2)	3989 (95.5)
>=6	2499 (94.3)	1438 (94.0)	3937 (94.2)
>=7	2476 (93.4)	1414 (92.5)	3890 (93.1)
>=8	2455 (92.6)	1391 (91.0)	3846 (92.0)
>=9	2436 (91.9)	1377 (90.1)	3813 (91.2)
>=10	2409 (90.9)	1349 (88.2)	3758 (89.9)
>=11	2395 (90.4)	1334 (87.2)	3729 (89.2)
>=12	2370 (89.4)	1305 (85.3)	3675 (87.9)
>=13	1863 (70.3)	1055 (69.0)	2918 (69.8)
>=14	1830 (69.1)	1042 (68.1)	2872 (68.7)
>=15	1809 (68.3)	1026 (67.1)	2835 (67.8)
>=16	1762 (66.5)	1008 (65.9)	2770 (66.3)
>=17	1636 (61.7)	945 (61.8)	2581 (61.8)
>=18	2 (0.1)	2 (0.1)	4 (0.1)

Phase 3a pool: STEP 1-4 data from subjects randomised to Sema 2.4 mg or Placebo during the controlled periods of the trials.
N: Number of subjects, %: Percentage of subjects.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

2.7.4.1.2.4　人口統計学的特性及びベースライン特性別の曝露

日本人被験者が参加した 3 つの第 3 相試験における被験者背景（年齢及び性別）によるサブグループ別の曝露を表 2.7.4.1-10、表 2.7.4.1-11 及び表 2.7.4.1-12 に示す。

4382 試験では、セマグルチド（1.7 及び 2.4 mg）及びプラセボの投与を受けた被験者はいずれも女性より男性の方が多く、4373 試験では、セマグルチド 2.4 mg 及びプラセボの投与を受けた被験者は男性より女性の方が多かった。4374 試験では、いずれの投与群でも曝露被験者数に男女で違いは認められなかった。日本人被験者が参加した 3 つの第 3 相試験では、65 歳以上の被験者より 65 歳未満の被験者が多かった。

日本人被験者が参加した 3 つの第 3 相試験における他のサブグループ別（体重、BMI、腎機能、脂質異常症の有無、高血圧の有無及び糖代謝の分類）の曝露は、付録 2.7.4.7.2、表 13、表 15、表 17、表 19、表 21、表 23、表 25、表 27、表 29、表 31、表 33、表 35、表 37、表 39、表 41、表 43 及び表 45 に示す。

表 2.7.4.1-10　サブグループ別の曝露状況－on-treatment 観察期間（4382 試験）

Subjects and exposure	Sema 1.7 mg N	Sema 1.7 mg PYE	Sema 2.4 mg N	Sema 2.4 mg PYE	Placebo N	Placebo PYE
	100	136.2	199	275.0	101	141.8
Sex						
Female	36	49.7	85	120.1	26	37.1
Male	64	86.5	114	154.9	75	104.8
Age (years)						
<65	90	122.4	166	229.0	95	133.3
>=65	10	13.8	33	46.0	6	8.6

Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

表 2.7.4.1-11　サブグループ別の曝露状況－on-treatment 観察期間（4373 試験）

Subjects and exposure	Sema 2.4 mg N	Sema 2.4 mg PYE	Placebo N	Placebo PYE
	1306	1706.1	655	829.6
Sex				
Female	955	1240.8	498	624.7
Male	351	465.3	157	204.9
Age (years)				
<65	1198	1562.8	607	766.3
>=65	108	143.3	48	63.2

Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

表 2.7.4.1-12　　サブグループ別の曝露状況－on-treatment 観察期間（4374 試験）

Subjects and exposure	Sema 1.0 mg N	Sema 1.0 mg PYE	Sema 2.4 mg N	Sema 2.4 mg PYE	Placebo N	Placebo PYE
	402	529.8	403	533.0	402	528.3
Sex						
Female	202	268.3	222	297.0	190	253.9
Male	200	261.5	181	236.1	212	274.4
Age (years)						
<65	319	420.5	315	422.2	317	422.6
>=65	83	109.3	88	110.9	85	105.7

Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

第 3 相試験併合データにおける被験者背景（年齢、性別、人種及び地域）によるサブグループ別の曝露を表 2.7.4.1-13 に示す。他のサブグループ別（民族、BMI、体重、腎機能及び糖代謝の分類）の曝露は Global summary of safety（Module 5.3.5.3）Appendix 7.1、Table 7.1.6 に示す。

セマグルチド 2.4 mg 及びプラセボの投与を受けた被験者は、いずれも男性より女性の方が多かった。セマグルチド 2.4 mg 及びプラセボの投与を受けた被験者で、最も割合が高かったのは 65 歳未満の被験者であった。65 歳以上 75 歳未満の被験者の占める割合は、セマグルチド 2.4 mg 及びプラセボを投与した被験者の約 10 分の 1 であった。75 歳以上の被験者については、計 23 例がセマグルチド 2.4 mg の投与を受け、13 例がプラセボの投与を受けた。

4375 試験は米国の被験者のみを組み入れ、4373、4374 及び 4376 試験は 26 ヵ国（米国を含む）の被験者を組み入れた国際共同試験であった。国別の曝露は Global summary of safety（Module 5.3.5.3）Appendix 7.1、Table 7.1.5 に示す。人種別の曝露は、国際共同試験であることを反映し、セマグルチド 2.4 mg の投与の受けた被験者は、その大部分は白人であり、次いでアジア人及び黒人又はアフリカ系アメリカ人であった（表 2.7.4.1-13）。地域別では北米及び欧州の割合が高かった。

表 2.7.4.1-13　　サブグループ別の曝露状況－on-treatment 観察期間（第 3 相試験併合データ）

	Sema 2.4 mg		Placebo		Total	
	N	PYE	N	PYE	N	PYE
Number of subjects	2650		1529		4179	
Age group (years)						
N	2650	3309	1529	1885	4179	5195
<65	2394	2987	1362	1676	3756	4663
65-<75	233	297	154	192	387	489
>=75	23	26	13	17	36	43
Sex						
N	2650	3309	1529	1885	4179	5195
Female	1920	2381	1073	1312	2993	3693
Male	730	928	456	574	1186	1502
Race						
N	2650	3309	1529	1885	4179	5195
White	1962	2439	1124	1378	3086	3816
Black or African American	255	311	147	166	402	477
Asian	313	409	198	266	511	675
Other	57	70	28	35	85	105
Not applicable	38	48	17	24	55	71
Region						
N	2650	3309	1529	1885	4179	5195
Europe	890	1088	516	624	1406	1713
North America	1304	1628	719	872	2023	2500
South America	103	141	66	88	169	229
Africa	57	62	38	46	95	108
East Asia	135	187	89	125	224	312
Asia (excluding East Asia)	161	203	101	130	262	333

Phase 3a pool: STEP 1-4 data from subjects randomised to Sema 2.4 mg or Placebo during the controlled periods of the trials.
N: Number of subjects, PYE: Patient years of exposure.
Ethnic origin and race are recorded as 'Not applicable' for France.
Region 'North America' includes United States and Canada. Region 'East Asia' includes Japan and Taiwan. Region 'Asia (excluding East Asia)' includes India and United Arab Emirates.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

2.7.4.1.2.5　結論

Module 2.7.3.3.1.1 に記載されているように、日本人被験者が参加した 3 つの第 3 相試験（4382、4373 及び 4374 試験）のいずれでも、試験を完了した被験者の割合は高く、投与群間で同程度であった。治験薬投与を中止した被験者の割合は、4382 試験ではプラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.7 mg 群でやや高く、4373 試験ではプラセボ群と比較してセマグルチド 2.4 mg 群で低く、4374 試験ではすべての投与群で同程度であった。セマグルチドの投与中止に至った有害事象のうち最も高頻度で認められたのは胃腸障害の有害事象であった（2.7.4.2.1.4.1 項）。肥満症のためのセマグルチド 2.4 mg の第 3 相試験プログラムでは、十分なセマグルチドへの曝露情報が得られている。

2.7.4.1.3　試験対象集団の人口統計学的特性及びその他の特性

2.7.4.1.3.1　ベースライン特性

評価方法

日本人被験者が参加した第 3 相試験（4373、4374 及び 4382 試験）の試験対象集団について、被験者背景及びその他の特性の詳細は Module 2.7.3.3.1.2 に提示する。以下の項では、第 3 相試験併合データにおける対象集団の被験者背景及びその他の特性の概要を記載する。

第 3 相試験の選択及び除外基準は、セマグルチド 2.4 mg の投与対象となる被験者を組み入れるために、被験者背景、併発疾患及び併用薬剤の観点から設定した。GLP-1 受容体作動薬を用いた他の試験と同様に、妊婦、小児、うっ血性心不全患者、ニューヨーク心臓協会（NYHA）クラス IV の心不全患者、慢性膵炎患者又は急性膵炎の最近の既往を有する患者、2 型多発性内分泌腺腫（MEN 2）の既往歴又は家族性甲状腺髄様癌を有する患者などは、安全性上の理由で試験から除外された。

様々な人種及び民族の被験者への投与を行うよう、治験実施医療機関は北米、南米、欧州、アフリカ及びアジアにおいて選択した。

結果

第 3 相試験併合データでは、男性より女性の方が多かった。ほとんどの被験者は白人及び非ヒスパニック系／非ラテン系であり、平均年齢は 48 歳、平均体重は 102.6 kg、平均 BMI は 36.8 kg/m^2 であった〔Global summary of safety（Module 5.3.5.3）Appendix 7.1、Table 7.1.8、7.1.9〕。被験者の 85%超はベースラインの BMI が 30 kg/m^2 以上であった。

ベースライン特性は投与群間で概ね同様であったが、正常血糖及び pre-diabetes の被験者はプラセボ併合群と比較してセマグルチド 2.4 mg 併合群で多く、2 型糖尿病を有する被験者はプラセボ併合群と比較してセマグルチド 2.4 mg 群で少なかった。これらの差は、無作為割り付けの比率が 4374 試験（1：1）と他の 3 つの第 3 相試験（2：1）とで異なっていたことによるものであり、有害事象プロファイルの評価にあたって、これらの差が有害事象の単位時間あたりの発現件数及び有害事象を発現した被験者の割合に影響しないよう、Cochran-Mantel-Haenszel 法を用いて調整した。

2 型糖尿病を有さない被験者を含む第 3 相試験併合データでは、ベースラインの空腹時血糖値及び HbA1c の平均は 2 つの投与群で同様であった。

2.7.4.1.3.2　既往歴及び併発疾患

評価方法

既往歴とは、過去に罹患した疾患でスクリーニング前に消失しているものと定義した。すべての第 3 相試験で既往歴の詳細を記録し、MedDRA の分類を用いてコーディングした。スクリーニング時に被験者の皮膚癌、大腸新生物、乳癌、胆嚢系疾患及び精神障害の既往歴を体系的に収集した。

併発疾患とは、試験開始時に存在する、もしくはスクリーニング手順又は治験薬への曝露の前に実施したその他の手順の結果として発見された疾患と定義した。すべての試験で併発疾患の詳細をスクリーニング時に記録し、MedDRA の分類を用いてコード化した。被験者の肥満に関連する合併症として、脂質異常症、高血圧、冠動脈疾患、脳血管疾患、閉塞性睡眠時無呼吸症候群、糖代謝異常、生殖器系疾患、肝疾患、腎疾患、変形性関節症、痛風及び喘息／慢性閉塞性肺疾患（COPD）に関する情報

をスクリーニング時に体系的に収集した。治験責任医師は被験者がこれらの各併発疾患を有するか否かを記録し、その情報を専用のフォームに入力することとした。「Comorbidity form」に記載された情報と一般既往歴及び併発疾患との一貫性を医学的モニタリングにおいて確認した。2 型糖尿病は、「comorbidity form」に併発疾患として含めなかった。

結果

全体として、日本人被験者が参加した 3 つの第 3 相試験では、既往歴及び併発疾患は組み入れられた試験対象集団において概ね予測されたとおりであり、投与群間に特記すべき違いはなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.1.12、14.1.13、4373 試験（Module 5.3.5.1）EOT Table 14.1.13、14.1.14、4374 試験（Module 5.3.5.1）EOT Table 14.1.10、14.1.11〕。

これらの 3 試験において、皮膚癌、大腸新生物、乳癌、胆嚢疾患及び精神障害の既往歴を有する被験者の割合は、組み入れられた試験対象集団において予測されたとおりであり、投与群間に特記すべき違いはなかった。4382 試験では、皮膚癌の既往がある被験者はいなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.1.14～14.1.18、4373 試験（Module 5.3.5.1）EOT Table 14.1.15～14.1.19、4374 試験（Module 5.3.5.1）EOT Table 14.1.12～14.1.16〕。

これらの 3 試験において、スクリーニング時に併発疾患を有する被験者の割合は投与群間で同様であった。4382 試験では、選択基準に従い、併発疾患のうち少なくとも 1 つが脂質異常症、高血圧、又は 2 型糖尿病（日本人被験者のみ）であったことから、これらの併発疾患を報告した被験者の割合は高かった〔4382 試験（Module 5.3.5.1）EOT Table 14.1.19、4373 試験（Module 5.3.5.1）EOT Table 14.1.20、4374 試験（Module 5.3.5.1）EOT Table 14.1.17〕。

2.7.4.1.3.3　併用薬剤

評価方法

スクリーニング時に服用していた併用薬及びスクリーニング後に服用した併用薬を試験中に記録し、解剖治療化学分類（ATC）を用いてコーディングした。併用薬とは、治験薬を除き、スクリーニング期間及び事後調査期間を含む試験期間中に投与されたすべての薬剤と定義した。各併用薬について収集された情報には、少なくとも、併用薬の販売名又は一般名、適応症、及び開始日と中止日が含まれた。

結果

日本人被験者が参加した 3 つの第 3 相試験では、ベースライン時に使用が報告された併用薬に投与群間で大きな違いはなく、第 3 相試験のデザイン及び組み入れられた試験対象集団を反映していた。併用薬剤の詳細は、各試験の治験総括報告書に示す〔4382 試験（Module 5.3.5.1）Section 10.2.2、4373 試験（Module 5.3.5.1）Section 10.2.2、4374 試験（Module 5.3.5.1）Section 10.2.3〕。

2.7.4.2　有害事象

2.7.4.2.1　有害事象の解析

2.7.4.2.1.1　有害事象（比較的よく見られる有害事象を含む）

2.7.4.2.1.1.1　背景及び評価方法

本項では、日本人被験者が参加した 3 つの第 3 相試験（4382、4373 及び 4374 試験）に基づき、セマグルチドの安全性プロファイルを検討する。

すべての安全性評価は、安全性解析対象集団に基づいて行う。安全性評価の観察期間は、主に on-treatment 観察期間に基づき、In-trial 観察期間は、発現から診断までの時間が長くなる可能性のある有害事象（死亡、心血管事象、新生物、精神障害の評価のためのメンタルヘルスに関する質問票、網膜障害及び妊娠中の使用）の評価に用いた。安全性の評価方法については 2.7.4.1.1.8 項、統計手法及びデータの提示については 2.7.4.1.1.9 項に示す。

GLP-1 受容体作動薬及びセマグルチにおいて評価が必要と判断した注目すべき安全性領域に関する詳細な評価を 2.7.4.2.2 項に示す。重篤な有害事象を 2.7.4.2.1.3 項、治験薬投与の中止に至った有害事象を 2.7.4.2.1.4 項に示す。また、2 つの第 3 相試験（4382 及び 4374 試験）及び 1 つの第 2 相用量設定試験（4153 試験）に基づいて行ったセマグルチドの用量反応関係に関する評価を 2.7.4.2.1.5 項に示す。

セマグルチドの安全性評価は、国際共同第 3 相試験の安全性併合データにより裏付けられる。この評価の結果を 2.7.4.2.3 項及び 2.7.4.5.9 項に示す。

第 2 相用量設定試験及び臨床薬理試験に基づくセマグルチドの安全性評価は Module 5 の各治験総括報告書に示す。これらの簡潔な要約を 2.7.4.2.1.1.4 項に示す。

2.7.4.2.1.1.2　有害事象の概観

各試験（4382、4373 及び 4374 試験）で報告された有害事象の詳細な評価は、各治験総括報告書（Module 5.3.5.1）に示す。以下に結果の要約を示す。

日本人被験者が参加した 3 つの第 3 相試験において、有害事象を発現した被験者の割合はプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で同様又は高かったが、単位時間あたりの有害事象の発現件数はプラセボ群と比較してすべてのセマグルチド群（1.0、1.7 及び 2.4 mg）で多かった（表 2.7.4.2-1、表 2.7.4.2-2 及び表 2.7.4.2-3）。有害事象の発現において認められた違いは、主にセマグルチド群において胃腸障害の有害事象が高頻度で報告されたことによるものであった（2.7.4.2.2.2 項）。胃腸障害は、GLP-1 受容体作動薬でよく知られた有害事象である。

3 つの第 3 相試験では、すべての投与群で一貫して、報告された有害事象の大部分が非重篤で、軽度又は中等度であり、転帰は回復と報告された。

4382 試験では、死亡は報告されなかった。4373 試験ではプラセボ群の 1 例が 1 件の転帰「死亡」の有害事象を on-treatment 観察期間に発現した。本被験者は、on-treatment 観察期間後の in-trial 観察期間内に 2 件の転帰「死亡」の有害事象も発現した。さらに、セマグルチド 2.4 mg 群の 1 例が、on-treatment 観察期間後の in-trial 観察期間内に 1 件の転帰「死亡」の有害事象を発現した。4374 試験では、セマグルチド 2.4 mg 群とプラセボ群の各 1 例が 1 件の転帰「死亡」の有害事象を on-treatment 観察期間に発現した。プラセボ群の 1 例は、on-treatment 観察期間後の in-trial 観察期間内に 2 件の転帰「死

亡」の有害事象も発現した。さらに、セマグルチド 1.0 mg 群の 1 例が、on-treatment 観察期間後の in-trial 観察期間内に 1 件の転帰「死亡」の有害事象を発現した。第 3 相試験において、日本人被験者に転帰「死亡」の有害事象は報告されなかった（2.7.4.2.1.2 項）。

3 つの第 3 相試験において、重篤な有害事象を発現した被験者の割合及び単位時間あたりの重篤な有害事象の発現件数は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）において同様又は高かった（2.7.4.2.1.3 項）。

いずれの試験においても、プラセボ群と比較してセマグルチド群でより多くの事象が治験責任医師により治験薬との因果関係が「あり」又は「可能性あり」と判定され、これらは主に胃腸障害の有害事象によるものであった（Module 2.7.6.10.2、表 2、Module 2.7.6.11.2、表 2 及び Module 2.7.6.12.2、表 2）。

治験薬投与の中止に至った有害事象を発現した被験者の割合は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高い傾向がみられた。これらの違いは、主に胃腸障害の有害事象によるものであった（2.7.4.2.1.4.1 項）。

表 2.7.4.2-1　有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
	N	(%)	E　R	N	(%)	E　R	N	(%)	E　R
Number of subjects	100			199			101		
Patient years of exposure (PYE)	136.2			275.0			141.8		
Adverse Events	82	(82.0)	483 354.6	171	(85.9)	834 303.3	80	(79.2)	235 165.7
Serious									
Yes	7	(7.0)	10　7.3	10	(5.0)	12　4.4	7	(6.9)	7　4.9
No	82	(82.0)	473 347.3	170	(85.4)	822 298.9	78	(77.2)	228 160.8
Severity									
Severe	3	(3.0)	3　2.2	3	(1.5)	4　1.5	5	(5.0)	5　3.5
Moderate	14	(14.0)	63　46.3	25	(12.6)	42　15.3	11	(10.9)	13　9.2
Mild	79	(79.0)	417 306.1	168	(84.4)	788 286.5	76	(75.2)	217 153.0
Relationship to trial product									
Probable	25	(25.0)	61　44.8	55	(27.6)	158　57.5	10	(9.9)	16　11.3
Possible	55	(55.0)	190 139.5	84	(42.2)	206　74.9	10	(9.9)	17　12.0
Unlikely	73	(73.0)	232 170.3	152	(76.4)	469 170.5	74	(73.3)	202 142.4
Missing	0			1	(0.5)	1　0.4	0		
Outcome									
Fatal	0			0			0		
Recovered	78	(78.0)	409 300.3	164	(82.4)	729 265.1	75	(74.3)	186 131.1
Recovering	9	(9.0)	16　11.7	16	(8.0)	21　7.6	5	(5.0)	5　3.5
Recovered With Sequelae	0			0			0		
Not Recovered	35	(35.0)	58　42.6	54	(27.1)	84　30.5	26	(25.7)	44　31.0
Unknown	0			0			0		
Leading to Permanent treatment discontinuation	3	(3.0)	6　4.4	5	(2.5)	9　3.3	1	(1.0)	1　0.7

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.

表 2.7.4.2-2　有害事象－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R
Number of subjects	1306				655			
Patient years of exposure (PYE)	1706.1				829.6			
Adverse Events	1171	(89.7)	9658	566.1	566	(86.4)	3302	398.0
Serious								
Yes	128	(9.8)	164	9.6	42	(6.4)	53	6.4
No	1169	(89.5)	9494	556.5	560	(85.5)	3249	391.7
Severity								
Severe	143	(10.9)	242	14.2	44	(6.7)	68	8.2
Moderate	723	(55.4)	2612	153.1	311	(47.5)	863	104.0
Mild	1079	(82.6)	6804	398.8	507	(77.4)	2371	285.8
Relationship to trial product								
Probable	571	(43.7)	2148	125.9	147	(22.4)	330	39.8
Possible	726	(55.6)	2700	158.3	223	(34.0)	555	66.9
Unlikely	1032	(79.0)	4780	280.2	536	(81.8)	2409	290.4
Missing	24	(1.8)	30	1.8	7	(1.1)	8	1.0
Outcome								
Fatal	0				1	(0.2)	1	0.1
Recovered	1140	(87.3)	8439	494.6	545	(83.2)	2710	326.7
Recovering	59	(4.5)	91	5.3	25	(3.8)	37	4.5
Recovered With Sequelae	11	(0.8)	19	1.1	4	(0.6)	5	0.6
Not Recovered	513	(39.3)	1106	64.8	265	(40.5)	548	66.1
Unknown	2	(0.2)	3	0.2	1	(0.2)	1	0.1
Leading to Permanent treatment discontinuation	92	(7.0)	123	7.2	20	(3.1)	23	2.8

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.

表 2.7.4.2-3　有害事象－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	402				403				402			
Patient years of exposure (PYE)	529.8				533.0				528.3			
Adverse Events	329	(81.8)	1859	350.9	353	(87.6)	2197	412.2	309	(76.9)	1388	262.7
Serious												
Yes	31	(7.7)	53	10.0	40	(9.9)	71	13.3	37	(9.2)	53	10.0
No	326	(81.1)	1806	340.9	352	(87.3)	2126	398.8	307	(76.4)	1335	252.7
Severity												
Severe	22	(5.5)	43	8.1	27	(6.7)	51	9.6	28	(7.0)	39	7.4
Moderate	135	(33.6)	315	59.5	173	(42.9)	508	95.3	118	(29.4)	264	50.0
Mild	306	(76.1)	1501	283.3	328	(81.4)	1638	307.3	279	(69.4)	1085	205.4
Relationship to trial product												
Probable	133	(33.1)	344	64.9	169	(41.9)	456	85.5	62	(15.4)	100	18.9
Possible	153	(38.1)	407	76.8	182	(45.2)	534	100.2	93	(23.1)	170	32.2
Unlikely	296	(73.6)	1097	207.1	301	(74.7)	1197	224.6	289	(71.9)	1111	210.3
Missing	10	(2.5)	11	2.1	10	(2.5)	10	1.9	6	(1.5)	7	1.3
Outcome												
Fatal	0				1	(0.2)	1	0.2	1	(0.2)	1	0.2
Recovered	315	(78.4)	1503	283.7	333	(82.6)	1812	339.9	285	(70.9)	1054	199.5
Recovering	19	(4.7)	32	6.0	17	(4.2)	26	4.9	17	(4.2)	19	3.6
Recovered With Sequelae	5	(1.2)	5	0.9	5	(1.2)	5	0.9	1	(0.2)	1	0.2
Not Recovered	147	(36.6)	319	60.2	163	(40.4)	345	64.7	156	(38.8)	310	58.7
Unknown	0				4	(1.0)	8	1.5	3	(0.7)	3	0.6
Leading to Permanent treatment discontinuation	20	(5.0)	23	4.3	25	(6.2)	34	6.4	14	(3.5)	18	3.4

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.

有害事象の発現時期

日本人被験者が参加した 3 つの第 3 相試験では、すべての投与群において有害事象は試験期間を通して発現がみられた。いずれの投与群においても、最初の有害事象の発現は主に用量漸増期間である投与開始後の最初の 20 週間に報告された。この期間では、プラセボ群と比較してセマグルチド群においてより多くの事象が報告された〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.1.3、4373 試験（Module 5.3.5.1）EOT Figure 14.3.1.3、4374 試験（Module 5.3.5.1）EOT Figure 14.3.1.3〕。いずれの投与群でも、最初の有害事象を発現した被験者の割合は 20 週以降に横ばいになったが、被験者 1 例あたりの有害事象の平均発現件数は、最初の 20 週間よりは少ないものの増え続けた。

2.7.4.2.1.1.3　比較的よく見られる有害事象

比較的よく見られる有害事象（いずれかの投与群の 5%以上の被験者に報告された有害事象）は、報告された基本語レベルで日本人被験者が参加した 3 つの第 3 相試験において概ね一貫しており（図 2.7.4.2-1、図 2.7.4.2-2 及び図 2.7.4.2-3）、比較的よく見られる有害事象の大部分が非重篤、軽度又は中等度であり、転帰は「回復」であった。

3 つのいずれの第 3 相試験においても、最も高頻度で発現した有害事象は胃腸障害の有害事象であった。胃腸障害の有害事象（特に「悪心」、「下痢」、「嘔吐」及び「便秘」）はプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）でより多く報告された。これらの事象は、セマグルチド及び他の GLP-1 受容体作動薬でよく知られた有害事象である。胃腸障害の有害事象は、セマグルチドにおける注目すべき安全性領域の事象として事前に規定された。詳細は 2.7.4.2.2.2 項に示す。

いずれの試験においても、器官別大分類「神経系障害」に含まれる事象は、セマグルチド 1.7 mg 群、セマグルチド 1.0 mg 群及びプラセボ群と比較してセマグルチド 2.4 mg 群でより多く報告された〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.1.6、4373 試験（Module 5.3.5.1）EOT Figure 14.3.1.6、4374 試験（Module 5.3.5.1）EOT Figure 14.3.1.6〕。これらの違いは、主に軽度又は中等度の「頭痛」及び「浮動性めまい」によるものであった。4373 試験のセマグルチド 2.4 mg 群において発現した 1 件の「頭痛」が重篤な有害事象であった（Module 2.7.6.11.2、表 4）。また、3 件の「頭痛」（4382 試験のセマグルチド 2.4 mg 群で 1 件、4373 試験のセマグルチド 2.4 mg 群で 1 件及び 4374 試験のセマグルチド 2.4 mg 群で 1 件）は治験薬投与の中止に至った有害事象であった（Module 2.7.6.10.2、表 5、Module 2.7.6.11.2、表 5 及び Module 2.7.6.12.2、表 5）。なお、「頭痛」はオゼンピック皮下注[14]、リベルサス錠[15]及びビクトーザ皮下注[16]の添付文書にも記載されている。「浮動性めまい」については、4382 試験のセマグルチド 1.7 mg 群の 1 件及び 4373 試験のセマグルチド 2.4 mg 群の 1 件が重篤な有害事象であった（Module 2.7.6.10.2、表 4 及び Module 2.7.6.11.2、表 4）。また、4374 試験のセマグルチド 2.4 mg 群及びプラセボ群の各 1 件の「浮動性めまい」は治験薬投与の中止に至った有害事象であった（Module 2.7.6.12.2、表 5）。

いずれの試験においても器官別大分類「代謝および栄養障害」に含まれる事象については、「食欲減退」がいずれかの投与群の 5%以上の被験者に報告されており、本事象を発現した被験者の割合は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった。4374 試験のセマグルチド 1.0 mg 群の 1 件が重篤な有害事象であり、治験薬投与の中止に至った（Module 2.7.6.12.2、表 4 及び 4374 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1）。また、4373 試験のセマグルチド 2.4 mg

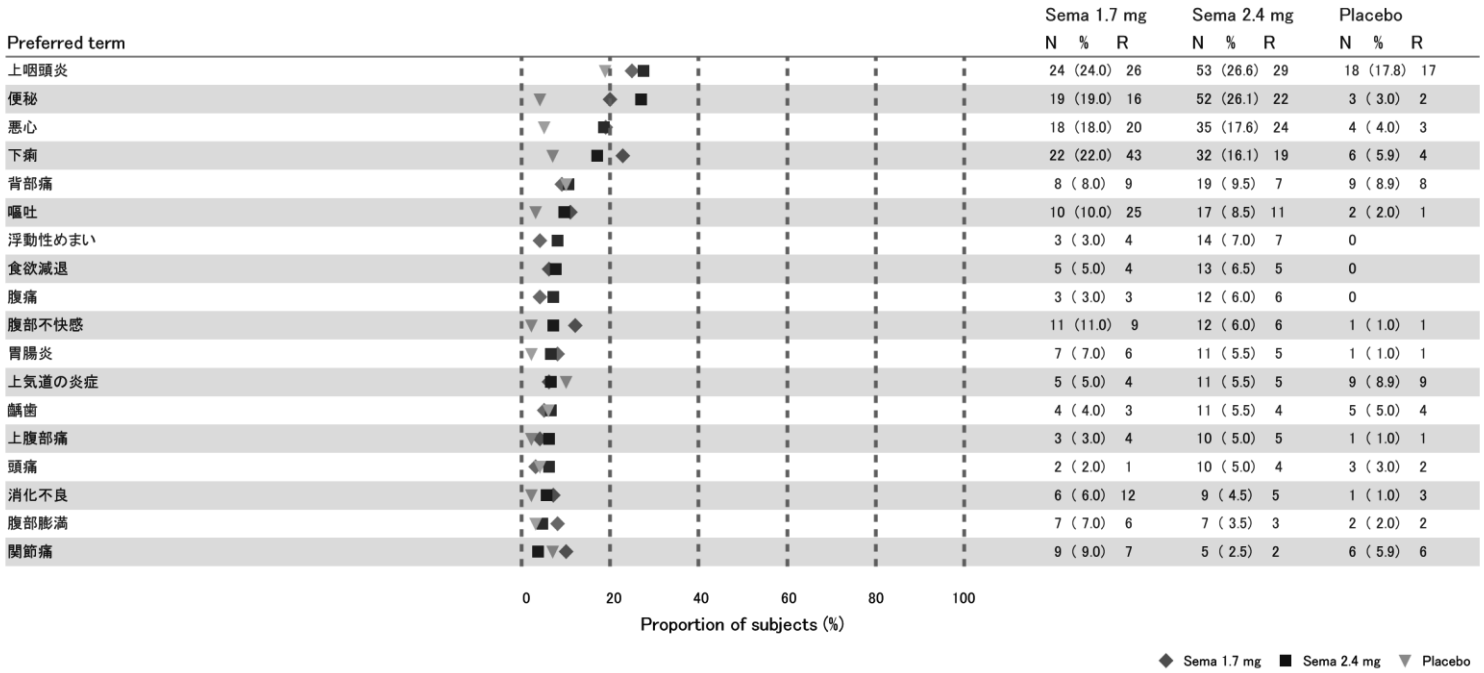
群で発現した 3 件の非重篤な「食欲減退」も治験薬投与の中止に至った。「食欲減退」は、中枢神経に対するセマグルチドの直接作用だと考えられている[17, 18, 19]。

4373 及び 4374 試験では、「疲労」がいずれかの投与群の 5%以上の被験者に報告されており、本事象を発現した被験者の割合は、セマグルチド 1.0 mg 群及びプラセボ群と比較してセマグルチド 2.4 mg 群でやや高かった。セマグルチド群の被験者で発現した「疲労」の大部分が、治験薬に関連した事象であると考えられた。4373 試験のセマグルチド 2.4 mg 群の 2 件の重度な事象を除き、すべての「疲労」が軽度又は中等度の事象だった。また、すべての事象が非重篤であった。3 件の「疲労」（4373 試験のセマグルチド 2.4 mg 群で 1 件、及び 4374 試験のセマグルチド 2.4 mg 群とセマグルチド 1.0 mg 群で各 1 件）が治験薬投与の中止に至った。

器官別大分類「感染症および寄生虫症」に含まれる事象については、3 つの試験において「上咽頭炎」と「胃腸炎」がいずれかの投与群の 5%以上の被験者に報告された。4382 試験では、「上咽頭炎」と「胃腸炎」を発現した被験者の割合はプラセボ群と比較してセマグルチド 1.7 mg 群及びセマグルチド 2.4 mg 群で高かったが、4373 及び 4374 試験では同様の傾向は認められなかった。

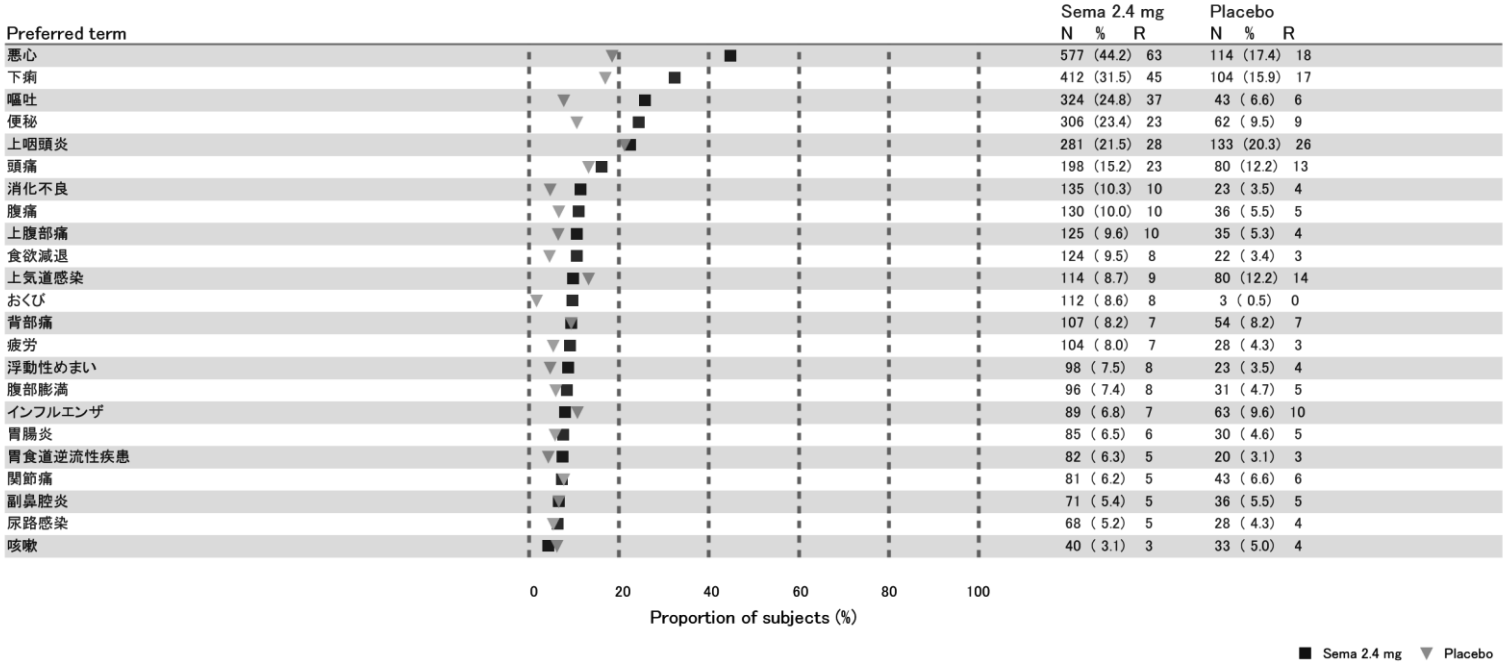
上記以外の比較的よく見られる有害事象を発現した被験者の割合は、プラセボ群と比較してセマグルチド群で同様又は低かった。

図 2.7.4.2-1　比較的よく見られる（いずれかの投与群の 5%以上の被験者）有害事象－要約プロット－on-treatment 観察期間－安全性解析対象集団（4382 試験）



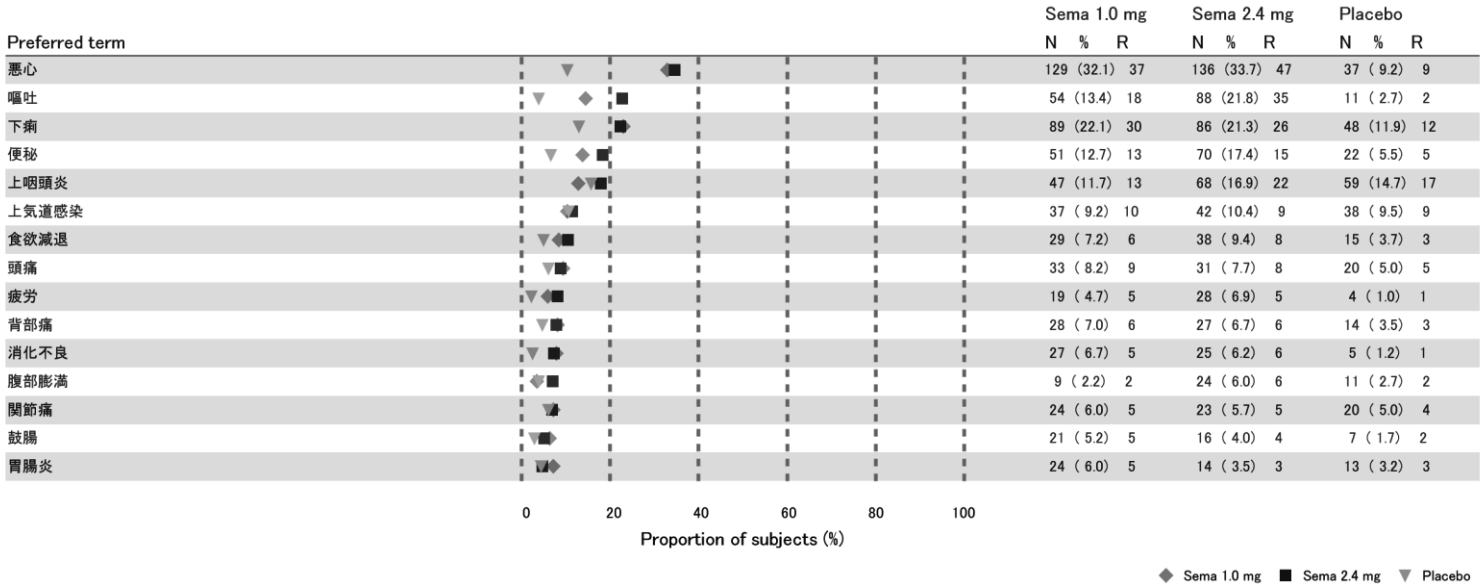
N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, R: Event rate per 100 years, NEC: Not elsewhere classified.
Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
Adverse events with preferred terms reported for at least 5% of subjects in any arm. Sorted in descending order by preferred term based on the percentage of subjects in the Sema 2.4 mg arm experiencing at least one event.
MedDRA version 23.1

図 2.7.4.2-2　比較的よく見られる（いずれかの投与群の 5%以上の被験者）有害事象－要約プロットーon-treatment 観察期間－安全性解析対象集団（4373 試験）



N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, R: Event rate per 100 years, NEC: Not elsewhere classified.
Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
Adverse events with preferred terms reported for at least 5% of subjects in any arm. Sorted in descending order by preferred term based on the percentage of subjects in the Sema 2.4 mg arm experiencing at least one event.
MedDRA version 22.1

図 2.7.4.2-3　比較的よく見られる（いずれかの投与群の 5%以上の被験者）有害事象－要約プロット－on-treatment 観察期間－安全性解析対象集団（4374 試験）



N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, R: Event rate per 100 years, NEC: Not elsewhere classified.
Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
Adverse events with preferred terms reported for at least 5% of subjects in any arm. Sorted in descending order by preferred term based on the percentage of subjects in the Sema 2.4 mg arm experiencing at least one event.
MedDRA version 22.1

すべての有害事象の器官別大分類及び基本語別の要約を Module 2.7.6.10.2、表 1、Module 2.7.6.11.2、表 1 及び Module 2.7.6.12.2、表 1 に示す。すべての有害事象の一覧は、各試験の治験総括報告書〔4382 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1、4373 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1、4374 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1〕に示す。

2.7.4.2.1.1.4 第 2 相試験及び臨床薬理試験で報告された有害事象

第 2 相用量設定試験（4153 試験）

第 2 相用量設定試験〔4153 試験（Module 5.3.5.1）〕では、計 957 例を異なる用量のセマグルチド〔0.05、0.1、0.2、0.3 又は 0.4 mg（4 週間ごとに用量漸増）〕の 1 日 1 回投与、リラグルチド（3.0 mg）又はプラセボに 6：1（実薬：プラセボ）の比率で無作為に割り付け、52 週間投与した。本試験から得られた結論を以下に示す。

全体として、52 週間の投与期間中、2 型糖尿病を有さない肥満患者においてセマグルチドは概ね安全で忍容性は良好であり、安全性と忍容性プロファイルは他の GLP-1 受容体作動薬と同様であった。有害事象の発現頻度は、セマグルチドの用量の増加に伴い高くなり（範囲：90.3～96.1%、5412～7427 件/1000 人・年）、併合したプラセボ群（78.7%、4845 件/1000 人・年）と比較してすべての用量で高かった。この用量依存性及びプラセボ群との違いは、主に胃腸障害の有害事象の違いによるものであった。

重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、セマグルチド群ごとに異なり、明らかな用量依存性は認められず（範囲：4.9～12.7%、66.4～213.3 件/1000 人・年）、発現頻度は併合したプラセボ群（8.1%、121.3 件/1000 人・年）と同様であった。重篤な有害事象の叙述は、4153 試験（Module 5.3.5.1）Section 14.3.3 に示す。

器官別大分類「胃腸障害」に含まれる有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、セマグルチド群では用量の増加に伴い増加し（範囲：62.1～82.4%、1526～3325 件/1000 人・年）、併合したプラセボ群（38.2%、811.4 件/1000 人・年）と比較してすべての用量で高かった。高頻度で認められた胃腸障害の有害事象（発現頻度の高い順）は、「悪心」、「下痢」、「便秘」及び「嘔吐」であり、いずれの事象もプラセボ群と比較してセマグルチド群でその発現頻度は高かった。

セマグルチドに関して新たな安全性所見は認められず、忍容性及び安全性プロファイルは GLP-1 受容体作動薬の薬剤クラス全般でこれまでに得られた結果と概ね同様であった。

臨床薬理試験

4455 試験（Module 5.3.4.2）：計 72 例の肥満被験者をセマグルチド 2.4 mg 又はプラセボのいずれかの盲検下での 20 週間投与（週 1 回投与を 21 回、すなわち 2.4 mg を 5 回投与）に 1：1 の比率で無作為に割り付け、セマグルチド 2.4 mg が胃内容排出、食欲及びエネルギー摂取量に及ぼす影響を比較した。死亡例は報告されなかった。重篤な有害事象が 2 件認められ、1 件はセマグルチド 2.4 mg 群の「交通事故」（基本語）であり、1 件はプラセボ群の重度な事象である「結腸膿瘍」（基本語）であった〔叙述は 4455 試験（Module 5.3.4.2）Section 14.3.3〕。報告された有害事象の大部分は、器官別大分類の「胃腸障害」に含まれる事象（主に軽度又は中等度）であり、プラセボ群（38.9%）と比較してセマグルチド群（69.4%）で事象を報告した被験者が多かった。セマグルチド 2.4 mg 群では平均脈拍数の 5

拍／分の増加が認められた。全体として、安全性及び忍容性プロファイルは、セマグルチドの過去の臨床薬理試験と同様であった。新たな安全性の所見は報告されなかった。

4590 試験（Module 5.3.1.2）：計 68 例の過体重又は肥満被験者を非盲検で 20 週間の試験デザイン（週 1 回投与を 21 回、すなわち 2.4 mg を 5 回投与）で 1：1 の比率で無作為に割り付け、単回使用ペン型注入器を用いた市販予定のセマグルチド製剤とセマグルチド 2.4 mg の第 3 相試験で使用した複数回使用可能な PDS290 ペン型注入器を用いたセマグルチド製剤の皮下投与時の生物学的同等性を検討した。死亡例の報告はなかった。本試験では 1 件の重篤な有害事象が認められ、本事象は単回使用ペン型注入器を用いたセマグルチド製剤で認められた「上室性不整脈」（基本語）の心臓障害の事象であった。治験責任医師により、治験薬との因果関係は「なし」と判定された〔叙述は 4590 試験（Module 5.3.1.2）Section 14.3.3 に示す〕。高頻度で報告された有害事象は器官別大分類「胃腸障害」、「神経系障害」、「一般・全身障害および投与部位の状態」及び「代謝および栄養障害」に含まれる事象であった。これらの事象は投与群間で同様の分布が認められた。単回使用ペン型注入器をも用いたセマグルチド製剤で認められた 1 件の非重篤で、軽度の注射部位反応〔「注射部位そう痒感」（基本語）〕は、治験責任医師により治験薬との因果関係は「あり」と判定された。当該事象は、局所症状としてそう痒感が報告された。また、本試験では用量漸増期間における投与群間の胃腸障害の有害事象についても評価した。投与週別及び用量別の胃腸障害の有害事象の発現状況に、単回使用のペン型注入器のセマグルチド製剤及び PDS290 ペン型注入器のセマグルチド製剤の間で明らかな違いは認められなかった（Module 2.7.1.3.3）。全体として、安全性及び忍容性プロファイルは、セマグルチドの過去の臨床薬理試験と同様であった。新たな安全性の所見は報告されなかった。

NN9535-4588 試験（Module 5.3.1.2）：計 68 例の過体重又は肥満の被験者を非盲検で 6 週間の試験デザイン（週 1 回投与を 7 回、最終投与はセマグルチド 1.0 mg）で 1：1 の比率で無作為に割り付け、単回使用ペン型注入器を用いたセマグルチド製剤と複数回使用の PDS290 ペン型注入器で用いたセマグルチド製剤の皮下投与時の生物学的同等性をセマグルチドの 1.0 mg と 0.25 mg の用量で検討した。重篤な有害事象、死亡例、治験の中止に至った有害事象は認められなかった。有害事象を発現した被験者の割合は両製剤間で同様であったが、有害事象の発現件数は、複数回使用の PDS290 ペン型注入器で投与するセマグルチド製剤の投与を受けた被験者と比較して単回使用ペン型注入器で投与するセマグルチド製剤の投与を受けた被験者で多かった。有害事象（基本語）の大部分が、「悪心」、「頭痛」、「食欲減退」であった。単回使用ペン型注入器で投与するセマグルチド製剤で計 3 件の非重篤で、軽度又は中等度の「注射部位反応」（基本語）が報告され、いずれの事象も回復した。1 件の過敏症反応が認められたが、転帰は「回復」であった。全体として、安全性及び忍容性プロファイルは、2 型糖尿病に対するセマグルチド皮下投与で確立されたプロファイルと同様であった。新たな安全性の所見は報告されなかった。

2.7.4.2.1.2　死亡

死亡は、治験責任医師が報告した転帰「死亡」の有害事象及びイベント判定委員会による死亡の評価に基づいて評価した（詳細は 2.7.4.1.1.8.2 項に示す）。死亡理由にかかわらずすべての死亡は、原因により心血管死又は非心血管死に分類し、さらに心突然死や悪性腫瘍などの死因を確定するためにイ

ベント判定委員会によって判定された。イベント判定委員会が死因を特定できなかった死亡は原因不明の死亡と分類することとした。

死亡は、in-trial 観察期間に基づき評価した。

4382 試験では死亡は報告されなかった。

4373 試験では、2 例の死亡例において計 4 件の転帰「死亡」の有害事象が報告された。セマグルチド 2.4 mg 群の 1 例は 1 件の転帰「死亡」の有害事象〔「死亡」（基本語）〕を on-treatment 観察期間後の in-trial 観察期間内に発現した。プラセボ群の 1 例は 3 件の転帰「死亡」の有害事象を発現した〔「神経膠芽細胞腫」（基本語）：on-treatment 観察期間に発現、「敗血症」（基本語）及び「誤嚥性肺炎」（基本語）：on-treatment 観察期間後の in-trial 観察期間内に発現〕（表 2.7.4.2-4）。すべての転帰「死亡」の有害事象が治験責任医師により治験薬との因果関係は「なし」と判定された〔4373 試験（Module 5.3.5.1）EOT Listing 14.3.2.2〕。イベント判定委員会により、セマグルチド 2.4 mg 群の死亡は心血管死、プラセボ群の死亡は悪性腫瘍による死亡（報告された「神経膠芽細胞腫」に関連する）と判定された。

4374 試験では、3 例の死亡例において計 5 例の転帰「死亡」の有害事象が報告された。セマグルチド 2.4 mg 群の 1 例は、1 件の転帰「死亡」の有害事象〔「心筋梗塞」（基本語）〕を on-treatment 観察期間に発現した。セマグルチド 1.0 mg 群の 1 例は、1 件の転帰「死亡」の有害事象〔「心肺停止」（基本語）〕を on-treatment 観察期間後の in-trial 観察期間内に発現した。プラセボ群の 1 例は、3 件の転帰「死亡」の有害事象を発現した〔「肝細胞癌」（基本語）：on-treatment 観察期間に発現、「肺塞栓症」（基本語）及び「呼吸不全」（基本語）：on-treatment 観察期間後の in-trial 観察期間内に発現〕（表 2.7.4.2-4）。すべての転帰「死亡」の有害事象が治験責任医師により治験薬との因果関係は「なし」と判定された〔4374 試験（Module 5.3.5.1）EOT Listing 14.3.2.2〕。イベント判定委員会により、セマグルチド 2.4 mg 群の死亡は心血管死、セマグルチド 1.0 mg 群の死亡は原因不明の死亡、プラセボ群の死亡は悪性腫瘍による死亡と判定された。

いずれの試験でも、日本人被験者において転帰「死亡」の有害事象は報告されなかった。

表 2.7.4.2-4　　死亡及び転帰「死亡」の有害事象（4373 及び 4374 試験）

Subject ID/ Age/Sex/BMI	Investigator reported information: Preferred term/ Onset (period)	EAC reported information: Outcome/Classification/ Day of death (period)	Other relevant details (investigator reported)
Trial 4373			
Semaglutide 2.4 mg			
305002/ 4[redacted]/M/83.0	死亡/311 (IT)	Cardiovascular death/Sudden cardiac death/ 311 (IT)	Medical history of hypertension, obstructive sleep apnoea syndrome and previous smoker. Day 198: Trial product permanently discontinued (due to the AE: Astenia). Day 282, 300 and 303: Loss of consciousness (SAEs). Day 311: Found dead in his bed in the morning. No autopsy performed.
Placebo			
450026/ 6[redacted]/F/35.7	神経膠芽細胞腫/43 (IT/OT) 誤嚥性肺炎/ 141 (IT) 敗血症/141 (IT)	Non-cardiovascular death/Malignancy/ 145 (IT)	No relevant medical history. Day 43: Brain tumour diagnosed by MRI. Biopsy showed grade 4 glioblastoma multiforme. Day 92: Trial product permanently discontinued (due to the AE: Glioblastoma). Day 141: Admitted to hospital with pneumonia and severe sepsis. Day 145: Fatal outcome due to severe sepsis, aspiration pneumonia and glioblastoma multiforme. No autopsy performed.
Trial 4374			
Semaglutide 1.0 mg			
218015 6[redacted]/F/28.4	心肺停止/393 (IT)	Undetermined cause of death/NA/ 395 (IT)	The subject was already known with coronary artery disease (CAD), Triple vessel disease (TVD), Dilated cardiomyopathy (DCMP) with reduced Left ventricular ejection fraction (LVEF) 20%
Semaglutide 2.4 mg			
450008 6[redacted]/M/46.2	心筋梗塞/154 (IT/OT)	Cardiovascular death/Sudden cardiac death/ 154 (OT)	Long-standing history of T2D, hypertension, obesity and previous smoking. In addition, the subject had 'T-wave inversion' detected on ECG approximately 4 years prior to the onset of the event.
Placebo			
508004 6[redacted]/M/29.4	肝細胞癌/105 (IT/OT) 肺塞栓症/156 (IT) 呼吸不全/156 (IT)	Non-cardiovascular death/Malignancy/ 161 (IT)	The subject had risk factors including previous alcohol abuse, hepatic cirrhosis, hepatopathy, obesity and T2D.

Age: baseline age in years, BMI: baseline body mass index (kg/m^2), EAC: Event Adjudication Committee; F: Female, IT: in-trial period, M: Male, NA: not applicable; OT: on-treatment period, PT: preferred term.

報告された死亡の叙述は、4373 試験（Module 5.3.5.1）Section 14.3.3 及び 4374 試験（Module 5.3.5.1）Section 14.3.3 に示す。

2.7.4.2.1.3　その他の重篤な有害事象

日本人被験者が参加した 3 つの第 3 相試験において、重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で同様又は高かった（表 2.7.4.2-5、表 2.7.4.2-6 及び表 2.7.4.2-7）。4382 及び 4374 試験では、セマグルチドの用量に依存した重篤な有害事象の発現頻度の増加はみられなかった（表 2.7.4.2-5 及び表 2.7.4.2-7）。

これらの第 3 相試験において、器官別大分類別の重篤な有害事象に関して一貫した発現傾向は認められず、特定の器官別大分類で多く発現することはなかった。いずれの試験においても、報告された重篤な有害事象（基本語）は各投与群で 5 例以下であり、事象（基本語）の大部分は 1 件のみの報告であった（Module 2.7.6.10.2、表 4、Module 2.7.6.11.2、表 4 及び Module 2.7.6.12.2、表 4）。

3 つのいずれの第 3 相試験でも、重篤な有害事象の大部分が中等度又は重度であり、転帰は「回復」又は「軽快」であった。セマグルチド群（1.0、1.7 及び 2.4 mg）で報告された重篤な有害事象の大部分は、治験責任医師により治験薬との因果関係は「なし」と判定された（表 2.7.4.2-5、表 2.7.4.2-6 及び表 2.7.4.2-7）。

4382 及び 4374 試験では、いずれの投与群においても治験薬投与の中止に至った重篤な有害事象は少なく（各投与群で 0～5 件）、これらの事象（基本語別）は 1 例の被験者に発現し、特定の事象が多く報告されることもなかった。4373 試験では、治験薬投与の中止に至った重篤な有害事象を発現した被験者は、セマグルチド 2.4 mg 群で 18 例（1.4%）、プラセボ群で 5 例（0.8%）であった。この違いは、主に胃腸障害の有害事象によるものであった。

すべての重篤な有害事象の叙述及び一覧は各試験の治験総括報告書〔4382 試験（Module 5.3.5.1）Section 14.3.3、EOT Listing 14.3.2、4373 試験（Module 5.3.5.1）Section 14.3.3、EOT Listing 14.3.2、4374 試験（Module 5.3.5.1）Section 14.3.3、EOT Listing 14.3.2〕に示す。

表 2.7.4.2-5　　重篤な有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	100			199			101		
Patient years of exposure (PYE)	136.2			275.0			141.8		
Serious Adverse Events	7 (7.0)	10	7.3	10 (5.0)	12	4.4	7 (6.9)	7	4.9
Severity									
Severe	3 (3.0)	3	2.2	3 (1.5)	4	1.5	4 (4.0)	4	2.8
Moderate	4 (4.0)	7	5.1	6 (3.0)	6	2.2	3 (3.0)	3	2.1
Mild	0			2 (1.0)	2	0.7	0		
Relationship to trial product									
Probable	0			1 (0.5)	1	0.4	1 (1.0)	1	0.7
Possible	0			4 (2.0)	4	1.5	1 (1.0)	1	0.7
Unlikely	7 (7.0)	10	7.3	6 (3.0)	7	2.5	5 (5.0)	5	3.5
Missing	0			0			0		
Outcome									
Fatal	0			0			0		
Recovered	6 (6.0)	9	6.6	8 (4.0)	10	3.6	6 (5.9)	6	4.2
Recovering	1 (1.0)	1	0.7	0			1 (1.0)	1	0.7
Recovered With Sequelae	0			0			0		
Not Recovered	0			2 (1.0)	2	0.7	0		
Unknown	0			0			0		
Leading to Permanent treatment discontinuation	1 (1.0)	1	0.7	2 (1.0)	3	1.1	0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.

表 2.7.4.2-6　　重篤な有害事象－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg N	(%)	E	R	Placebo N	(%)	E	R
Number of subjects	1306				655			
Patient years of exposure (PYE)	1706.1				829.6			
Serious Adverse Events	128	(9.8)	164	9.6	42	(6.4)	53	6.4
Severity								
Severe	61	(4.7)	75	4.4	22	(3.4)	27	3.3
Moderate	62	(4.7)	70	4.1	16	(2.4)	18	2.2
Mild	16	(1.2)	19	1.1	8	(1.2)	8	1.0
Relationship to trial product								
Probable	10	(0.8)	11	0.6	3	(0.5)	3	0.4
Possible	17	(1.3)	23	1.3	1	(0.2)	1	0.1
Unlikely	103	(7.9)	130	7.6	39	(6.0)	49	5.9
Missing	0				0			
Outcome								
Fatal	0				1	(0.2)	1	0.1
Recovered	115	(8.8)	150	8.8	33	(5.0)	43	5.2
Recovering	3	(0.2)	3	0.2	2	(0.3)	2	0.2
Recovered With Sequelae	0				1	(0.2)	1	0.1
Not Recovered	11	(0.8)	11	0.6	5	(0.8)	5	0.6
Unknown	0				1	(0.2)	1	0.1
Leading to Permanent treatment discontinuation	18	(1.4)	23	1.3	5	(0.8)	5	0.6

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.

表 2.7.4.2-7　重篤な有害事象－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg N (%)	E	R	Sema 2.4 mg N (%)	E	R	Placebo N (%)	E	R
Number of subjects	402			403			402		
Patient years of exposure (PYE)	529.8			533.0			528.3		
Serious Adverse Events	31 (7.7)	53	10.0	40 (9.9)	71	13.3	37 (9.2)	53	10.0
Severity									
Severe	12 (3.0)	25	4.7	17 (4.2)	36	6.8	19 (4.7)	25	4.7
Moderate	16 (4.0)	20	3.8	21 (5.2)	30	5.6	18 (4.5)	22	4.2
Mild	6 (1.5)	8	1.5	4 (1.0)	5	0.9	6 (1.5)	6	1.1
Relationship to trial product									
Probable	3 (0.7)	9	1.7	4 (1.0)	4	0.8	0		
Possible	1 (0.2)	1	0.2	6 (1.5)	8	1.5	3 (0.7)	5	0.9
Unlikely	29 (7.2)	42	7.9	32 (7.9)	59	11.1	35 (8.7)	48	9.1
Missing	1 (0.2)	1	0.2	0			0		
Outcome									
Fatal	0			1 (0.2)	1	0.2	1 (0.2)	1	0.2
Recovered	29 (7.2)	46	8.7	33 (8.2)	60	11.3	32 (8.0)	47	8.9
Recovering	0			2 (0.5)	3	0.6	0		
Recovered With Sequelae	3 (0.7)	3	0.6	1 (0.2)	1	0.2	0		
Not Recovered	3 (0.7)	4	0.8	6 (1.5)	6	1.1	5 (1.2)	5	0.9
Unknown	0			0			0		
Leading to Permanent treatment discontinuation	3 (0.7)	3	0.6	3 (0.7)	3	0.6	5 (1.2)	5	0.9

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.

2.7.4.2.1.4　その他の重要な有害事象－治療の介入に至った有害事象

本臨床概要では、その他の重要な有害事象として治験薬投与の中止に至った有害事象について記載する。

2.7.4.2.1.4.1　治験薬投与の中止に至った有害事象

日本人被験者が参加した 3 つの第 3 相試験（4382、4373 及び 4374 試験）において、治験薬投与の中止に至った有害事象を発現した被験者の割合は、プラセボ群と比較してセマグルチド群（1.0、1.7、2.4 mg）で高く、この違いは主に胃腸障害の有害事象によるものであった。高頻度で報告された事象（基本語）は、4382 試験では「悪心」、4373 試験では「悪心」、「嘔吐」、「下痢」、「便秘」及び「上腹部痛」、ならびに 4374 試験では「悪心」、「嘔吐」及び「下痢」であった（Module 2.7.6.10.2、表 5、Module 2.7.6.11.2、表 5 及び Module 2.7.6.12.2、表 5）。

治験薬投与の中止に至った有害事象の大部分は非重篤で、軽度又は中等度の事象であり、転帰は「回復」又は「軽快」であった。プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）でより多くの事象が治験責任医師より治験薬との因果関係が「あり」又は「可能性あり」と判定された〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.20、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.20、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.20〕。治験薬との因果関係が「あり」又は「可能性あり」と判定された有害事象の大部分が胃腸障害の有害事象であったこと（2.7.4.2.2.2 項）及び最も高頻度で報告された治験薬投与の中止に至った有害事象の種類が器官別大分類「胃腸障害」に含まれるものであったことから〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.22、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.22、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.22〕、この違いは胃腸障害の有害事象によるものであると考えられた。

試験を通して、治験薬投与の中止に至った有害事象の発現状況、ならびに事象の重篤性及び重症度の分布について、セマグルチドの用量の増加に伴う特定の傾向はみられなかった。4374 試験では、治験薬投与の中止に至った有害事象の報告において用量反応性がみられた。4382 試験では、治験薬投与の中止に至った有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、セマグルチド 2.4 mg 群とセマグルチド 1.7 mg 群で同様であった。

3 つのいずれの第 3 相試験においても、すべての投与群において治験薬投与の中止に至った有害事象は試験期間を通して発現がみられた。4373 及び 4374 試験では、セマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群において用量漸増期間（それぞれ最初の 20 週及び 12 週）に治験薬投与の中止に至った有害事象が大きく増加した。各セマグルチド群の最終用量漸増後の期間は、治験薬投与の中止に至った有害事象を発現した被験者の割合は安定し、プラセボ群の被験者で見られた曲線の傾きと同様となった。これは、治験薬の投与中止の主な理由であったセマグルチドによる胃腸障害の有害事象が 20 週間の用量漸増期間以降に減少したことによるものと考えられる〔4373 試験（Module 5.3.5.1、EOT Figure 14.3.1.21、4374 試験（Module 5.3.5.1）EOT Figure 14.3.1.21）。4382 試験では、治験薬投与の中止に至った有害事象の発現件数は少なかったため、特定の傾向はみられなかった〔4382 試験（Module 5.3.5.1、EOT Figure 14.3.1.21）。

治験薬の一時的な投与の中断に至った有害事象及び投与量の減量に至った有害事象の要約は各治験総括報告書〔4382 試験（Module 5.3.5.1）Section 12.4.3、Section 12.4.4、4373 試験（Module 5.3.5.1）

Section 12.4.3、Section 12.4.4、4374 試験（Module 5.3.5.1）Section 12.4.3、Section 12.4.4〕に示す。いずれの試験においても、治験薬の一時的な投与の中断に至った有害事象及び投与量の減量に至った有害事象の多くは胃腸障害の有害事象であった。

2.7.4.2.1.5　用量反応関係の評価

2.7.4.2.1.5.1　背景及び評価方法

GLP-1 受容体作動薬は、一部の胃腸障害の有害事象（「悪心」、「嘔吐」及び「下痢」等）及びセマグルチドの作用機序に直接的又は間接的に関連する他の有害事象（「食欲減退」等）が用量依存的に増加することが知られている[20]。これは、体重管理のためのリラグルチド 3.0 mg（Saxenda）[21]や 2 型糖尿病に対するセマグルチド皮下投与[22]の曝露量－反応解析により裏付けられており、これらの解析において胃腸障害の有害事象における明らかな用量反応性が認められた（すなわち、曝露量の増加に伴い悪心と嘔吐の発現が増加した）。

用量反応は、日本人被験者が参加し、かつセマグルチドの 2 つ以上の用量を検討した第 3 相試験〔4382 試験（1.7 及び 2.4 mg）及び 4374 試験（1.0 及び 2.4 mg）〕に基づき評価した。

4382 試験、4374 試験又は国際共同第 3 相試験の併合データにおいてセマグルチド 2.4 mg に好ましくない投与群間の違いが認められた注目すべき安全性領域について、用量反応の評価を行った。

- 胃腸障害（2.7.4.2.2.2 項）
- 胆嚢関連障害（2.7.4.2.2.3 項）
- 低血糖（2.7.4.2.2.9 項）
- 網膜障害（2.7.4.2.2.10 項）
- リパーゼ及びアミラーゼ（2.7.4.2.2.4.4.1 項）
- 脈拍数（2.7.4.2.2.5.4 項）

4153 試験（第 2 相用量設定試験）では、被験者は 52 週間まで各用量のセマグルチド（0.05、0.1、0.2、0.3 及び 0.4 mg）の 1 日 1 回皮下投与を受けた。全体的な有害事象及び治験薬投与の中止に至った有害事象の報告では用量反応性が認められ、これらは胃腸障害の有害事象（主に「悪心」、「下痢」、「嘔吐」、「便秘」及び「おくび」）の報告における用量反応性によるものと考えられた。

4382、4373 及び 4374 試験で報告されたすべての胃腸障害の有害事象、ならびに「悪心」及び「嘔吐」の有害事象について、曝露量－反応関係を検討した。予想されたように、胃腸障害の有害事象、特に「悪心」と「嘔吐」を発現した被験者の割合は、セマグルチドの曝露量に伴ってわずかに増えた。なお、曝露量の増加に対するこれらの事象を発現した被験者の割合はほぼプラトーに達し、検討したセマグルチド 2.4 mg の曝露量範囲ではほぼ一定であった。これらは、すべての試験で用いられた用量漸増法によるものと考えられた。薬物動態モデルと曝露量－反応関係評価の包括的な説明は、Module 2.7.2.3.3.2 及び J-Modelling report‐phase 3a（Module 5.3.3.5）Section 5.3.4、Section 5.3.6 に示す。

2.7.4.2.1.5.2　第 3 相試験（4374 及び 4382 試験）における用量反応関係

4382 試験では、すべての有害事象、重篤な有害事象、重度の有害事象又は治験薬投与の中止に至った有害事象について明らかな用量反応関係は認められなかった。有害事象を発現した被験者の割合

は、セマグルチド 1.7 mg 群、セマグルチド 2.4 mg 群及びプラセボ群で同様であった。単位時間あたりの発現件数は、セマグルチド 1.7 mg 群とセマグルチド 2.4 mg 群で同様であり、プラセボ群よりも多かった（表 2.7.4.2-1）。重篤な有害事象を発現した被験者の割合は、セマグルチド 1.7 mg 群、セマグルチド 2.4 mg 群及びプラセボ群で同様であった。単位時間あたりの重篤な有害事象の発現件数は、セマグルチド 2.4 mg 群とプラセボ群が同様であり、セマグルチド 1.7 mg 群ではわずかに多かった。すべての投与群において、重度の有害事象の発現件数は少なく、重度の有害事象を発現した被験者の割合及び単位時間あたりの発現件数に投与群間で明らかな違いはみられなかった。いずれの投与群でも、有害事象により治験薬の投与を中止した被験者は非常に少なかった。治験薬投与の中止に至った有害事象を発現した被験者の割合は、セマグルチド 1.7 mg 群とセマグルチド 2.4 mg 群で同様であり、プラセボ群と比較してわずかに高かった。これらの違いは、主に胃腸障害の有害事象によるものであった。「悪心」（計 3 例で報告された）が、2 例以上の被験者で報告された唯一の基本語であった。胃腸障害の有害事象に明らかな用量反応性は認められなかった。胃腸障害の有害事象及び治験薬投与の中止に至った胃腸障害の有害事象を発現した被験者の割合ならびに単位時間あたりの発現件数は、セマグルチド 1.7 mg 群と比較してセマグルチド 2.4 mg 群で同様又は低かった（表 2.7.4.2-8）。

4374 試験では、有害事象を発現した被験者の割合と単位時間あたりの発現件数は、セマグルチド 1.0 mg 群と比較してセマグルチド 2.4 mg 群で高く、プラセボ群と比較してセマグルチド 1.0 mg 群で高かった（表 2.7.4.2-3）。重篤な有害事象及び重度の有害事象について、明らかな用量反応性は認められなかった。重篤な有害事象を発現した被験者の割合は、セマグルチド 2.4 mg 群とプラセボ群で同程度であり、セマグルチド 1.0 mg 群が最も低かったが、重篤な有害事象の単位時間あたりの発現件数は、セマグルチド 1.0 mg 群及びプラセボ群と比較してセマグルチド 2.4 mg 群でわずかに多かった。これは、セマグルチド 2.4 mg 群の 1 例で交通事故に関連して 13 件の重篤な有害事象が報告されたためである。重度の有害事象を発現した被験者の割合はすべての投与群で同様であったが、単位時間あたりの重度の有害事象の発現件数はプラセボ群で最も少なかった。治験薬投与の中止に至った有害事象を発現した被験者の割合は、セマグルチド 1.0 mg 群と比較してセマグルチド 2.4 mg 群で高く、プラセボ群と比較してセマグルチド 1.0 mg 群で高かった。治験薬投与の中止に至った有害事象の大部分は、胃腸障害の有害事象であり、「悪心」及び「嘔吐」が両セマグルチド群において高頻度で認められた治験薬投与の中止に至った胃腸障害の有害事象であった。胃腸障害の有害事象及び治験薬投与の中止に至った胃腸障害の有害事象について、用量増加に伴う増加が認められた（表 2.7.4.2-10）。

胃腸障害以外の注目すべき安全性領域

4382 及び 4374 試験では、胆嚢関連障害の有害事象の発現件数は少なく（各投与群で 4 件以下）、用量反応性はみられなかった（表 2.7.4.2-11 及び表 2.7.4.2-13）。

4382 試験では臨床的に問題となる低血糖（レベル 2）は報告されなかった。4374 試験では臨床的に問題となる低血糖（レベル 2）について明らかな用量反応性は認められなかった。1 件以上の低血糖を発現した被験者の割合は、セマグルチド 2.4 mg 群とセマグルチド 1.0 mg 群で同様であったが、既に低血糖を 1 回発現した被験者では、さらに低血糖を発現するリスクがセマグルチド 1.0 mg 群と比較してセマグルチド 2.4 mg 群で高かった（2.7.4.2.2.9.3 項）。

4382 と 4374 試験において、網膜障害の有害事象（表 2.7.4.2-59 及び表 2.7.4.2-60）、ベースライン後のアミラーゼ及びリパーゼの増加〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.10、14.3.5.20、4374

試験（Module 5.3.5.1）EOT Figure 14.3.5.10、14.3.5.21〕、又は脈拍数の増加〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.6.3、4374 試験（Module 5.3.5.1）EOT Figure 14.3.6.3〕について明らかな用量反応性は認められなかった。

2.7.4.2.1.6　器官別又は症候別有害事象の解析

器官別大分類及び基本語別の有害事象（いずれかの投与群の 5%以上の被験者に報告された有害事象）の有害事象については、2.7.4.2.1.1.3 項に示す。

すべての有害事象の器官別大分類及び基本語別の要約は Module 2.7.6.10.2、表 1、Module 2.7.6.11.2、表 1 及び Module 2.7.6.12.2、表 1 に、すべての有害事象の一覧は、各試験の治験総括報告書〔4382 試験（Module 5.3.5.1）EOT Listing 14.3.2、4373 試験（Module 5.3.5.1）EOT Listing 14.3.2、4374 試験（Module 5.3.5.1）EOT Listing 14.3.2〕に示す。

GLP-1 受容体作動薬でよく知られている臨床及び非臨床の安全性情報に基づき、セマグルチドにおいて影響があることがすでに知られているか又は疑われる医学的領域を、注目すべき安全性領域と規定し、以下の 2.7.4.2.2 項に示す。これらのデータの収集方法を 2.7.4.1.1.8 項に示した。

2.7.4.2.2　注目すべき安全性領域

2.7.4.2.2.1　注目すべき安全性領域における結果の概要

GLP-1 受容体作動薬における治療経験、ならびに規制当局からの助言及び要求事項に基づき、肥満症のためのセマグルチド 2.4 mg の安全性評価において注目すべき安全性領域として、以下を事前に規定した：

- 胃腸障害
- 胆嚢関連障害
- 急性膵炎
- 心血管障害
- 新生物
- 肝障害
- 急性腎不全
- 低血糖
- 網膜障害
- 免疫原性
- 精神障害
- 稀な事象

個々の注目すべき安全性領域は、当該領域に特化した MedDRA 検索、イベント判定結果、特定のイベントフォームを用いて収集された追加データ、特定の臨床検査項目及び他の検査項目を含む、当該領域に関連する評価方法とデータに基づき評価する。各領域で用いられた評価方法の概要を 2.7.4.1.1.5 項に示し、個々の領域における評価方法の詳細をそれぞれの安全性領域の「背景及び評価方法」の項に示す。

注目すべき安全性領域のうち、急性膵炎及び心血管障害はいずれも MedDRA 検索及びイベント判定の両方により評価した。これらの領域では、治験責任医師から報告された情報に基づく事象とイベント判定委員会の判定結果に基づく事象を要約することにより、2 つ評価方法の結果は相互に補完された（各評価方法の違いについては、2.7.4.1.1.9.3 項に示す）。急性膵炎については、MedDRA 検索で特定された膵炎の事象はすべて、イベント判定委員会に送付された。イベント判定では、MedDRA 検索で特定されたよりも多くの事象が特定された。心血管障害の事象については、イベント判定で特定された事象は MedDRA 検索で特定された事象よりも少なかった。

2.7.4.2.2.2　胃腸障害

2.7.4.2.2.2.1　背景及び評価方法

胃腸障害の有害事象は、GLP-1 受容体作動薬で最も高頻度で認められている有害反応である[14, 15, 16, 23, 24, 25, 26]。しかしながら、胃腸障害は一般集団においても最も一般的な障害のひとつであり、これは臨床試験においてプラセボ群で胃腸障害の有害事象を報告した被験者の割合が高いことからも明らかである。また、肥満は、上腹部痛、胃食道逆流性疾患、下痢、嘔吐、痔核などの特定の胃腸障害の頻度が高いと考えられている[27, 28]。

胃腸障害の有害事象は、MedDRA 検索で特定された事象（器官別大分類「胃腸障害」に含まれる有害事象）に基づき、on-treatment 観察期間のデータを用いて評価した。

2.7.4.2.2.2.2　胃腸障害の有害事象

日本人被験者が参加した 3 つのいずれの第 3 相試験でも、胃腸障害はすべての用量（1.0、1.7 及び 2.4 mg）のセマグルチド群において最も高頻度で認められた有害事象であった。

胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してすべてのセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった（表 2.7.4.2-8、表 2.7.4.2-9 及び表 2.7.4.2-10）。セマグルチド群において高頻度で報告された胃腸障害の有害事象は、「悪心」、「下痢」、「嘔吐」及び「便秘」であった。すべての胃腸障害の有害事象の要約は、Module 2.7.6.10.2、表 1、Module 2.7.6.11.2、表 1 及び Module 2.7.6.12.2、表 1 に示す。

いずれの投与群及び試験でも、胃腸障害の有害事象の大部分は、非重篤で、軽度又は中等度であり、転帰は「回復」であった。死亡に至った胃腸障害の有害事象はなかった。プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）において、治験責任医師により治験薬との因果関係が「あり」又は「可能性あり」と判定された胃腸障害を発現した被験者の割合が高かった（表 2.7.4.2-8、表 2.7.4.2-9 及び表 2.7.4.2-10）。

4382 及び 4374 試験では、いずれの投与群でも重篤な胃腸障害の有害事象の発現件数は少なく（各投与群で 0～7 件）、重篤な胃腸障害の有害事象の発現状況に投与群間で明らかな違いはみられなかった（表 2.7.4.2-8 及び表 2.7.4.2-10）。4373 試験では、セマグルチド 2.4 mg 群において計 18 例（1.4%）の被験者が重篤な胃腸障害の有害事象を発現したが、プラセボ群において重篤な胃腸障害の有害事象を発現した被験者はいなかった（表 2.7.4.2-9）。転帰が「未回復」であった 4373 試験のセマグルチド 2.4 mg 群で発現した 1 件の「裂孔ヘルニア」及び 4374 試験のセマグルチド 1.0 mg 群で発現した 1 件の「胃潰瘍」を除き、3 つのいずれの第 3 相試験でも、すべての重篤な胃腸障害の有害事象の転帰は「回

復」であった〔4382 試験（Module 5.3.5.1）Section 12.5.3、4373 試験（Module 5.3.5.1）Section 12.5.3、4374 試験（Module 5.3.5.1）Section 12.5.3〕。

3 つのいずれの第 3 相試験でも、治験薬投与の中止に至った胃腸障害の有害事象を発現した被験者の割合は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった（表 2.7.4.2-8、表 2.7.4.2-9、及び表 2.7.4.2-10）。治験薬投与の中止に至った有害事象の詳細については 2.7.4.2.1.4.1 項に示す。

試験を通して、胃腸障害の有害事象及び治験薬投与の中止に至った胃腸障害の有害事象の発現状況について、セマグルチドの用量の増量に伴う特定の傾向はみられなかった。4374 試験では、胃腸障害の有害事象及び治験薬投与の中止に至った有害事象の報告において用量反応性がみられた（表 2.7.4.2-10）が、4382 試験では胃腸障害の有害事象を発現した被験者の割合及び治験薬投与の中止に至った胃腸障害の有害事象を発現した被験者の割合ならびにこれらの事象の単位時間あたりの発現件数は、セマグルチド 1.7 mg 群と比較してセマグルチド 2.4 mg 群で同様又は低かった（表 2.7.4.2-8）。

表 2.7.4.2-8　　胃腸障害の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	100			199			101		
Patient years of exposure (PYE)	136.2			275.0			141.8		
Adverse Events	64 (64.0)	256	187.9	118 (59.3)	343	124.7	30 (29.7)	43	30.3
Serious									
yes	0			2 (1.0)	2	0.7	1 (1.0)	1	0.7
No	64 (64.0)	256	187.9	118 (59.3)	341	124.0	29 (28.7)	42	29.6
Severity									
Severe	0			1 (0.5)	1	0.4	1 (1.0)	1	0.7
Moderate	5 (5.0)	37	27.2	9 (4.5)	16	5.8	1 (1.0)	1	0.7
Mild	63 (63.0)	219	160.8	115 (57.8)	326	118.5	28 (27.7)	41	28.9
Relationship to trial product									
Probable	22 (22.0)	56	41.1	48 (24.1)	119	43.3	9 (8.9)	14	9.9
Possible	45 (45.0)	166	121.9	67 (33.7)	143	52.0	5 (5.0)	7	4.9
Unlikely	22 (22.0)	34	25.0	54 (27.1)	81	29.5	18 (17.8)	22	15.5
Missing	0			0			0		
Outcome									
Fatal	0			0			0		
Recovered	60 (60.0)	238	174.7	114 (57.3)	311	113.1	27 (26.7)	36	25.4
Recovering	2 (2.0)	3	2.2	8 (4.0)	9	3.3	1 (1.0)	1	0.7
Recovered With Sequelae	0			0			0		
Not Recovered	12 (12.0)	15	11.0	17 (8.5)	23	8.4	5 (5.0)	6	4.2
Unknown	0			0			0		
Leading to Permanent treatment discontinuation	2 (2.0)	5	3.7	4 (2.0)	5	1.8	0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 23.1

表 2.7.4.2-9　胃腸障害の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R
Number of subjects	1306				655			
Patient years of exposure (PYE)	1706.1				829.6			
Adverse Events	969	(74.2)	4309	252.6	314	(47.9)	739	89.1
Serious								
yes	18	(1.4)	25	1.5	0			
No	967	(74.0)	4284	251.1	314	(47.9)	739	89.1
Severity								
Severe	58	(4.4)	88	5.2	4	(0.6)	8	1.0
Moderate	436	(33.4)	1073	62.9	93	(14.2)	146	17.6
Mild	871	(66.7)	3148	184.5	272	(41.5)	585	70.5
Relationship to trial product								
Probable	520	(39.8)	1751	102.6	105	(16.0)	196	23.6
Possible	635	(48.6)	1939	113.7	164	(25.0)	347	41.8
Unlikely	362	(27.7)	618	36.2	132	(20.2)	195	23.5
Missing	1	(0.1)	1	0.1	1	(0.2)	1	0.1
Outcome								
Fatal	0				0			
Recovered	931	(71.3)	4056	237.7	292	(44.6)	662	79.8
Recovering	20	(1.5)	25	1.5	6	(0.9)	6	0.7
Recovered With Sequelae	6	(0.5)	7	0.4	0			
Not Recovered	169	(12.9)	219	12.8	60	(9.2)	71	8.6
Unknown	2	(0.2)	2	0.1	0			
Leading to Permanent treatment discontinuation	59	(4.5)	78	4.6	5	(0.8)	5	0.6

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

表 2.7.4.2-10　胃腸障害の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	402			403			402		
Patient years of exposure (PYE)	529.8			533.0			528.3		
Adverse Events	231 (57.5)	724	136.7	256 (63.5)	924	173.3	138 (34.3)	262	49.6
Serious									
Yes	3 (0.7)	7	1.3	6 (1.5)	7	1.3	3 (0.7)	3	0.6
No	230 (57.2)	717	135.3	255 (63.3)	917	172.0	137 (34.1)	259	49.0
Severity									
Severe	7 (1.7)	10	1.9	9 (2.2)	12	2.3	4 (1.0)	5	0.9
Moderate	50 (12.4)	115	21.7	93 (23.1)	222	41.6	26 (6.5)	38	7.2
Mild	220 (54.7)	599	113.1	226 (56.1)	690	129.4	121 (30.1)	219	41.5
Relationship to trial product									
Probable	120 (29.9)	285	53.8	143 (35.5)	379	71.1	42 (10.4)	61	11.5
Possible	125 (31.1)	302	57.0	148 (36.7)	403	75.6	58 (14.4)	102	19.3
Unlikely	83 (20.6)	136	25.7	92 (22.8)	142	26.6	72 (17.9)	98	18.5
Missing	1 (0.2)	1	0.2	0			1 (0.2)	1	0.2
Outcome									
Fatal	0			0			0		
Recovered	216 (53.7)	657	124.0	242 (60.0)	861	161.5	121 (30.1)	224	42.4
Recovering	4 (1.0)	5	0.9	5 (1.2)	5	0.9	3 (0.7)	3	0.6
Recovered With Sequelae	0			1 (0.2)	1	0.2	0		
Not Recovered	42 (10.4)	62	11.7	42 (10.4)	54	10.1	25 (6.2)	34	6.4
Unknown	0			1 (0.2)	3	0.6	1 (0.2)	1	0.2
Leading to Permanent treatment discontinuation	14 (3.5)	16	3.0	17 (4.2)	24	4.5	4 (1.0)	6	1.1

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

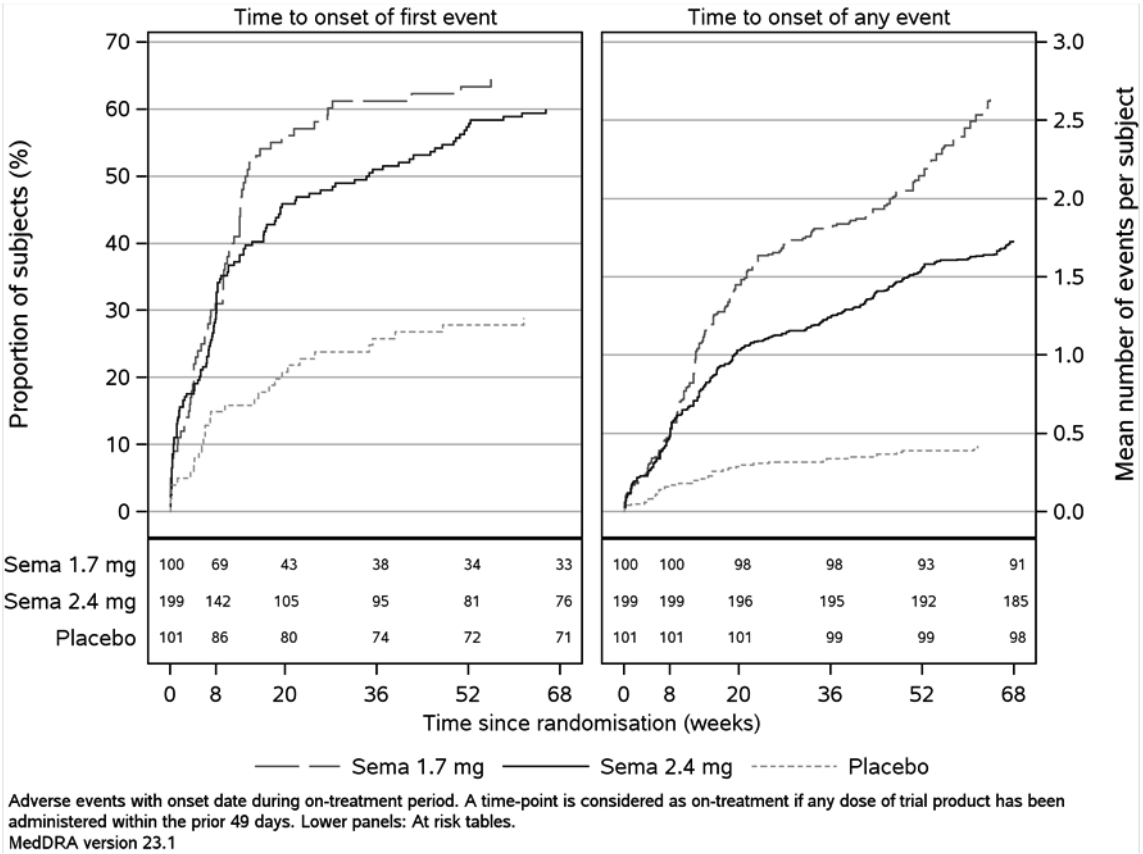
2.7.4.2.2.2.3　胃腸障害の有害事象の発現時期

胃腸障害の有害事象の発現までの時間

日本人被験者が参加した 3 つのいずれの第 3 相試験でも、すべての投与群において胃腸障害の有害事象は試験期間を通して発現がみられた。最初の胃腸障害の有害事象の発現に関する経時推移に基づくと、いずれの投与群でも最初に発現した胃腸障害の有害事象の大部分が投与開始後最初の 20 週間に発現したが、曲線の傾きはプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で大きかった。いずれのセマグルチド群でも、最初の胃腸障害の有害事象を発現した被験者の割合の増加は 20 週以降に横ばいになり、プラセボ群とほぼ同程度の増加になった（図 2.7.4.2-4、左図）。累積頻度プロット（図 2.7.4.2-4、右図）に基づくと、曲線の傾きの大きさから示されるように、胃腸障害の有害事象の大部分が報告された最初の約 20 週間以降の残りの試験期間を通して、プラセボの投与を受けた被験者と比較してセマグルチドの投与を受けた被験者でより多くの胃腸障害の有害事象が報告された。

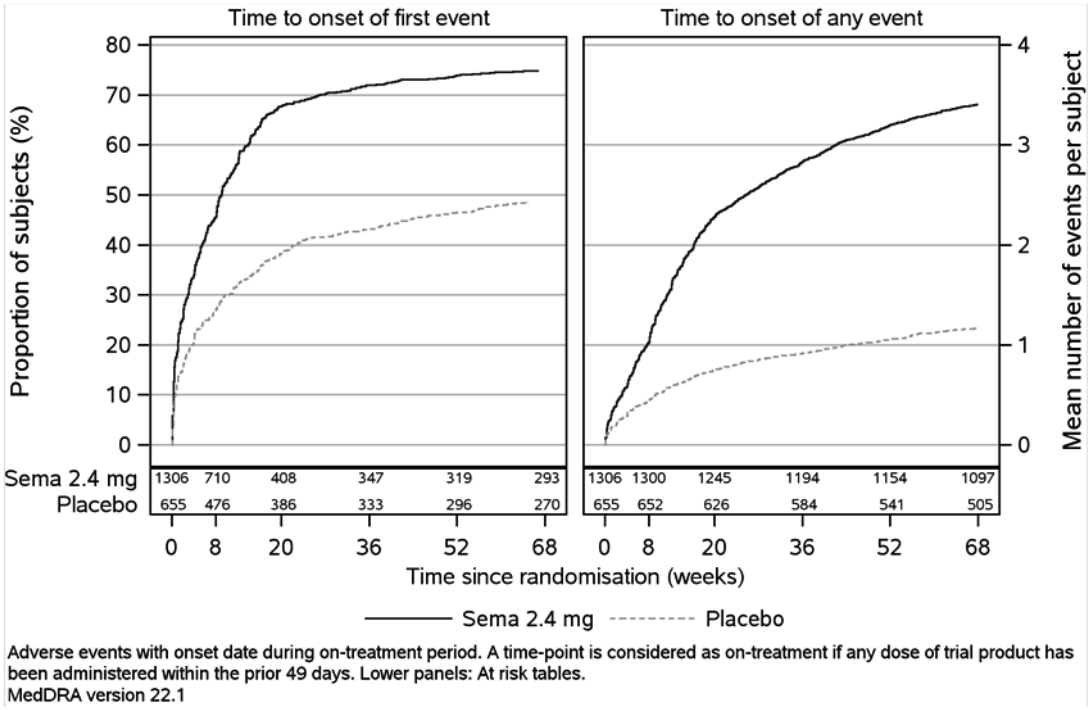
図 2.7.4.2-4　　胃腸障害の有害事象（MedDRA 検索）の経時推移－on-treatment 観察期間－安全性解析対象集団（4382、4373 及び 4374 試験）

4382 試験



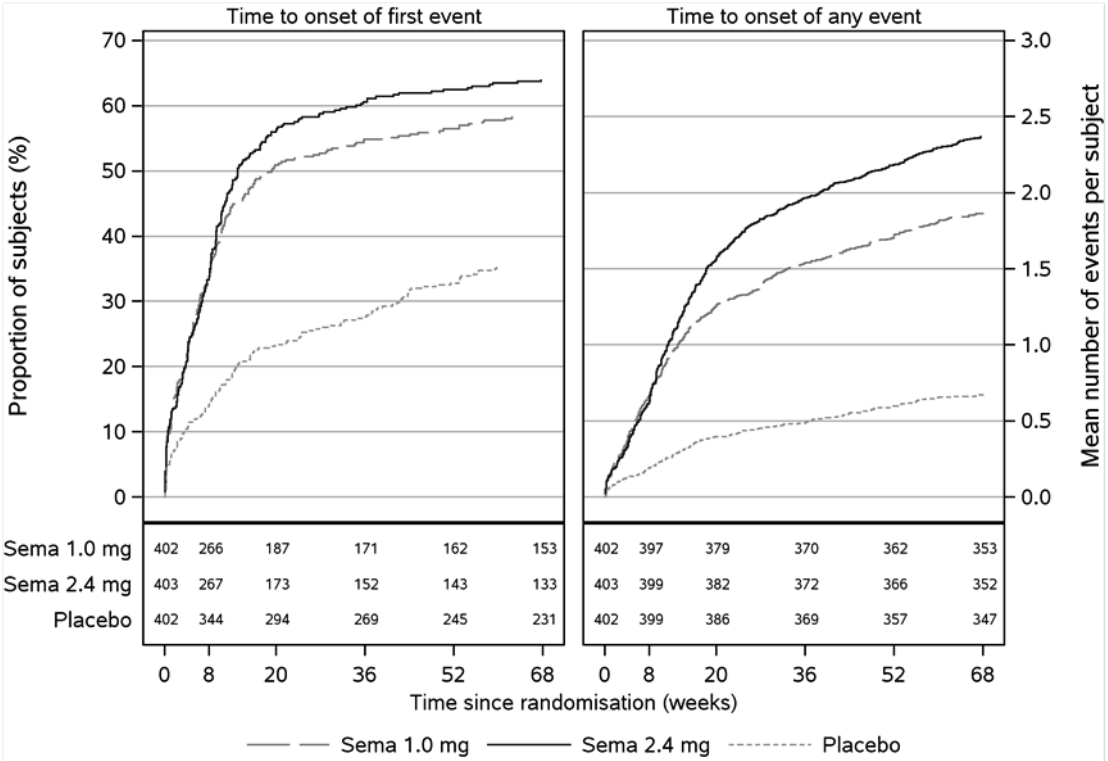
Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. Lower panels: At risk tables.
MedDRA version 23.1

4373 試験



Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. Lower panels: At risk tables.
MedDRA version 22.1

4374 試験



Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. Lower panels: At risk tables.
MedDRA version 22.1

胃腸障害の有害事象を発現している被験者の割合

日本人被験者が参加した 3 つのいずれの第 3 相試験でも、胃腸障害の有害事象（軽度、中等度及び重度）を発現している被験者の割合〔prevalence（特定の週で胃腸障害の有害事象を発現しているすべての被験者の割合）〕は、すべてのセマグルチド群（1.0、1.7 及び 2.4 mg）で試験期間を通してプラセボ群よりも高いまま推移した。胃腸障害の有害事象を発現している被験者の割合（prevalence）は、20 週前後で最も高く、20 週以降は、4382 試験では試験期間を通して安定しており、4373 及び 4374 試験では低下した〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.1.28、4373 試験（Module 5.3.5.1）EOT Figure 14.3.1.28、4374 試験（Module 5.3.5.1）EOT Figure 14.3.1.28〕。

3 つのいずれの第 3 相試験においても、すべての用量のセマグルチド群（1.0、1.7 及び 2.4 mg）で「悪心」及び「下痢」を発現している被験者の割合（prevalence）は、最初の約 20 週間で増加し、その後は時間の経過とともに徐々に低下した。「嘔吐」を発現している被験者の割合（prevalence）は試験期間を通して低いまま推移した。また、「便秘」を発現している被験者の割合（prevalence）は、すべての用量のセマグルチド群で試験期間を通してプラセボ群よりも高いまま推移した〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.1.29～14.3.1.32、4373 試験（Module 5.3.5.1）EOT Figure 14.3.1.29～14.3.1.32、4374 試験（Module 5.3.5.1）EOT Figure 14.3.1.29～14.3.1.32〕。「悪心」、「嘔吐」及び「下痢」の持続期間の中央値は短期間であり、投与群間で同程度であった（3 つの試験全体ですべての投与群におけるこれらの事象の持続期間の中央値は、「悪心」が 5～10 日間、「嘔吐」が 1～2 日間及び「下痢」が 2～5 日間であった）。「便秘」については、持続期間の中央値は、「悪心」、「下痢」及び「嘔吐」より長期間であり、試験ごとに違いがみられた（セマグルチド群で 35～179 日間、プラセボ群で 21～406 日間）〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.33、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.33、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.33〕。

2.7.4.2.2.2.4　結論

日本人被験者が参加した 3 つの第 3 相試験（4382、4373 及び 4374 試験）において、胃腸障害の有害事象が最も高頻度で報告された事象であり、プラセボ群と比較してすべての用量のセマグルチド群（1.0、1.7 及び 2.4 mg）で発現頻度が高かった。胃腸障害の有害事象の大部分は、非重篤で、軽度又は中等度の事象であり、用量漸増期間に発現し、転帰は「回復」であった。高頻度で報告された胃腸障害の有害事象は「悪心」、「下痢」、「嘔吐」及び「便秘」であった。胃腸障害の有害事象により死亡した被験者はいなかった。胃腸障害の有害事象は、比較的よく見られる治験薬投与の中止に至った有害事象でもあり、治験薬投与の中止に至った胃腸障害の有害事象を発現した被験者の割合は、プラセボ群と比較してすべての用量のセマグルチド群で高かった。胃腸障害の有害事象及び治験薬投与の中止に至った胃腸障害の有害事象の発現状況について、セマグルチドの用量の増加に伴う特定の傾向はみられなかった。全体的に、「悪心」、「嘔吐」及び「下痢」の持続時間は短く、「便秘」の持続時間は長かった。

以上のことから、胃腸障害に関連する安全性プロファイルはセマグルチドの 2 型糖尿病に対する皮下投与（オゼンピック皮下注）[14]及び経口投与（リベルサス錠）[15]を含む他の GLP-1 受容体作動薬と類似していると考えられた。

2.7.4.2.2.3　胆嚢関連障害

2.7.4.2.2.3.1　背景及び評価方法

肥満（特に中心性肥満）[29, 30, 31]、女性[32]、及び急激かつ大幅な体重減少[31, 33, 34, 35]は、胆石（胆石症）発症の危険因子であることが知られている。胆石は、胆嚢炎や急性膵炎などの合併症を引き起こすことがある。

また、胆石は一部の GLP-1 受容体作動薬との関連性が指摘されている[36]ため、すべての第 3 相試験において胆嚢関連障害を追加のデータ収集を必要とする注目すべき安全性領域に含めた。

胆石症は、2 型糖尿病に対するセマグルチド皮下投与（オゼンピック皮下注）[14]及びセマグルチド経口投与（リベルサス錠）[15]の添付文書にも記載されている。

胆嚢関連障害の有害事象は、事前に規定した MedDRA 検索〔検索に含まれる用語は 4382 試験（Module 5.3.5.1）Appendix 16.1.9、4373 試験（Module 5.3.5.1）Appendix 16.1.9、4374 試験（Module 5.3.5.1）Appendix 16.1.9 に示す〕により特定し、on-treatment 観察期間に基づき評価した。

症候性の急性胆嚢疾患の有害事象については追加のデータ収集を行った。

2.7.4.2.2.3.2　有害事象に基づく胆嚢関連障害

4382 及び 4374 試験では、胆嚢関連障害の有害事象の発現件数は少なく（各投与群で 1～4 件）、胆嚢関連障害の発現頻度及び単位時間あたりの発現件数について投与群間で明らかな違いはみられず、用量反応性もみられなかった（表 2.7.4.2-11 及び表 2.7.4.2-13）。また、重症度、治験責任医師による治験薬との因果関係の評価、転帰又は治験薬の投与への対応について投与群間で明らかな違いはみられなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.40、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.40〕。4382 試験では 2 件（いずれもセマグルチド 2.4 mg 群）及び 4374 試験では 4 件（セマグルチド 1.0 mg 群で 1 件、セマグルチド 2.4 mg 群で 2 件、プラセボ群で 1 件）の重篤な有害事象が報告された。治験薬投与の中止に至った胆嚢関連障害の有害事象はなかった。

4373 試験では、セマグルチド 2.4 mg 群で 2.6%の被験者及びプラセボ群で 1.2%の被験者が胆嚢関連障害の有害事象を発現した（表 2.7.4.2-12）。胆嚢関連障害の有害事象の大部分は軽度又は中等度であり、転帰は「回復」であった。セマグルチド 2.4 mg 群で発現した事象の約半数、及びプラセボ群で発現した事象の 25%が重篤であった。また、セマグルチド 2.4 mg 群で発現した事象の約半数が治験責任医師により治験薬との因果関係が「あり」又は「可能性あり」と判定された〔4373 試験（Module 5.3.5.1）EOT Table 14.3.1.40〕。セマグルチド 2.4 mg 群の 2 例が、胆嚢関連障害の有害事象〔「胆石症」（基本語）〕のため治験薬の投与を中止した（表 2.7.4.2-12）。

日本人被験者が参加した 3 つのいずれの第 3 相試験においても、MedDRA 検索で特定された最も高頻度で報告された事象（基本語）は「胆石症」であった。4382 及び 4374 試験では、「胆石症」を除き、胆嚢関連障害の有害事象（基本語別）はいずれかの投与群で 1 例 1 件の発現であった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.42、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.42〕。4373 試験では、胆嚢関連障害の有害事象及び重篤な有害事象における投与群間の違いは、主に「胆石症」ならびに「胆嚢炎」及び「急性胆嚢炎」などの合併症によるものであった〔4373 試験（Module 5.3.5.1）EOT Table 14.3.1.42〕。

胆石症

- 4382 試験の 2 件（いずれもセマグルチド 2.4 mg 群）、4373 試験の 13 件（セマグルチド 2.4 mg 群で 2 件、プラセボ群で 1 件）及び 4374 試験の 2 件（セマグルチド 2.4 mg 群で 1 件、セマグルチド 1.0 mg 群で 1 件）が重篤な有害事象であった。
- 転帰が「未回復」であった 4382 試験のセマグルチド 2.4 mg 群の 2 件を除き、すべての「胆石症」の重篤な有害事象の転帰は「回復」であった。
- 4373 試験のセマグルチド 2.4 mg 群において発現した 1 件の「胆石症」の重篤な有害事象は、治験薬投与の中止に至った。

胆嚢炎又は急性胆嚢炎

- 「胆嚢炎」については、4373 試験のセマグルチド 2.4 mg 群の 4 件が重篤な有害事象であった。
- 「急性胆嚢炎」については、4373 試験のセマグルチド 2.4 mg 群の 3 件及び 4374 試験のプラセボ群の 1 件が重篤な有害事象であった。
- すべての「胆嚢炎」及び「急性胆嚢炎」の重篤な有害事象の転帰は「回復」であった。
- 治験薬投与の中止に至った「胆嚢炎」及び「急性胆嚢炎」の重篤な有害事象はなかった。

なお、「胆嚢炎」の事象は 4382 及び 4374 試験では報告はなかった。「急性胆嚢炎」は、4382 試験のすべての投与群、4373 試験のプラセボ群、ならびに 4374 試験のセマグルチド 1.0 mg 群及びセマグルチド 2.4 mg 群で報告はなかった。

セマグルチド 2.4 mg 群で発現した「胆嚢炎」及び「急性胆嚢炎」のすべての事象について、胆石の徴候（「胆石症」の有害事象をともに報告、画像診断により認められた胆石又は胆石を含む報告用語）が認められた。

叙述の詳細は 4382 試験（Module 5.3.5.1）Section 14.3.3、4373 試験（Module 5.3.5.1）Section 14.3.3、4374 試験（Module 5.3.5.1）Section 14.3.3 に、症候性の急性胆嚢疾患の有害事象で収集された追加情報の詳細は 4382 試験（Module 5.3.5.1）Section 12.5.4、Appendix 16.2.7、Listing 16.2.7.19、4373 試験（Module 5.3.5.1）Section 12.5.4、Appendix 16.2.7、Listing 16.2.7.18、4374 試験（Module 5.3.5.1）Section 12.5.4、Appendix 16.2.7、Listing 16.2.7.19 に示す。

表 2.7.4.2-11　胆嚢関連障害－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	100			199			101		
Patient years of exposure (PYE)	136.2			275.0			141.8		
Adverse Events	1	(1.0)	1 0.7	2	(1.0)	2 0.7	1	(1.0)	1 0.7
SAEs	0			2	(1.0)	2 0.7	0		
Severe AEs	0			0			0		
Leading to Permanent treatment discontinuation	0			0			0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 23.1

表 2.7.4.2-12　胆嚢関連障害－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg			Placebo		
	N	(%)	E R	N	(%)	E R
Number of subjects	1306			655		
Patient years of exposure (PYE)	1706.1			829.6		
Adverse Events	34	(2.6)	42 2.5	8	(1.2)	8 1.0
SAEs	17	(1.3)	21 1.2	2	(0.3)	2 0.2
Severe AEs	11	(0.8)	15 0.9	1	(0.2)	1 0.1
Leading to Permanent treatment discontinuation	2	(0.2)	2 0.1	0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

表 2.7.4.2-13　胆嚢関連障害－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	402				403				402			
Patient years of exposure (PYE)	529.8				533.0				528.3			
Adverse Events	4	(1.0)	4	0.8	1	(0.2)	2	0.4	3	(0.7)	4	0.8
SAEs	1	(0.2)	1	0.2	1	(0.2)	2	0.4	1	(0.2)	1	0.2
Severe AEs	0				1	(0.2)	1	0.2	1	(0.2)	1	0.2
Leading to Permanent treatment discontinuation	0				0				0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

「胆石症」、「胆嚢炎」及び「急性胆嚢炎」の発現時期

4382 及び 4374 試験では、「胆石症」、「胆嚢炎」及び「急性胆嚢炎」の発現件数が少なかったため、いずれの投与群においてもこれらの事象の発現について明らかな経時的な傾向はみられなかった〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.1.41、4374 試験（Module 5.3.5.1）EOT Figure 14.3.1.41〕。4373 試験では、最初の「胆石症」、「胆嚢炎」及び「急性胆嚢炎」の有害事象の発現に関する経時推移に基づくと、両方の投与群において、試験期間を通してこれらの最初の事象の発現がみられたが、曲線の傾きはプラセボ群と比較してセマグルチド 2.4 mg 群で大きかった。すべての「胆石症」、「胆嚢炎」及び「急性胆嚢炎」の有害事象の発現時期も同様の結果であった〔4373 試験（Module 5.3.5.1）EOT Figure 14.3.1.41〕。

2.7.4.2.2.3.3　結論

4382 及び 4374 試験では、胆嚢関連障害の有害事象の発現件数は少なく（各投与群で 4 件以下）、胆嚢関連障害の発現に投与群間で明らかな違いはみられなかった。4373 試験では、胆嚢関連障害の有害事象はプラセボ群と比較してセマグルチド 2.4 mg 群で多く発現し、これは「胆石症」ならびに「胆嚢炎」及び「急性胆嚢炎」などの合併症によるものであった。同様の結果が他の GLP-1 受容体作動薬でも報告されている [36, 37]。

「胆石症」、「胆嚢炎」及び「急性胆嚢炎」の有害事象は試験期間を通して発現し、特定の時期に多く発現することはなかった。

2.7.4.2.2.4　急性膵炎

2.7.4.2.2.4.1　背景及び評価方法

すべてのインクレチン関連薬において、急性膵炎のリスクはクラスラベリングとして扱われている。このため、直近（スクリーニング前 180 日以内）に急性膵炎を発症した被験者及び慢性膵炎を有する又は既往歴を有する被験者は第 3 相試験から除外した。

GLP-1 受容体作動薬によって膵酵素が増加するが、他の徴候や症状がない場合には急性膵炎を予測できない[38]。また、大規模なメタアナリシスでは、GLP-1 受容体作動薬の投与によって急性膵炎のリスクが増加しないことが示唆されている [36, 39, 40]。

急性膵炎のリスクは、注目すべき安全性領域として、事前に規定した膵炎の MedDRA 検索、急性膵炎が疑われる事象のイベント判定結果及び急性膵炎に関する追加のデータ収集に基づき評価した。急性膵炎が疑われる場合は治験薬の投与を中断し、急性膵炎の診断基準及びその他の症状及び実施された治療に関する追加データの収集を含めて、適切な対応を開始することとした。表 2.7.4.2-14 に示すように、急性膵炎は診断、イベント判定及びアトランタ分類を用いた重症度分類が行われた。イベント判定に関する全体的な方法は 2.7.4.1.1.8.2 項に示す。MedDRA 検索に含まれる用語は 4382 試験については（Module 5.3.5.1）Appendix 16.1.9、4373 及び 4374 試験については Global summary of safety (Module 5.3.5.3), Appendix 7.8、Section 20 に示す。

表 2.7.4.2-14　　急性膵炎－追加のデータ収集及びイベント判定結果

Event category	Description for evaluation of diagnosis	Adjudication outcome(s)
Acute pancreatitis	The diagnosis of acute pancreatitis required two of the following three features: • Abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back) • Serum lipase activity (and/or amylase activity) at least three times greater than the upper limit of normal • Characteristic findings of acute pancreatitis on imaging	Acute pancreatitis by severity (Atlanta classification [41]): • Mild • Moderately severe • Severe

血清リパーゼ活性（及び／又はアミラーゼ活性）が基準値上限の 3 倍を超えることが、急性膵炎の診断基準の 1 つであることから、急性膵炎の評価の一環としてリパーゼ及びアミラーゼの値についても検討した（データ収集の詳細については、2.7.4.1.1.8.5 項に示す）。リパーゼ及びアミラーゼの増加は、セマグルチドを含む GLP-1 受容体作動薬においてよく知られている。この所見の背景にある詳細なメカニズムは現時点では不明であるが、膵臓の腺房に対する GLP-1 受容体作動薬の薬理作用によるものと考えられる。動物試験では、GLP-1 受容体の活性化はタンパク質合成の増加を誘発するが、細胞増殖を誘発しないことが示されている[42, 43]。

膵炎に関する事前に規定した MedDRA 検索ならびにリパーゼ及びアミラーゼの臨床検査に基づく評価は、on-treatment 観察期間を用いた。急性膵炎が疑われる事象のイベント判定に基づく評価には、in-trial 観察期間を用いた。

2.7.4.2.2.4.2　　有害事象に基づく膵炎

4382 試験では、MedDRA 検索により膵炎は特定されなかった。

4373 試験ではセマグルチド 2.4 mg 群で 2 件、4374 試験ではセマグルチド 2.4 mg 群とプラセボ群でそれぞれ 1 件の膵炎が MedDRA 検索により特定された（表 2.7.4.2-15 及び表 2.7.4.2-16）。セマグルチド 2.4 mg 群で発現した事象については、4373 試験の 2 件が重篤な有害事象であり、転帰は「回復」であった。このうち 1 件は治験薬投与の中止に至った。4374 試験の 1 件は非重篤であり、治験薬投与の中止に至った。本事象の転帰は「回復したが後遺症あり」であった（付録 2.7.4.7.1、表 1 及び表 5）。また、4374 試験のプラセボ群で発現した事象は重篤であり、転帰は「回復」であった。セマグルチド 2.4 mg 群で発現した 3 件の事象（基本語）はいずれも「急性膵炎」であり、プラセボ群の 1 件の事象（基本語）は「閉塞性膵炎」であった（付録 2.7.4.7.1、表 2 及び表 6）。

MedDRA 検索により特定された 4 件のすべての事象が、イベント判定委員会により急性膵炎と確定された。

表 2.7.4.2-15　膵炎に関する有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R
Number of subjects	1306				655			
Patient years of exposure (PYE)	1706				829.6			
Adverse Events	2	(0.2)	2	0.1	0			
SAEs	2	(0.2)	2	0.1	0			
Severe	0				0			
Leading to Permanent treatment discontinuation	1	(0.1)	1	0.1	0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years, PYE: The duration of the on-treatment period in years,
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

表 2.7.4.2-16　膵炎に関する有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	402				403				402			
Patient years of exposure (PYE)	529.8				533.0				528.3			
Adverse Events	0				1	(0.2)	1	0.2	1	(0.2)	1	0.2
SAEs	0				0				1	(0.2)	1	0.2
Severe	0				0				0			
Leading to Permanent treatment discontinuation	0				1	(0.2)	1	0.2	0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years, PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.2.2.4.3　イベント判定に基づく急性膵炎の有害事象

4382 試験では、イベント判定に送付された事象はなかった。

4373 試験では、計 4 例 6 件（いずれもセマグルチド 2.4 mg 群）がイベント判定委員会に送付され、これらのうち 3 例 5 件がイベント判定委員会により急性膵炎と確定された。2 例の被験者は on-treatment 観察期間にそれぞれ 1 件発現し、1 例の被験者が計 3 件の事象（on-treatment 観察期間に発現した 1 件と on-treatment 観察期間後の in-trial 観察期間内に発現した 2 件）を発現した。On-treatment 観察期間内に発現した事象のみに注目すると、セマグルチド 2.4 mg 群において、3 例 3 件がイベント判定により急性膵炎と確定され、いずれも軽症急性膵炎（mild acute pancreatitis）に分類された（表 2.7.4.2-17）。

表 2.7.4.2-17　イベント判定委員会により確定された急性膵炎の有害事象－in-trial 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R
Number of subjects	1306				655			
Patient years of observation (PYO)	1856.4				918.5			
Events sent for adjudication	4	(0.3)	6	0.3	0			
Diagnostic criteria unmet	1	(<0.1)	1	0.1	0			
EAC confirmed pancreatitis events	3	(0.2)	5	0.3	0			
Acute pancreatitis	3	(0.2)	5	0.3	0			
Mild	3	(0.2)	4	0.2	0			
Moderately severe	1	(<0.1)	1	0.1	0			
On-treatment								
Yes	3	(0.2)	3	0.2	0			
No	1	(<0.1)	2	0.1	0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years, EAC: Event adjudication committee PYO: The duration of the in-trial period in years. The on-treatment evaluation of events is based on EAC confirmed events only. MedDRA version 22.1

4374 試験では、セマグルチド 2.4 mg 群及びプラセボ群の各 1 例で計 4 件がイベント判定委員会に送付され、これらのうち 3 件（セマグルチド 2.4 mg 群の 1 例 2 件、プラセボ群の 1 件）がイベント判定委員会により急性膵炎と確定された。いずれの事象も on-treatment 観察期間に発現した。セマグルチド 2.4 mg 群の 1 例 2 件は中等度～重症急性膵炎（moderately severe acute pancreatitis）に、プラセボ群の 1 件は軽症急性膵炎（mild acute pancreatitis）に分類された（表 2.7.4.2-18）。

表 2.7.4.2-18　　イベント判定委員会により確定された急性膵炎の有害事象－in-trial 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	402				403				402			
Patient years of observation (PYO)	569.1				572.8				566.6			
Events sent for adjudication	0				1	(0.2)	3	0.5	1	(0.2)	1	0.2
Diagnostic criteria unmet	0				1	(0.2)	1	0.2	0			
EAC confirmed pancreatitis events	0				1	(0.2)	2	0.3	1	(0.2)	1	0.2
Acute pancreatitis	0				1	(0.2)	2	0.3	1	(0.2)	1	0.2
Mild	0				0				1	(0.2)	1	0.2
Moderately severe	0				1	(0.2)	2	0.3	0			
On-treatment												
Yes	0				1	(0.2)	2	0.3	1	(0.2)	1	0.2

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years, EAC: Event adjudication committee PYO: The duration of the in-trial period in years. The on-treatment evaluation of events is based on EAC confirmed events only.
MedDRA version 22.1

イベント判定委員会により確定された 8 件の急性膵炎の詳細を表 2.7.4.2-19 に示す。

表 2.7.4.2-19　　イベント判定委員会により確定された急性膵炎の詳細－in-trial 観察期間（4373 及び 4374 試験）

Subject ID Age/Sex/BMI/ Case no.	**Investigator reported information:** **Preferred term/Onset (period)/ Symptoms/ Imaging (results)/ Complications/ Treatment/ Confounding factors**	**Seriousness/ Severity/ Causality/ Action/ Outcome**	**EAC reported information:** **Outcome (Classification)/ Onset (period)/ Criteria fulfilled/ Source/Documentation**
Trial 4373			
Sema 2.4 mg			
305001/ 4[redacted]/F/45.0/ 649700	リパーゼ増加/260 (IT/OT)/ Significant upper abdominal pain/ Imaging performed (findings consistent with gallstones)/ No acute complications/ No treatment/ No confounding factors	Serious/ Severe/ Probable/ Permanent treatment discontinuation/ Recovered	Acute pancreatitis (Mild)/260 (IT/OT)/ Severe acute upper abdominal pain and elevated blood levels of pancreatic enzymes/ Investigator/Full documentation
919022/ 3[redacted]/F/36.3/ 661853 703575 715466	急性膵炎/234 (IT/OT)/ Significant upper abdominal pain, nausea and vomiting/ Imaging performed (no findings)/ No acute complications/ Standard treatment/ Confounding factors included: history of acute pancreatitis and alcohol consumption	Serious/ Moderate/ Possible/ Permanent treatment discontinuation/ Recovered	Acute pancreatitis (Mild)/232 (IT/OT)/ Investigator reported/ Severe acute upper abdominal pain and elevated blood levels of pancreatic enzymes/ Investigator/Full documentation
	急性膵炎/415 (IT)/ Significant upper abdominal pain, nausea and vomiting/ Imaging performed (findings consistent with acute pancreatitis: peri-pancreatic fluid)/ No acute complications/ Standard treatment/ Confounding factors: history of acute pancreatitis	Serious/ Moderate/ Possible/ Not Applicable/ Recovered	Acute pancreatitis (Moderately severe)/ 417 (IT) Severe acute upper abdominal pain and characteristic imaging findings/ Investigator/Full documentation
	急性膵炎/526 (IT)/ Significant upper abdominal pain, nausea and vomiting/ Imaging performed (findings consistent with acute pancreatitis: peri-pancreatic fluid)/ Standard treatment/ Confounding factors: history of acute pancreatitis	Serious/ Moderate/ Unlikely/ Not Applicable/ Recovered	Acute pancreatitis (Mild)/526 (IT)/ Severe acute upper abdominal pain and characteristic imaging findings/ Investigator/Full documentation

Subject ID Age/Sex/BMI/ Case no.	Investigator reported information: Preferred term/Onset (period)/ Symptoms/ Imaging (results)/ Complications/ Treatment/ Confounding factors	Seriousness/ Severity/ Causality/ Action/ Outcome	EAC reported information: Outcome (Classification)/ Onset (period)/ Criteria fulfilled/ Source/Documentation
938015/ 3[redacted]/M/35.5/ 707153	急性膵炎/508 (IT/OT)/ Significant upper abdominal pain and nausea/ Imaging performed (findings consistent with gallstones)/ No acute complications/ Standard treatment/ No confounding factors	Serious/ Mild/ Unlikely/ Not Applicable/ Recovered	Acute pancreatitis (Mild)/508 (IT/OT)/ Severe acute upper abdominal pain and elevated blood levels of pancreatic enzymes/ Investigator/Full documentation
Trial 4374			
Sema 2.4 mg			
306012 6[redacted]/M/39.1 NA	急性膵炎/ 84 (IT/OT)/ Significant upper abdominal pain, nausea and vomiting/ Imaging not performed/ No acute complications/ Unknown/ No confounding factors included	Non-serious/ Moderate/ Probable/ Permanent treatment discontinuation/ Recovered with sequelae	Acute pancreatitis (Moderately severe)/87 (IT/OT)/Severe acute upper abdominal pain and elevated blood levels of pancreatic enzymes/ Preferred term search/Full documentation
	膵仮性嚢胞/149 (IT)/ No additional data were provided[a]	Non-serious/ Mild/ Probable/ Not Applicable/ Not recovered	Acute pancreatitis (Moderately severe)/ 84 (IT/OT)/ Severe acute upper abdominal pain and elevated blood levels of pancreatic enzymes/Investigator/Full documentation
Placebo			
400004/ 5[redacted]/M/29.3 663039	閉塞性膵炎/254 (IT/OT)/ Significant upper abdominal pain/ Imaging performed (findings consistent with gallstones and acute pancreatitis)/No acute complications/Standard treatment/No confounding factors	Serious/ Mild/ Unlikely/ Dose not changed/ Recovered	Acute pancreatitis (Mild)/253 (IT/OT)/ Severe acute upper abdominal pain and elevated blood levels of pancreatic enzymes/ Investigator/Full documentation

F: Female, M: Male, Age: Age in years, BMI: Body mass index (kg/m^2), IT: in-trial period, OT: on-treatment period.

[a] Additional data were to be collected in case of acute pancreatitis,

[b] The event had onset in the 7-week follow-up period after last dose of trial product.

叙述の詳細は 4373 試験（Module 5.3.5.1）Section 14.3.3、4374 試験（Module 5.3.5.1）Section 14.3.3 に示し、急性膵炎の有害事象で収集された追加情報の詳細は 4373 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.20、4374 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.21 に示す。

2.7.4.2.2.4.4　膵酵素：リパーゼ及びアミラーゼ

2.7.4.2.2.4.4.1　リパーゼ及びアミラーゼの臨床検査評価

平均値の経時推移

日本人被験者が参加した 3 つの第 3 相試験では、リパーゼの平均値は on-treatment 観察期間中にすべての用量のセマグルチド群（1.0、1.7 及び 2.4 mg）において 68 週で増加したが、プラセボ群の平均値は安定していた（表 2.7.4.2-20、表 2.7.4.2-21 及び表 2.7.4.2-22）。セマグルチド群のリパーゼは、投与開始後の最初の 20 週間に増加した。その後は、4382 及び 4373 試験では平均値のわずかな減少が認められ、4374 試験ではセマグルチド 2.4 mg 群は on-treatment 観察期間の残りの期間にわずかではあるがさらに増加し、セマグルチド 1.0 mg 群では安定していた〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.20、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.20、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.21〕。

アミラーゼについては、4382 試験において、セマグルチド 2.4 mg 群とセマグルチド 1.7 mg 群では on-treatment 観察期間中にわずかに増加したのに対し、プラセボ群では減少した。4373 及び 4374 試験においては、セマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群では平均値が増加したが、プラセボ群の平均値は安定していた（表 2.7.4.2-20、表 2.7.4.2-21 及び表 2.7.4.2-22）。4382、4373 及び 4374 試験において、セマグルチド群のアミラーゼも、投与開始後の最初の 20 週間に増加し、その後は on-treatment 観察期間の残りの期間にわずかではあるがさらに増加した〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.10、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.10、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.10〕。

4382 及び 4374 試験において、アミラーゼとリパーゼのベースライン以降の増加に対するセマグルチドの明らかな用量反応関係はみられなかった〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.10、14.3.5.20、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.10、14.3.5.21〕。

個々の被験者における高値

日本人被験者が参加した 3 つの第 3 相試験では、ベースラインにおいてリパーゼが基準範囲を超えていた被験者の割合は、投与群間で概ね同程度であった。68 週では、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）でリパーゼが基準範囲を超えた被験者が多かった（表 2.7.4.2-20、表 2.7.4.2-21 及び表 2.7.4.2-22）。リパーゼの経時推移、ならびにベースライン以降の最低値及び最高値を示す箱ひげ図〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.19、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.19、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.20〕に基づくと、20 週から 68 週までのリパーゼ値の分布に大きな変化はなく、平均の推移でみられた傾向が同様に認められた〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.20、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.20、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.21〕。

アミラーゼについては、いずれの試験でもベースラインにおいて基準範囲を超えていた被験者の割合は、投与群間で概ね同程度であった。68 週では、プラセボ群と比較してセマグルチド群（1.0、1.7、2.4 mg）でアミラーゼが基準範囲を超えた被験者が多かった（表 2.7.4.2-20、表 2.7.4.2-21 及び表 2.7.4.2-22）。アミラーゼの経時推移、ならびにベースライン以降の最低値と最高値を示す箱ひげ図〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.9、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.9、

4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.9〕に基づくと、20 週から 68 週までのアミラーゼ値の分布に変化はなく、平均の推移でみられた傾向が同様に認められた〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.10、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.10、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.10〕。

表 2.7.4.2-20　リパーゼ及びアミラーゼのベースライン値、68 週のベースラインに対する比ならびにベースライン及び 68 週のカテゴリーの要約－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg	Sema 2.4 mg	Placebo
Number of subjects	100	199	101
Lipase (U/L)			
Descriptive statistics (Geometric mean (CV))			
Mean level at baseline	23 (69.1)	23 (52.2)	24 (59.3)
Ratio to baseline at week 68	1.56 (39.8)	1.56 (45.4)	0.96 (40.5)
Categorical summary (N (%))			
Visit 1 (week -1)			
N	100 (100)	199 (100)	101 (100)
Low (<LLN)	3 (3.0)	3 (1.5)	3 (3.0)
Normal	95 (95.0)	195 (98.0)	97 (96.0)
High (>ULN)	2 (2.0)	1 (0.5)	1 (1.0)
Visit 24 (week 68)			
N	93 (93.0)	186 (93.5)	98 (97.0)
Low (<LLN)	0	1 (0.5)	3 (3.1)
Normal	88 (94.6)	176 (94.6)	95 (96.9)
High (>ULN)	5 (5.4)	9 (4.8)	0
Amylase (U/L)			
Descriptive statistics (Geometric mean (CV))			
Mean level at baseline	53 (31.0)	56 (38.7)	52 (34.7)
Ratio to baseline at week 68	1.09 (20.9)	1.08 (23.2)	0.93 (25.1)
Categorical summary (N (%))			
Visit 1 (week -1)			
N	100 (100)	199 (100)	101 (100)
Low (<LLN)	0	4 (2.0)	2 (2.0)
Normal	99 (99.0)	192 (96.5)	98 (97.0)
High (>ULN)	1 (1.0)	3 (1.5)	1 (1.0)
Visit 24 (week 68)			
N	93 (93.0)	186 (93.5)	98 (97.0)
Low (<LLN)	0	1 (0.5)	0
Normal	92 (98.9)	180 (96.8)	98 (100)
High (>ULN)	1 (1.1)	5 (2.7)	0

CV: Coefficient of variation in %. N: Number of subjects with an observation at the visit, %: Percentages are based on subjects with an observation at the visit, LLN: Lower limit normal, ULN: Upper limit normal.
Observed data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.

表 2.7.4.2-21　リパーゼ及びアミラーゼのベースライン値、68 週のベースラインに対する比ならびにベースライン及び 68 週のカテゴリーの要約－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg	Placebo
Number of subjects	1306	655
Lipase (U/L)		
Descriptive statistics (Geometric mean (CV))		
Mean level at baseline	25 (53.8)	25 (52.6)
Ratio to baseline at week 68	1.41 (49.3)	0.97 (37.3)
Categorical summary (N (%))		
Visit 1 (week -1)		
N	1306 (100)	654 (100)
Low (<LLN)	17 (1.3)	6 (0.9)
Normal	1270 (97.2)	638 (97.6)
High (>ULN)	19 (1.5)	10 (1.5)
Visit 24 (week 68)		
N	1053 (80.6)	497 (75.9)
Low (<LLN)	0	6 (1.2)
Normal	989 (93.9)	486 (97.8)
High (>ULN)	64 (6.1)	5 (1.0)
Amylase (U/L)		
Descriptive statistics (Geometric mean (CV))		
Mean level at baseline	48 (35.7)	48 (35.5)
Ratio to baseline at week 68	1.14 (21.6)	1.03 (21.4)
Categorical summary (N (%))		
Visit 1 (week -1)		
N	1306 (100)	655 (100)
Low (<LLN)	40 (3.1)	19 (2.9)
Normal	1258 (96.3)	635 (96.9)
High (>ULN)	8 (0.6)	1 (0.2)
Visit 24 (week 68)		
N	1053 (80.6)	497 (75.9)
Low (<LLN)	17 (1.6)	13 (2.6)
Normal	1026 (97.4)	482 (97.0)
High (>ULN)	10 (0.9)	2 (0.4)

CV: Coefficient of variation in %. N: Number of subjects with an observation at the visit, %: Percentages are based on subjects with an observation at the visit, LLN: Lower limit normal, ULN: Upper limit normal.
Observed data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.

表 2.7.4.2-22　リパーゼ及びアミラーゼのベースライン値、68 週のベースラインに対する比ならびにベースライン及び 68 週のカテゴリーの要約－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg	Sema 2.4 mg	Placebo
Number of subjects	402	403	402
Lipase (U/L)			
Descriptive statistics (geometric mean (CV))			
Men level at baseline	34 (63.4)	33 (64.3)	34 (73.9)
Ratio to baseline at week 68	1.31 (57.2)	1.41 (57.2)	0.99 (51.8)
Categorical summary (N (%))			
Visit 1 (week -1)			
N	402 (100)	403 (100)	402 (100)
Low (<LLN)	2 (0.5)	1 (0.2)	3 (0.7)
Normal	368 (91.5)	379 (94.0)	360 (89.6)
High (>ULN)	32 (8.0)	23 (5.7)	39 (9.7)
Visit 24 (week 68)			
N	350 (87.1)	350 (86.8)	338 (84.1)
Low (<LLN)	1 (0.3)	1 (0.3)	5 (1.5)
Normal	296 (84.6)	287 (82.0)	306 (90.5)
High (>ULN)	53 (15.1)	62 (17.7)	27 (8.0)
Amylase (U/L)			
Descriptive statistics (Geometric mean (CV))			
Mean level at baseline	50 (45.0)	50 (44.3)	50 (47.3)
Ratio to baseline at week 68	1.19 (32.8)	1.24 (28.3)	1.06 (25.0)
Categorical summary (N (%))			
Visit 1 (week -1)			
N	402 (100)	403 (100)	402 (100)
Low (<LLN)	24 (6.0)	17 (4.2)	23 (5.7)
Normal	370 (92.0)	377 (93.5)	370 (92.0)
High (>ULN)	8 (2.0)	9 (2.2)	9 (2.2)
Visit 24 (week 68)			
N	350 (87.1)	350 (86.8)	338 (84.1)
Low (<LLN)	9 (2.6)	5 (1.4)	18 (5.3)
Normal	327 (93.4)	328 (93.7)	312 (92.3)
High (>ULN)	14 (4.0)	17 (4.9)	8 (2.4)

CV: Coefficient of variation in %. N: Number of subjects with an observation at the visit, %: Percentages are based on subjects with an observation at the visit, LLN: Lower limit normal, ULN: Upper limit normal.
Observed data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.

2.7.4.2.2.4.5　結論

4382 試験では、膵炎の MedDRA 検索により事象は特定されず、イベント判定委員会により急性膵炎として確定された事象もなかった。4373 及び 4374 試験では、on-treatment 期間において、MedDRA 検索で特定された膵炎及びイベント判定委員会により確定された急性膵炎のいずれの事象についても少なかったことから、急性膵炎のリスクがプラセボと比較してセマグルチド 2.4 mg で増加することはなかった。

4373 試験のセマグルチド 2.4 mg 群において、イベント判定委員会により確定された急性膵炎を発現した 3 例のうち、2 例では症状の説明が可能な胆石の事象がともに報告され、1 例には急性膵炎の既往歴があった。また 4374 試験では、イベント判定委員会により確定された急性膵炎がセマグルチド 2.4 mg 群及びプラセボ群で各 1 例に報告された。

3 つの第 3 相試験において、セマグルチド群（1.0、1.7 及び 2.4 mg）ではリパーゼ及びアミラーゼの平均値は試験初期の期間に増加した。その後リパーゼはほぼ一定になったが、アミラーゼはその後も増加し、横ばいにはならなった。このことは、他の GLP-1 受容体作動薬での報告と同様であった。

他の検討と一致して[38]、急性膵炎の他の徴候や症状がない場合には、膵酵素の増加のみでは急性膵炎を予測することはできないと考えられた。

2.7.4.2.2.5 心血管障害

2.7.4.2.2.5.1 背景及び評価方法

心血管リスク因子の改善が進んでも、過体重又は肥満を有する人は心血管疾患のリスクが高い[44]。心血管疾患は、過体重又は肥満を有する人の主な死因の 1 つである[44, 45]ことから、肥満症のためのセマグルチドの第 3 相試験において、注目すべき安全性領域として定義した。

これまでに、2 型糖尿病患者を対象とした GLP-1 受容体作動薬の 7 つの CVOT から結果が報告されており、いずれの試験でも心血管リスクの増加は認められず[46, 47, 48, 49]、さらに心血管ベネフィットが認められた[50, 51, 52]。NN9535-3744 試験（SUSTAIN 6）では、セマグルチドの週 1 回皮下投与（0.5 mg 投与群と 1.0 mg 投与群の併合）のプライマリー複合アウトカム（心血管死、非致死性心筋梗塞又は非致死性脳卒中の最初の発現）の発現リスクがプラセボと比較して 26%低下することが示された〔ハザード比は 0.74（95%信頼区間：0.58; 0.95）〕〔3744 試験（Module 5.3.5.1）Table 11-4〕。

QT 間隔に対するセマグルチド皮下投与の影響は、2 型糖尿病のためのセマグルチド皮下投与の through QT/QTc 評価試験（NN9535-3652 試験）で検討され、1.5 mg までの用量のセマグルチド週 1 回皮下投与で QTc 間隔の延長は認められなかった（Module 2.7.2.4.1）。

肥満症のためのセマグルチド 2.4 mg の開発プログラムにおいて、心血管障害のリスクは、治験責任医師が報告した有害事象に対して行った事前に規定した心血管障害の MedDRA 検索〔検索に含まれる用語は、4382 試験（Module 5.3.5.1）Appendix 16.1.9、4373 試験（Module 5.3.5.1）Appendix 16.1.9、4374 試験（Module 5.3.5.1）Appendix 16.1.9 に示す〕、及び表 2.7.4.2-23 に示した事前に規定した心血管系事象のイベント判定結果に基づき評価した。イベント判定のプロセスは、2.7.4.1.1.8.2.2 項に示す。発現から診断までの時間が長くなる可能性があることから、これらの評価は in-trial 観察期間を用いた。MedDRA 検索ではより多くの種類の事象が含まれるが、イベント判定の対象として事前に規定した心血管事象ほど特異的ではない。

表 2.7.4.2-23　　心血管障害のイベント判定

Event type	Description	Adjudication outcome(s)
Death	All-cause death	Cardiovascular death (including undetermined cause of death) Non-cardiovascular death
Acute Coronary Syndrome	Acute coronary syndrome conditions include all types of acute myocardial infarction and hospitalisation for unstable angina pectoris	Acute myocardial infarction (including subgroup classifications) Hospitalisation for unstable angina pectoris
Cerebrovascular events	Episode of focal or global neurological dysfunction that could be caused by brain, spinal cord, or retinal vascular injury as a result of haemorrhage or infarction	Ischaemic stroke Haemorrhagic stroke Undetermined stroke Transient Ischaemic Attack
Coronary artery revascularisation	A coronary revascularisation procedure is a catheter-based (PCI) or a surgical procedure (CABG) designed to improve myocardial blood flow	Coronary revascularisation procedure
Heart failure	Presentation of the patient for an urgent, unscheduled clinic/office/emergency department visit or hospital admission, with a primary diagnosis of heart failure (new episode or worsening of existing heart failure)	Heart failure hospitalisation Urgent heart failure visit

脈拍数（2.7.4.2.2.5.4 項）及び心電図（2.7.4.2.2.5.5 項）も、心血管障害の評価の一部として検討した。脈拍数、心電図及びその他のバイタルサインに関連する臨床的に問題となる異常（治験責任医師の判断による）が認められた場合には、有害事象として報告することとした。さらに、個々の外れ値について検討するために、ベースラインの脈拍数別にベースライン値から最高値（すなわち、最も悪い値）までの変化量の評価も提示する。脈拍数と心電図については、on-treatment 観察期間に基づいて検討した。

さらに、4382 試験では心血管系における安全性の評価に含まれる心電図結果の一部として、QTc 間隔の推定値を評価した。QTc の推定は心電図の中央評価実施機関によって実施されたが、臨床的に問題がある異常所見の評価のために治験責任医師は無作為割り付け時に心電図の確認を行うこととした。無作為割り付け時に認められた臨床的に問題がある心電図所見は併発疾患として報告され、試験期間中に認められた臨床的に問題がある新たな所見又は臨床的に問題となる悪化が認められた場合には有害事象として報告することとした。

2.7.4.2.2.5.2　有害事象に基づく心血管障害

日本人被験者が参加した 3 つのいずれの第 3 相試験でも、in-trial 観察期間において心血管障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数に、投与群間で明らかな違いはみられなかった（表 2.7.4.2-24、表 2.7.4.2-25 及び表 2.7.4.2-26）。器官別大分類及び基本語別の違いについても、投与群間で明らかな傾向は認められなかった。セマグルチド群において最も高頻度で報告された事象（基本語）は、4382 試験では「血中クレアチンホスホキナーゼ増加」、4373 試験では「失神」、4374 試験では「心房細動」であった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.57、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.55、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.55〕。

また、発現した事象の重症度、治験責任医師による因果関係の評価、転帰又は治験薬の投与への対応についても投与群間で明らかな違いは認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.56、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.54、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.54〕。

3 つのいずれの試験においても心血管障害の重篤な有害事象を発現した被験者の割合はセマグルチド群（1.0、1.7 及び 2.4 mg）及びプラセボ群で同様であった。

表 2.7.4.2-24　心血管障害の有害事象－MedDRA 検索－in-trial 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg N	(%)	E	R	Sema 2.4 mg N	(%)	E	R	Placebo N	(%)	E	R
Number of subjects	100				199				101			
Patient years of observation	142.2				285.9				145.8			
Adverse Events	9	(9.0)	10	7.0	16	(8.0)	17	5.9	7	(6.9)	7	4.8
SAEs	0				1	(0.5)	1	0.3	2	(2.0)	2	1.4
Severe	0				1	(0.5)	1	0.3	2	(2.0)	2	1.4
Leading to Permanent treatment discontinuation	0				0				0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYO: The duration of the in-trial period in years.
MedDRA version 23.1

表 2.7.4.2-25　心血管障害の有害事象－MedDRA 検索－in-trial 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg N	(%)	E	R	Placebo N	(%)	E	R
Number of subjects	1306				655			
Patient years of observation (PYO)	1856.4				918.5			
Adverse Events	107	(8.2)	134	7.2	75	(11.5)	96	10.5
SAEs	16	(1.2)	22	1.2	12	(1.8)	13	1.4
Severe AEs	9	(0.7)	12	0.6	7	(1.1)	7	0.8
Leading to Permanent treatment discontinuation	0				4	(0.6)	4	0.4

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYO: The duration of the in-trial period in years.
MedDRA version 22.1

表 2.7.4.2-26　　心血管障害の有害事象－MedDRA 検索－in-trial 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	402			403			402		
Patient years of observation (PYO)	569.1			572.8			566.6		
Adverse Events	35 (8.7)	44	7.7	50 (12.4)	72	12.6	39 (9.7)	55	9.7
SAEs	12 (3.0)	16	2.8	13 (3.2)	18	3.1	12 (3.0)	14	2.5
Severe AEs	6 (1.5)	9	1.6	10 (2.5)	14	2.4	7 (1.7)	9	1.6
Leading to Permanent treatment discontinuation	2 (0.5)	2	0.4	1 (0.2)	1	0.2	1 (0.2)	1	0.2

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYO: The duration of the in-trial period in years.
MedDRA version 22.1

2.7.4.2.2.5.3　イベント判定に基づく心血管障害

4382 試験において、セマグルチド 2.4 mg 群で計 2 例（1.0%）3 件、プラセボ群で 1 例（1.0%）1 件がイベント判定委員会に送付された。セマグルチド 2.4 mg 群の 3 件中 2 件がイベント判定委員会により心血管系事象として確定された。プラセボ群ではイベント判定委員会により確定された事象はなかった。イベント判定委員会により確定された 2 件（セマグルチド 2.4 mg 群の 1 例の被験者で認められた急性心筋梗塞及び冠動脈血行再建）は on-treatment 観察期間に報告された（表 2.7.4.2-27）。

表 2.7.4.2-27　　イベント判定委員会により確定された心血管障害の有害事象－in-trial 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	100				199				101			
Patient years of observation (PYO)	142.2				285.9				145.8			
Events sent for adjudication	0				2	(1.0)	3	1.0	1	(1.0)	1	0.7
Diagnostic criteria unmet	0				1	(0.5)	1	0.3	1	(1.0)	1	0.7
EAC confirmed cardiovascular events	0				1	(0.5)	2	0.7	0			
Acute coronary syndrome	0				1	(0.5)	1	0.3	0			
Acute myocardial infarction	0				1	(0.5)	1	0.3	0			
Indeterminate	0				1	(0.5)	1	0.3	0			
Coronary artery revascularisation	0				1	(0.5)	1	0.3	0			
Percutaneous coronary intervention	0				1	(0.5)	1	0.3	0			
On-treatment												
Yes	0				1	(0.5)	2	0.7	0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years, EAC: Event adjudication committee PYO: The duration of the in-trial period in years. The on-treatment evaluation of events is based on EAC confirmed events only. MedDRA version 23.1

4373 試験では、セマグルチド 2.4 mg 群で計 11 例（0.8%）16 件、プラセボ群で計 4 例（0.6%）5 件がイベント判定委員会に送付された。セマグルチド 2.4 mg 群では、16 件中 8 件が心血管系事象としてイベント判定委員会により確定された。プラセボ群では、5 件中 4 件が心血管系事象としてイベント判定委員会により確定された。イベント判定委員会により確定された心血管系事象を発現した被験者の割合は全体的に低く、投与群間で同様であった（セマグルチド 2.4 mg 群で 0.5%及びプラセボ群で 0.6%）。イベント判定委員会により確定された事象には、急性心筋梗塞、不安定狭心症、脳卒中及び冠動脈血行再建が含まれた。On-treatment 観察期間後の in-trial 観察期間内に発現したセマグルチド 2.4 mg 群の 1 例 2 件（急性心筋梗塞及び冠動脈血行再建）を除き、イベント判定委員会により確定されたいずれの事象も on-treatment 観察期間に報告された（表 2.7.4.2-28）。

表 2.7.4.2-28　　イベント判定委員会により確定された心血管障害の有害事象－in-trial 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R
Number of subjects	1306				655			
Patient years of observation (PYO)	1856.4				918.5			
Events sent for adjudication	11	(0.8)	16	0.9	4	(0.6)	5	0.5
Duplicate events	3	(0.2)	3	0.2	0			
Diagnostic criteria unmet	5	(0.4)	5	0.3	1	(0.2)	1	0.1
EAC confirmed cardiovascular events	6	(0.5)	8	0.4	4	(0.6)	4	0.4
Acute coronary syndrome	4	(0.3)	4	0.2	3	(0.5)	3	0.3
Acute myocardial infarction	3	(0.2)	3	0.2	3	(0.5)	3	0.3
ST elevation myocardial infarction	1	(<0.1)	1	0.1	0			
Non-ST elevation myocardial infarction	1	(<0.1)	1	0.1	1	(0.2)	1	0.1
Indeterminate	1	(<0.1)	1	0.1	2	(0.3)	2	0.2
Unstable angina pectoris	1	(<0.1)	1	0.1	0			
Resting ECG changes	1	(<0.1)	1	0.1	0			
Cerebrovascular events	1	(<0.1)	1	0.1	1	(0.2)	1	0.1
Stroke	1	(<0.1)	1	0.1	1	(0.2)	1	0.1
Ischemic stroke	1	(<0.1)	1	0.1	1	(0.2)	1	0.1
Coronary artery revascularisation	3	(0.2)	3	0.2	0			
Percutaneous coronary intervention	2	(0.2)	2	0.1	0			
Coronary artery bypass graft	1	(<0.1)	1	0.1	0			
On-treatment								
Yes	5	(0.4)	6	0.3	4	(0.6)	4	0.4
No	1	(<0.1)	2	0.1	0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years, EAC: Event adjudication committee PYO: The duration of the in-trial period in years. The on-treatment evaluation of events is based on EAC confirmed events only. MedDRA version 22.1

4374 試験では、セマグルチド 2.4 mg 群で計 13 例（3.2%）17 件、セマグルチド 1.0 mg 群で計 7 例（1.7%）10 件、プラセボ群で計 8 例（2.0%）13 件がイベント判定委員会に送付された。セマグルチド 2.4 mg 群、セマグルチド 1.0 mg 群及びプラセボ群で、それぞれ 17 件中 6 件、10 件中 7 件及び 13 件中 7 件がイベント判定委員会により心血管系事象として確定された。イベント判定委員会により確定された心血管系事象を発現した被験者の割合は、全体的に低く、投与群間で同様であった（セマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群で 1.5%、プラセボ群で 1.2%）（表 2.7.4.2-29）。イベント判定委員会により確定された事象には、急性心筋梗塞、不安定狭心症、脳卒中、一過性脳虚血発作、冠動脈

血行再建及び心不全が含まれた。イベント判定委員会により確定されたすべての事象が on-treatment 観察期間に報告された。

表 2.7.4.2-29　　イベント判定委員会により確定された心血管障害の有害事象－in-trial 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	402				403				402			
Patient years of observation (PYO)	569.1				572.8				566.6			
Events sent for adjudication	7	(1.7)	10	1.8	13	(3.2)	17	3.0	8	(2.0)	13	2.3
Events unable to adjudicate due to insufficient information	0				1	(0.2)	1	0.2	0			
Duplicate events	0				0				3	(0.7)	3	0.5
Diagnostic criteria unmet	2	(0.5)	3	0.5	8	(2.0)	10	1.7	3	(0.7)	3	0.5
EAC confirmed cardiovascular events	6	(1.5)	7	1.2	6	(1.5)	6	1.0	5	(1.2)	7	1.2
Acute coronary syndrome	3	(0.7)	3	0.5	2	(0.5)	2	0.3	1	(0.2)	1	0.2
Acute myocardial infarction	3	(0.7)	3	0.5	1	(0.2)	1	0.2	1	(0.2)	1	0.2
ST elevation myocardial infarction	0				1	(0.2)	1	0.2	0			
Non-ST elevation myocardial infarction	3	(0.7)	3	0.5	0				0			
Indeterminate	0				0				1	(0.2)	1	0.2
Unstable angina pectoris	0				1	(0.2)	1	0.2	0			
Resting ECG changes	0				1	(0.2)	1	0.2	0			
Coronary lesion on angiography	0				1	(0.2)	1	0.2	0			
Cerebrovascular events	1	(0.2)	1	0.2	3	(0.7)	3	0.5	3	(0.7)	3	0.5
Stroke	1	(0.2)	1	0.2	3	(0.7)	3	0.5	2	(0.5)	2	0.4
Ischemic stroke	1	(0.2)	1	0.2	3	(0.7)	3	0.5	2	(0.5)	2	0.4
Transient ischemic attack	0				0				1	(0.2)	1	0.2
Coronary artery revascularisation	3	(0.7)	3	0.5	0				1	(0.2)	1	0.2
Percutaneous coronary intervention	3	(0.7)	3	0.5	0				1	(0.2)	1	0.2
Heart failure	0				1	(0.2)	1	0.2	2	(0.5)	2	0.4
Heart failure hospitalization	0				1	(0.2)	1	0.2	2	(0.5)	2	0.4
On-treatment												
Yes	6	(1.5)	7	1.2	6	(1.5)	6	1.0	5	(1.2)	7	1.2

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years, EAC: Event adjudication committee PYO: The duration of the in-trial period in years. The on-treatment evaluation of events is based on EAC confirmed events only. MedDRA version 22.1

2.7.4.2.2.5.4　脈拍数

日本人被験者が参加した 3 つのいずれの第 3 相試験でも、セマグルチド群（1.0、1.7 及び 2.4 mg）で脈拍数の増加が認められた。脈拍数の増加は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で同様又は大きかった。脈拍数のベースラインから 68 週までの変化量の平均における投与群間の差の推定値（セマグルチド 2.4 mg 群 - プラセボ群）は、3 つの試験において 1.95～4.26 拍／分であった。4382 試験における脈拍数のベースラインから 68 週までの変化量の平均における投与群間の差の推定値（セマグルチド 1.7 mg 群 - プラセボ群）は 3.86 拍／分であり、4374 試験における脈拍数のベースラインから 68 週までの変化量の平均における投与群間の差の推定値（セマグルチド 2.4 mg 群 - セマグルチド 1.0 mg 群）は 0.71 拍／分であった（表 2.7.4.2-30）。4382 及び 4374 試験のベースライン以降の脈拍数の増加において、セマグルチドの明らかな用量反応関係はみられなかった〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.6.3、4374 試験（Module 5.3.5.1）EOT Figure 14.3.6.3〕。セマグルチドで認められた脈拍数の増加は、2 型糖尿病に対するセマグルチド皮下投与（オゼンピック皮下注）[52, 53, 54]及びセマグルチド経口投与（リベルサス錠）[47, 55]で報告された所見と同様であった。

表 2.7.4.2-30　　脈拍数（拍／分）のベースライン値及びベースラインから投与終了時の変化量－on-treatment 観察期間（4382、4373 及び 4374 試験）

	Trial 4382			Trial 4373		Trial 4374		
	Sema 2.4 mg	Sema 1.7 mg	Placebo	Sema 2.4 mg	placebo	Sema 2.4 mg	Sema 1.0 mg	Placebo
N (baseline/week 68)	199/186	100/93	101/98	1306/950	655/443	403/320	402/326	402/313
Baseline	73	73	73	72	72	75	76	76
Change from baseline at week 68	4.38	6.29	2.43	3.52	-0.74	2.49	1.77	-0.23
Treatment difference (Sema 2.4 mg – Placebo) [95% CI]	1.95 [-0.13; 4.03]	-	-	4.26 [3.38; 5.15]*	-	2.71 [1.43; 3.99]*	-	-
Treatment difference (Sema 1.7 mg – Placebo) [95% CI]	-	3.86 [1.45; 6.27]**	-	-	-	-	-	-
Treatment difference (Sema 2.4 mg – Sema 1.0 mg) [95% CI]	-	-	--	-	-	-	0.71 [-0.56; 1.99]	-

* p<0.0001, ** p<0.01

N: Number of subjects, CI: Confidence interval.

Analysis of data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days. MMRM: All responses for all randomised subject prior to first discontinuation of treatment (or initiation of other anti-obesity medication or bariatric surgery) were included in a mixed model for repeated measurements with randomised treatment as factor and baseline pulse as covariate, all nested within visit.

セマグルチド群における脈拍数の増加は、試験初期の期間に増加し、その後はわずかな減少が認められた。投与終了後に実施された事後調査来院（75 週）では、脈拍数の平均はベースライン値のレベルに戻っていた〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.6.3、4373 試験（Module 5.3.5.1）EOT Figure 14.3.6.3、4374 試験（Module 5.3.5.1）EOT Figure 14.3.6.3〕。

いずれの試験においても、on-treatment 観察期間に脈拍数の増加の最高値が 20 拍／分以上であった被験者の割合は、プラセボ群と比較してセマグルチド群で高かった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.6.4、4373 試験（Module 5.3.5.1）EOT Table 14.3.6.4、4374 試験（Module 5.3.5.1）EOT Table 14.3.6.4〕。

2.7.4.2.2.5.5　心電図

日本人被験者が参加した 3 つの第 3 相試験では、無作為割り付け時（0 週）、20 週及び 68 週に 12 誘導心電図を測定した。

ベースラインから 20 週及び 68 週のまでの全体的な心電図評価の変化の要約に基づくと、いずれの試験でも投与群間で明らかな違いは認められなかった。被験者の大部分においてベースライン時の心電図所見は「正常」であり、治験期間を通して「正常」のままであった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.6.6、4373 試験（Module 5.3.5.1）EOT Table 14.3.6.6、4374 試験（Module 5.3.5.1）EOT Table 14.3.6.6〕。

2.7.4.2.2.5.6　QTc 評価

4382 試験では東アジア人集団（日本及び韓国）を対象に、セマグルチド 2.4 mg の曝露量における QTcF の変化量についての曝露量－反応関係を評価するために、心電図評価時に定常状態の薬物動態評価用検体を採取した。セマグルチド 2.4 mg の用量において、QTcF 間隔の変化量について曝露量－反応関係を示す所見は認められなかった（詳細は Module 2.7.2.4.1 に示す）。

QTcF 間隔が事前に規定した閾値である 450 msec、480 msec 又は 500 msec を超えた被験者の割合は、ベースライン、20 週及び 68 週のいずれにおいても低く、その頻度について投与群間で明らかな違いはなかった〔4382 試験（Module 5.3.5.1）Table 12-17〕。セマグルチド 1.7 mg 群の 1 例の男性被験者が on-treatment 観察期間中に QTcF 間隔が 500 msec 超であった〔4382 試験（Module 5.3.5.1）EOT Listing 14.3.7.8〕。

ベースラインからの QTcF 間隔の変化量が 30 msec を超えた被験者の割合は、20 週及び 68 週のいずれにおいても低く、投与群間で明らかな違いは認められなかった〔4382 試験（Module 5.3.5.1）Table 12-18〕。QTcF 間隔のベースラインからの変化量が 60 msec を超えた被験者はいなかった。

2 例の被験者（いずれもセマグルチド 1.7 mg 群）において、QTc に関連する有害事象が報告された。これらの被験者については表 2.7.4.2-31 に示す。

表 2.7.4.2-31　　QTc に関する有害事象の詳細－on-treatment 観察期間

Subject ID/ Age/Sex/BMI	Week/Trial day/ Duration	Preferred term/Seriousness/Severity/ Causality/Action/Outcome	Relevant details
Sema 1.7 mg			
120006/ 5[redacted]/F/33.0	20/141/ 113	Electrocardiogram QT Prolonged/Non-serious/ Mild/Unlikely/No changes/Recovered	QTcF interval 444 msec
115028/ 4[redacted]/M/28.7	20/141/ 57	Electrocardiogram QRS Complex/Non-serious/ Mild/Unlikely/No changes/Recovered	QTcF interval 426 msec

2.7.4.2.2.5.7　　結論

結論として、日本人被験者が参加した 3 つの第 3 相試験（4382、4373 及び 4374 試験）において、心血管障害の MedDRA 検索で特定された事象、イベント判定委員会により確定された心血管系事象及び心電図評価に基づくと、心血管系事象に関連するリスクの増加は認められなかった。4382 試験における推定された QTcF 間隔の評価に基づくと、QTcF 間隔に対するセマグルチドの影響は認められなかった。いずれの試験でも、セマグルチド群（1.0、1.7 及び 2.4 mg）で平均脈拍数の増加が認められたが、2 型糖尿病に対するセマグルチド皮下投与及びセマグルチド経口投与で報告された所見と同様であった。

現在得られている包括的な非臨床及び臨床のエビデンスにより、セマグルチドが心血管イベントリスクを上昇させることは示唆されておらず、このことは市販されている GLP-1 受容体作動薬から得られた広範なデータと同様である[46, 47, 48, 49, 50, 51, 52]。

2.7.4.2.2.6　　新生物

2.7.4.2.2.6.1　　背景及び評価方法

疫学的エビデンスから、肥満は、消化器系の癌（食道腺癌、胃噴門部癌及び結腸直腸癌など）、膵癌及び乳癌（閉経後の女性）を含む様々な種類の悪性新生物の発症リスクが高いことが示唆されている[56, 57]。このことから、肥満症のためのセマグルチドの第 3 相試験において悪性新生物を注目すべき安全性領域として定義した。

セマグルチド[14, 15]及び他の既承認の GLP-1 受容体作動薬[16, 23, 24, 25, 26]は、変異原性又は遺伝毒性はないと考えられている。

ヒト甲状腺に GLP-1 受容体が認められないことから、ヒトでの関連は低いと考えられるげっ歯類の C 細胞腫瘍の所見に基づき、甲状腺髄様癌（MTC）は GLP-1 受容体作動薬における注目すべき安全性領域である。このことから、C 細胞過形成を特定するために、試験期間を通してカルシトニン値を測定した。

インクレチン関連薬と膵新生物との関連の可能性がこれまでに示されている[58]。現時点では、GLP-1 受容体作動薬による治療より膵癌のリスクが増加することを示すことは、非臨床試験、臨床試験及び市販後のデータから裏付けられていないが[59, 60]、GLP-1 受容体作動薬を投与する臨床試験における膵新生物の評価は依然として注目すべき安全性領域である。

全体として、GLP-1 受容体作動薬はヒトにおいて悪性新生物のリスクの増加には関連しないと考えられている [60, 61, 62]。

肥満症のためのセマグルチド 2.4 mg のすべての第 3 相試験では、以下に該当する被験者は、試験への組み入れから除外した：

- 悪性腫瘍（皮膚の基底細胞癌又は有棘細胞癌、及びすべての上皮内癌を除く）の既往歴（過去 5 年以内）を有する被験者
- 本人又は家族（第一度近親者）が、多発性内分泌腫瘍症候群 2 型又は甲状腺髄様癌の既往歴を有する被験者
- スクリーニング時のカルシトニンが 100 ng/L 以上の被験者

試験期間中のいずれかの時点でカルシトニンが 100 ng/L 以上であった被験者は、さらなる評価のために甲状腺の専門医に紹介され、治験薬の投与を中止することとした。

肥満症のためのセマグルチド 2.4 mg の開発プログラムで報告された新生物の事象〔良性及び悪性（ポリープ及び嚢胞を含む）〕を特定し、提示するために、治験責任医師が報告したすべての有害事象に対して事前に規定した MedDRA 検索を実施した。すべての悪性新生物を特定するために、悪性腫瘍の有害事象を特定するための事前に規定した MedDRA 検索を実施した。これらすべての検索に含まれる用語は、4382 試験（Module 5.3.5.1）Appendix 16.1.9、4373 試験（Module 5.3.5.1）Appendix 16.1.9 及び 4374 試験（Module 5.3.5.1）Appendix 16.1.9 に示す。投与と関連のある新生物の発現には長い時間を要すると考えられたため、これらの事象は in-trial 観察期間に基づき評価した。

第 3 相試験では、悪性新生物に関する追加データを事象特有のフォームで収集した。乳癌、大腸新生物及び皮膚癌については、スクリーニング時に既往歴を収集した。さらに、乳癌及び大腸新生物については、投与終了来院及び試験終了来院において全集団（乳癌についてはすべての女性被験者）を対象に検査及び検査理由（スクリーニング目的又は症状）に関する追加データを収集した。

2.7.4.2.2.6.2　新生物の有害事象

日本人被験者が参加した 3 つの第 3 相試験において、すべての新生物の有害事象を発現した被験者の割合はいずれの投与群でも同程度であった（表 2.7.4.2-32、表 2.7.4.2-33 及び表 2.7.4.2-34）。器官別大分類での全体的な新生物の発現頻度についても、投与群間で違いは認められなかった。新生物の事象は、複数の器官別大分類及び基本語に分布しており、器官別大分類及び個々の基本語に特定の傾向は認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.72、4373 試験（Module 5.3.5.1）EOT Table14.3.1.61、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.68〕。

いずれの試験及び投与群においても、新生物の事象の大部分は非重篤、軽度又は中等度であり、治験責任医師により治験薬との因果関係は「なし」と判定された〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.71、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.60、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.67〕。3 つのいずれの試験でも、新生物の重篤な有害事象を発現した被験者の割合について投与群間で明らかな違いは認められなかった（表 2.7.4.2-32、表 2.7.4.2-33 及び表 2.7.4.2-34）。各試験において、約半分の新生物の有害事象の転帰は「回復」と報告され、残りの約半分の事象の転帰は「未回復」と報告された。4373 試験及び 4374 試験のプラセボ群の各 1 例が、転帰「死亡」の新生物の事象

（「神経膠芽細胞腫」及び「肝細胞癌」）を発現した。転帰「死亡」の事象に関する詳細な情報については、2.7.4.2.1.2 項に示す。3 つの第 3 相試験において、治験薬投与の中止に至った新生物の事象の発現件数は少なく、投与群間で明らかな違いは認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.71、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.60、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.67〕。

4382 及び 4374 試験において、新生物のすべての有害事象及び重篤な有害事象に用量反応性を示唆される所見は認められなかった（表 2.7.4.2-32 及び表 2.7.4.2-34）。

表 2.7.4.2-32　新生物の有害事象－MedDRA 検索－in-trial 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	100			199			101		
Patient years of observation (PYO)	142.2			285.9			145.8		
Adverse Events	8 (8.0)	8	5.6	10 (5.0)	14	4.9	4 (4.0)	5	3.4
SAEs	3 (3.0)	3	2.1	1 (0.5)	1	0.3	1 (1.0)	1	0.7

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYO: The duration of the in-trial period in years. MedDRA version 23.1

表 2.7.4.2-33　新生物の有害事象－MedDRA 検索－in-trial 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R
Number of subjects	1306			655		
Patient years of observation (PYO)	1856.4			918.5		
Adverse Events	93 (7.1)	112	6.0	49 (7.5)	56	6.1
SAEs	12 (0.9)	12	0.6	5 (0.8)	5	0.5

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYO: The duration of the in-trial period in years. MedDRA version 22.1

表 2.7.4.2-34　新生物の有害事象－MedDRA 検索－in-trial 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	402			403			402		
Patient years of observation (PYO)	569.1			572.8			566.6		
Adverse Events	29 (7.2)	36	6.3	21 (5.2)	27	4.7	28 (7.0)	34	6.0
SAEs	8 (2.0)	8	1.4	4 (1.0)	4	0.7	5 (1.2)	6	1.1

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYO: The duration of the in-trial period in years. MedDRA version 22.1

2.7.4.2.2.6.3　悪性新生物

日本人被験者が参加した 3 つの第 3 相試験において、悪性新生物の有害事象を発現した被験者の割合は投与群間で同程度であった（表 2.7.4.2-35、表 2.7.4.2-36 及び表 2.7.4.2-37）。いずれの試験及び投与群間においても、特定の種類の悪性新生物の有害事象が多く認められることはなかった。3 つの試験において、甲状腺髄様癌及び膵癌の報告はなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.35、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.35、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.35〕。

4382 試験では、すべての悪性新生物の事象が重篤な有害事象であった。4373 試験では、両投与群で約半分の悪性新生物の事象が重篤な有害事象であった。4374 試験では、セマグルチド 2.4 mg 群は 3 分の 1 の事象が重篤な有害事象であったが、セマグルチド 1.0 mg 群とプラセボ群では大部分の事象が重篤な有害事象であった。3 つの第 3 相試験において、事象の重症度について投与群間で明らかな違いは認められなかった（表 2.7.4.2-35、表 2.7.4.2-36 及び表 2.7.4.2-37）。大部分の事象が治験責任医師により治験薬との因果関係は「なし」と判定され、転帰は「回復」であった。4373 及び 4374 試験のプラセボ群の各 1 例が、転帰「死亡」の事象（「神経膠芽細胞腫」及び「肝細胞癌」）を発現した。3 つの第 3 相試験において、悪性新生物の事象により治験薬の投与を中止した被験者は少なく（各投与群で 3 例以下）、投与群間で明らかな違いは認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.34、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.34、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.34〕。

4382 及び 4374 試験において、悪性新生物のすべての有害事象及び重篤な有害事象に用量反応性を示す所見は認められなかった（表 2.7.4.2-35 及び表 2.7.4.2-37）。

表 2.7.4.2-35　悪性新生物の有害事象－MedDRA 検索－in-trial 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg N (%) E R	Sema 2.4 mg N (%) E R	Placebo N (%) E R
Number of subjects	100	199	101
Patient years of observation (PYO)	142.2	285.9	145.8
Adverse Events	2 (2.0) 2 1.4	0	1 (1.0) 1 0.7
SAEs	2 (2.0) 2 1.4	0	1 (1.0) 1 0.7
Severity			
Severe	2 (2.0) 2 1.4	0	1 (1.0) 1 0.7
Moderate	0	0	0
Mild	0	0	0
Outcome			
Fatal	0	0	0
Recovered	2 (2.0) 2 1.4	0	1 (1.0) 1 0.7
Recovering	0	0	0
Recovered With Sequelae	0	0	0
Not Recovered	0	0	0
Unknown	0	0	0

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYO: The duration of the in-trial period in years. MedDRA version 23.1

表 2.7.4.2-36　悪性新生物の有害事象－MedDRA 検索－in-trial 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R
Number of subjects	1306				655			
Patient years of observation (PYO)	1856.4				918.5			
Adverse Events	14	(1.1)	14	0.8	7	(1.1)	7	0.8
SAEs	7	(0.5)	7	0.4	3	(0.5)	3	0.3
Severity								
Severe	2	(0.2)	2	0.1	2	(0.3)	2	0.2
Moderate	4	(0.3)	4	0.2	4	(0.6)	4	0.4
Mild	8	(0.6)	8	0.4	1	(0.2)	1	0.1
Outcome								
Fatal	0				1	(0.2)	1	0.1
Recovered	8	(0.6)	8	0.4	4	(0.6)	4	0.4
Recovering	3	(0.2)	3	0.2	0			
Recovered With Sequelae	0				0			
Not Recovered	3	(0.2)	3	0.2	2	(0.3)	2	0.2
Unknown	0				0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYO: The duration of the in-trial period in years. MedDRA version 22.1

表 2.7.4.2-37　悪性新生物の有害事象－MedDRA 検索－in-trial 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	402			403			402		
Patient years of observation (PYO)	569.1			572.8			566.6		
Adverse Events	7 (1.7)	8	1.4	5 (1.2)	6	1.0	8 (2.0)	9	1.6
SAEs	7 (1.7)	7	1.2	2 (0.5)	2	0.3	5 (1.2)	6	1.1
Severity									
Severe	2 (0.5)	3	0.5	1 (0.2)	1	0.2	4 (1.0)	5	0.9
Moderate	5 (1.2)	5	0.9	3 (0.7)	4	0.7	1 (0.2)	1	0.2
Mild	0			1 (0.2)	1	0.2	3 (0.7)	3	0.5
Outcome									
Fatal	0			0			1 (0.2)	1	0.2
Recovered	2 (0.5)	2	0.4	3 (0.7)	4	0.7	2 (0.5)	2	0.4
Recovering	0			0			0		
Recovered With Sequelae	2 (0.5)	2	0.4	0			0		
Not Recovered	3 (0.7)	4	0.7	2 (0.5)	2	0.3	6 (1.5)	6	1.1
Unknown	0			0			0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYO: The duration of the in-trial period in years. MedDRA version 22.1

2.7.4.2.2.6.4　カルシトニン

C 細胞過形成の可能性のある事象を特定するために、試験期間を通してカルシトニン値を測定した。カルシトニンのデータは、on-treatment 観察期間に基づき評価した。

平均値の経時推移

日本人被験者が参加した 3 つの第 3 相試験において、ベースライン時のカルシトニンの平均値はセマグルチド群（1.0、1.7 及び 2.4 mg）とプラセボ群で同様であった。On-treatment 観察期間において、いずれの投与群でもカルシトニンの平均値はわずかに減少したものの安定していた（表 2.7.4.2-38、表 2.7.4.2-39 及び表 2.7.4.2-40）。

個々の被験者における高値

日本人被験者が参加した 3 つの第 3 相試験において、高値を示したそれぞれのカルシトニンについて注目すると、ベースラインから 68 週までに基準範囲上限を超えた被験者の割合に、明らかな変化は認められなかった（表 2.7.4.2-38、表 2.7.4.2-39 及び表 2.7.4.2-40）。

カルシトニンの経時推移、ならびにベースライン以降の最低値と最高値を示す箱ひげ図〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.14、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.13、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.14〕に基づくと、20 週から 68 週のカルシトニン値に変化はなく、ベースライン以降の最高値について投与群間で違いはみられなかった〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.15、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.14、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.15〕。

4374 試験では、on-treatment 観察期間においてカルシトニン値が 50 ng/L 以上であった検体が 1 つ認められた。セマグルチド 2.4 mg 群の男性被験者から得られた検体であり、スクリーニング来院時のカルシトニン値が 50 ng/L 以上であった。本被験者は甲状腺の専門医を受診するよう勧められ、その後、甲状腺乳頭癌と診断された〔詳細は 4374 試験（Module 5.3.5.1）Section 12.5.7.2、12.5.7.3 に示す〕。3 つの試験において、カルシトニン値が 100 ng/L 以上に増加した被験者はいなかった。

表 2.7.4.2-38　カルシトニンのベースライン値、68 週のベースラインに対する比ならびにベースライン及び 68 週のカテゴリーの要約－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg Geometric mean (CV)	Sema 2.4 mg Geometric mean (CV)	Placebo Geometric mean (CV)
Number of subjects	100	199	101
Calcitonin (ng/L)			
Mean level at baseline	1.4 (77.5)	1.3 (66.8)	1.2 (47.7)
Ratio to baseline at week 68	0.98 (32.4)	0.95 (34.6)	0.94 (30.6)
Categorical summary (N (%))			
Visit 1 (week -1)			
N	100 (100)	199 (100)	101 (100)
Low (<LLN)	0	0	0
Normal	96 (96.0)	195 (98.0)	100 (99.0)
High (>ULN)	4 (4.0)	4 (2.0)	1 (1.0)
Visit 24 (week 68)			
N	93 (93.0)	186 (93.5)	98 (97.0)
Low (<LLN)	0	0	0
Normal	90 (96.8)	184 (98.9)	98 (100)
High (>ULN)	3 (3.2)	2 (1.1)	0

CV: Coefficient of variation in %. N: Number of subjects with an observation at the visit,
%: Percentages are based on subjects with an observation at the visit, LLN: Lower limit normal,
ULN: Upper limit normal.
Observed data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.

表 2.7.4.2-39　カルシトニンのベースライン値、68 週のベースラインに対する比ならびにベースライン及び 68 週のカテゴリーの要約－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg Geometric mean (CV)	Placebo Geometric mean (CV)
Number of subjects	1306	655
Calcitonin (ng/L)		
Mean level at baseline	1.4 (77.3)	1.3 (77.4)
Ratio to baseline at week 68	0.99 (37.6)	0.95 (40.9)
Categorical summary (N (%))		
Visit 1 (week -1)		
N	1306 (100)	655 (100)
Low (<LLN)	0	0
Normal	1242 (95.1)	623 (95.1)
High (>ULN)	64 (4.9)	32 (4.9)
Visit 24 (week 68)		
N	1050 (80.4)	497 (75.9)
Low (<LLN)	0	0
Normal	992 (94.5)	478 (96.2)
High (>ULN)	58 (5.5)	19 (3.8)

CV: Coefficient of variation in %. N: Number of subjects with an observation at the visit,
%: Percentages are based on subjects with an observation at the visit, LLN: Lower limit normal,
ULN: Upper limit normal.
Observed data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.

表 2.7.4.2-40　カルシトニンのベースライン値、68 週のベースラインに対する比ならびにベースライン及び 68 週のカテゴリーの要約－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg Geometric mean (CV)	Sema 2.4 mg Geometric mean (CV)	Placebo Geometric mean (CV)
Number of subjects	401	403	402
Calcitonin (ng/L)			
Mean level at baseline	1.8 (112.6)	1.7 (111.9)	1.7 (108.1)
Ratio to baseline at week 68	0.95 (50.9)	0.94 (60.3)	0.96 (38.6)
Categorical summary (N (%))			
Visit 1 (week -1)			
N	401 (99.8)	403 (100)	402 (100)
Low (<LLN)	0	0	0
Normal	359 (89.5)	364 (90.3)	366 (91.0)
High (>ULN)	42 (10.5)	39 (9.7)	36 (9.0)
Visit 24 (week 68)			
N	350 (87.1)	348 (86.4)	339 (84.3)
Low (<LLN)	0	0	0
Normal	321 (91.7)	317 (91.1)	322 (95.0)
High (>ULN)	29 (8.3)	31 (8.9)	17 (5.0)

CV: Coefficient of variation in %. N: Number of subjects with an observation at the visit, %: Percentages are based on subjects with an observation at the visit, LLN: Lower limit normal, ULN: Upper limit normal.
Observed data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.

2.7.4.2.2.6.5　結論

全体として、プラセボと比較してセマグルチドですべての新生物（良性及び悪性）又は悪性新生物のリスクの増加は認められなかった。

日本人被験者が参加した 3 つの第 3 相試験（4382、4373 及び 4374 試験）において、すべての新生物（良性及び悪性）の有害事象を発現した被験者の割合は、投与群間で同様であった。

3 つの第 3 相試験において、悪性新生物の有害事象の発現件数は少なく、これらの事象を発現した被験者の割合は、投与群間で同様であった。報告された悪性新生物の種類についても、セマグルチド群（1.0、1.7 及び 2.4 mg）とプラセボ群の間で明らかな違いは認められなかった。また 3 つの第 3 相試験において、甲状腺髄様癌及び膵癌の報告はなかった。

4374 試験では、1 例の被験者のスクリーニング時におけるカルシトニン値が 50 ng/L を超えた。3 つの試験について、カルシトニン値が 100 ng/L を超えた被験者はいなかった。

以上のことから、臨床開発プログラムから得られたデータに基づくと、いずれの種類の新生物もセマグルチドとの関連性は裏付けられなかった。これは、2 型糖尿病に対するセマグルチド皮下投与（オゼンピック皮下注）[14]及びセマグルチド経口投与（リベルサス錠）[15]を含む GLP-1 受容体作動薬での現在の知見[61, 62]と同様であった。

2.7.4.2.2.7　肝障害

2.7.4.2.2.7.1　背景及び評価方法

市販されている GLP-1 受容体作動薬[16, 23, 26]において肝毒性は認められておらず、セマグルチドの毒性試験でもセマグルチドの投与に関連する肝毒性は示されていない。セマグルチドは全身に広く分布する酵素によって代謝され、セマグルチドの代謝を単独で担う臓器はない。2 型糖尿病に対するセマグ

ルチド皮下投与の臨床開発プログラムで実施された肝機能障害（軽度、中等度及び重度）を有する被験者を対象とした臨床薬理試験（NN9535-3651 試験）では、セマグルチドの曝露量は肝機能障害の影響を受けず、軽度、中等度、重度の肝機能障害を有する被験者でのセマグルチドの薬物動態特性は、肝機能正常の被験者と同様であった（2.7.4.5.2 項）。2 型糖尿病に対するセマグルチド皮下投与及びセマグルチド経口投与の臨床開発プログラムにおいて、肝に対する安全性に関連する問題は認められなかった。

セマグルチドの肝に対する安全性を評価するために、肝障害を注目すべき安全性領域とし、事前に規定した MedDRA 検索で特定された肝障害の有害事象〔検索に含まれる用語は、4382 試験（Module 5.3.5.1）Appendix 16.1.9、4373 試験（Module 5.3.5.1）Appendix 16.1.9、4374 試験（Module 5.3.5.1）Appendix 16.1.9〕、ならびに肝機能パラメータ〔ALT、AST、アルカリホスファターゼ及び総ビリルビン（日本人被験者が参加したすべての第 3 相試験で検討）及び GGT（4373 及び 4374 試験で検討）〕を評価した。肝機能の悪化又は肝障害を有する被験者は、肥満症のための第 3 相試験から除外されなかった。

以下に示す 2 つの評価を除き、すべての肝機能障害及び臨床検査データに関するすべてのデータは、on-treatment 観察期間に基づき評価した：

- ALT 又は AST が基準範囲上限の 3 倍を超え、かつ総ビリルビンが基準範囲上限の 2 倍を超えた被験者については、in-trial 観察期間を用い、予定来院及び予定外来院のデータを含めて評価した。
- ベースライン以降のいずれかの時点（予定来院及び予定外来院を含む）で ALT が基準範囲上限の 5 倍を超えた被験者については、in-trial 観察期間を用いて評価した。

2.7.4.2.2.7.2　肝障害の有害事象

日本人被験者が参加した 3 つの第 3 相試験において、4382 と 4374 試験では少ない発現件数に基づくが、すべての用量のセマグルチド群（1.0、1.7 及び 2.4 mg）での肝障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と同様であった（表 2.7.4.2-41、表 2.7.4.2-42 及び表 2.7.4.2-43）。肝障害の有害事象の大部分が、非重篤で、軽度又は中等度であり、治験薬投与の中止には至らなかった。事象の重症度、治験責任医師による治験薬との因果関係の評価、及び転帰について、投与群間で明らかな違いは認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.45、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.43、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.43〕。4374 試験において、プラセボ群の 1 例が肝障害（「肝細胞癌」）のために死亡した〔4374 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.8〕。

4382 試験では、器官別大分類及び基本語について投与群間で明らかな違いは認められず、特定の事象が多く報告されることもなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.46〕。4373 試験では、高頻度で報告された肝臓に関する有害事象は、「脂肪肝」、「γ-グルタミルトランスフェラーゼ増加」及び「肝酵素上昇」であり、これらの事象の発現頻度及び単位時間あたりの発現件数に投与群間で明らかな違いは認められなかった〔4373 試験（Module 5.3.5.1）EOT Table 14.3.1.44〕。4374 試験では、高頻度で報告された肝臓に関する有害事象は「脂肪肝」であり、発現頻度及び単位時間あたりの発現件数に投与群間で明らかな違いは認められなかった〔4374 試験（Module 5.3.5.1）EOT Table 14.3.1.44〕。

4382 及び 4374 試験において、肝臓に関する有害事象を発現した被験者の割合及び単位時間あたりの発現件数について、セマグルチドとの用量反応関係は認められなかった（表 2.7.4.2-41 及び表 2.7.4.2-43）

肝臓に関する有害事象について追加データ収集のためのフォームで収集された個々の事象の詳細は、4382 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.22、4373 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.21 及び 4374 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.22 に示す。

表 2.7.4.2-41　肝障害の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	100			199			101		
Patient years of exposure (PYE)	136.2			275.0			141.8		
Adverse Events	1 (1.0)	1	0.7	4 (2.0)	4	1.5	5 (5.0)	5	3.5
SAEs	0			0			0		
Severe AEs	0			0			0		
Leading to Permanent treatment discontinuation	0			0			0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 23.1

表 2.7.4.2-42　肝障害の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R
Number of subjects	1306			655		
Patient years of exposure (PYE)	1706.1			829.6		
Adverse Events	31 (2.4)	37	2.2	20 (3.1)	24	2.9
SAEs	1 (0.1)	1	0.1	0		
Severe AEs	2 (0.2)	2	0.1	1 (0.2)	1	0.1
Leading to Permanent treatment discontinuation	1 (0.1)	1	0.1	0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

表 2.7.4.2-43　肝障害の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	402				403				402			
Patient years of exposure (PYE)	529.8				533.0				528.3			
Adverse Events	10	(2.5)	11	2.1	10	(2.5)	12	2.3	14	(3.5)	21	4.0
SAEs	0				1	(0.2)	2	0.4	1	(0.2)	1	0.2
Severe AEs	0				1	(0.2)	2	0.4	1	(0.2)	1	0.2
Leading to Permanent treatment discontinuation	1	(0.2)	1	0.2	0				1	(0.2)	1	0.2

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.2.2.7.3　肝臓に関連する臨床検査パラメータに基づく肝臓の安全性

肝機能のマーカー〔AST、ALT、アルカリホスファターゼ及び総ビリルビン（日本人被験者が参加したすべての第 3 相試験で検討）、ならびに GGT（4373 及び 4374 試験で検討）〕は、試験期間中、定期的に評価した。

日本人被験者が参加した 3 つの第 3 相試験において、Hy's law の定義（ALT 又は AST が基準範囲上限の 3 倍を超え、かつ総ビリルビンが基準範囲上限の 2 倍を超え、他の原因が認められない）に合致する被験者は認められなかった。4382 試験では、セマグルチド 2.4 mg 群の 1 例（被験者番号：113005、case no：673549）が Hy's law の生化学的定義に合致したが、他の原因として胆嚢疾患が認められた〔本被験者の胆嚢疾患の詳細については、4382 試験（Module 5.3.5.1）Section 12.5.8.2 及び Section 14.3.3（叙述）に示す〕。

平均値の経時推移

日本人被験者が参加した 3 つの第 3 相試験について、ベースライン時の ALT、AST、アルカリホスファターゼの平均値は投与群間で同様であった。ALT の平均値は、すべての投与群においてベースラインから 68 週まで減少したが、いずれの試験でもセマグルチド群（1.0、1.7 及び 2.4 mg）でより減少した。AST の平均値は、すべての試験において、セマグルチド群（1.0、1.7 及び 2.4 mg）において 68 週で減少した。プラセボ群については、4374 試験ではセマグルチド群と同様の傾向がみられたが、4382 と 4373 試験では AST の平均値に変化は認められなかった。アルカリホスファターゼの平均値は、4382 と 4373 試験では、セマグルチド群（1.7 及び 2.4 mg）で減少したが、プラセボ群では変化は認められなかった。4374 試験では、3 つのいずれの投与群でも、アルカリホスファターゼの平均値はベースラインから 68 週まで安定したままであった（表 2.7.4.2-44、表 2.7.4.2-45 及び表 2.7.4.2-46）。

4382 及び 4373 試験では、ベースライン時の総ビリルビンの平均値は投与群間で同様であったが、すべての投与群において 68 週で増加した。4374 試験では、ベースライン時の総ビリルビンの平均値は、セマグルチド 1.0 mg 群及びプラセボ群と比較して、セマグルチド 2.4 mg 群でわずかに低かった。ベースラインから 68 週までに、総ビリルビンの平均値は、セマグルチド 2.4 mg 群で 10%増加し、セマグルチド 1.0 mg 群とプラセボ群ではベースラインと同様の値であった。

4373 及び 4374 試験では、ベースライン時の GGT の平均値は投与群間で同様であった。ベースラインから 68 週までに、GGT の平均値は、両試験においてすべての投与群で減少した。

表 2.7.4.2-44　肝機能に関する血液生化学的検査パラメータのベースライン値及び 68 週のベースラインに対する比－on-treatment 観察期間（4382 試験）

	Sema 1.7 mg Geometric mean (CV)	Sema 2.4 mg Geometric mean (CV)	Placebo Geometric mean (CV)
Number of subjects	100	199	101
Alanine aminotransferase (U/L)			
Baseline level	32 (58.0)	33 (63.3)	34 (63.8)
Ratio to baseline at week 68	0.71 (55.3)	0.61 (59.3)	0.91 (42.2)
Alkaline phosphatase (U/L)			
Baseline level	66 (32.0)	70 (25.2)	69 (27.8)
Ratio to baseline at week 68	0.89 (17.0)	0.89 (16.7)	0.99 (16.9)
Aspartate aminotransferase (U/L)			
Baseline level	23.9 (39.2)	24.7 (45.7)	24.8 (46.1)
Ratio to baseline at week 68	0.82 (36.2)	0.75 (39.2)	0.94 (34.5)
Total bilirubin (umol/L)			
Baseline level	11.9 (44.8)	11.3 (46.8)	12.1 (49.8)
Ratio to baseline at week 68	1.04 (43.9)	1.15 (42.4)	1.15 (43.8)

CV: Coefficient of variation in %.
Observed data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.

表 2.7.4.2-45　肝機能に関する血液生化学的検査パラメータのベースライン値及び 68 週のベースラインに対する比－on-treatment 観察期間（4373 試験）

	Sema 2.4 mg Geometric mean (CV)	Placebo Geometric mean (CV)
Number of subjects	1306	655
Alanine aminotransferase (U/L)		
Baseline level	23 (57.1)	23 (56.8)
Ratio to baseline at week 68	0.74 (55.4)	0.90 (48.4)
Alkaline phosphatase (U/L)		
Baseline level	75 (27.7)	75 (28.7)
Ratio to baseline at week 68	0.90 (19.1)	0.98 (18.9)
Gamma glutamyl transferase (U/L)		
Baseline level	26 (64.0)	26 (65.8)
Ratio to baseline at week 68	0.74 (42.0)	0.92 (37.4)
Aspartate aminotransferase (U/L)		
Baseline level	20 (35.5)	20 (33.3)
Ratio to baseline at week 68	0.88 (32.6)	0.97 (32.8)
Total bilirubin (umol/L)		
Baseline level	8.7 (46.1)	8.8 (48.4)
Ratio to baseline at week 68	1.15 (38.5)	1.08 (41.1)

CV: Coefficient of variation in %.
Observed data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.

表 2.7.4.2-46　肝機能に関する血液生化学的検査パラメータのベースライン値及び 68 週のベースラインに対する比－on-treatment 観察期間（4374 試験）

	Sema 1.0 mg Geometric mean (CV)	Sema 2.4 mg Geometric mean (CV)	Placebo Geometric mean (CV)
Number of subjects	402	403	402
Alanine aminotransferase (U/L)			
Baseline level	29 (65.9)	27 (60.3)	28 (62.9)
Ratio to baseline at week 68	0.76 (57.1)	0.74 (66.1)	0.85 (44.4)
Alkaline phosphatase (U/L)			
Baseline level	77 (29.2)	77 (29.1)	79 (29.9)
Ratio to baseline at week 68	0.97 (18.8)	0.95 (17.6)	0.98 (17.8)
Gamma glutamyl transferase (U/L)			
Baseline level	35 (63.3)	33 (65.9)	34 (69.7)
Ratio to baseline at week 68)	0.75 (41.0)	0.71 (48.7)	0.86 (36.3)
Aspartate aminotransferase (U/L)			
Baseline level	22 (47.6)	22 (52.0)	22 (49.9)
Ratio to baseline at week 68	0.89 (41.8)	0.88 (55.5)	0.93 (35.8)
Total bilirubin (umol/L)			
Baseline level	9.3 (47.3)	8.8 (47.3)	9.6 (49.0)
Ratio to baseline at week 68	1.03 (38.7)	1.10 (35.8)	1.03 (38.7)

CV: Coefficient of variation in %.
Observed data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.

個々の被験者における高値

日本人被験者が参加した 3 つの第 3 相試験では、ベースライン時に、ALT 及び AST（3 つすべての試験で検討）ならびに GGT（4373 及び 4374 試験で検討）についていずれの投与群でも 70%以上の被験者が基準範囲内の値を有していた。AST が基準値範囲内であった被験者の割合に変化がみられなかった 4373 試験のプラセボ群を除き、すべての投与群において、ベースラインと比較して 68 週で改善が認められ、ALT、AST 及び GGT について基準範囲内の値を有する被験者の割合は高く、投与群間で明らかな違いは認められなかった。

すべての試験において、いずれの投与群でも 88%以上の被験者が、アルカリホスファターゼ及び総ビリルビンについて基準範囲内の値を有していた。4382 及び 4373 試験では、すべての投与群において総ビリルビンが基準範囲内であった被験者の割合はベースラインと比較して 68 週で低下したが、すべての試験のアルカリホスファターゼ及び 4374 試験の総ビリルビンについては、値が基準範囲内であった被験者の割合に変化はなかった。いずれも投与群間で明らかな違いは認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.5.3、4373 試験（Module 5.3.5.1）EOT Table 14.3.5.3、4374 試験（Module 5.3.5.1）EOT Table 14.3.5.3〕。

いずれの試験でも、ベースライン以降のいずれかの時点（予定来院及び予定外来院を含む）で、事前に規定した基準を満たす臨床検査項目の外れ値を示した被験者は少なかった：

- ALT が基準範囲上限の 5 倍超：4373 試験のプラセボ群で 1 例
- AST が基準範囲上限の 5 倍超：4382 試験のセマグルチド 2.4 mg 群で 1 例、4373 試験のセマグルチド 2.4 mg 群で 1 例及びプラセボ群で 2 例、4374 試験のプラセボ群で 1 例
- ALT が基準範囲上限の 5 倍超、かつ AST が基準範囲上限の 5 倍超：4382 試験のセマグルチド 2.4 mg 群で 1 例、4373 試験のプラセボ群で 1 例

外れ値を示した被験者の叙述については、各治験総括報告書〔4382 試験（Module 5.3.5.1）Section 14.3.3、4373 試験（Module 5.3.5.1）Section 14.3.3、4374 試験（Module 5.3.5.1）Section 14.3.3〕に示す。

2.7.4.2.2.7.4　結論

日本人被験者が参加した 3 つの第 3 相試験（4382、4373 及び 4374 試験）において、肝障害に関する事象の全体的な発現にセマグルチド群（1.0、1.7 及び 2.4 mg）とプラセボ群との間に明らかな違いはみられず、セマグルチドの用量間（1.0、1.7 及び 2.4 mg）にも明らかな違いはみられなかった。3 つの第 3 相試験において、Hy's law の定義に該当する被験者は認められなかった。試験中に ALT が基準範囲上限の 5 倍を超えた又は AST が基準範囲上限の 5 倍を超えた被験者は少なく、投与群間で明らかな違いはみられなかった。

以上のことから、肝臓の安全性データはセマグルチドの投与が肝障害を誘発しないことを支持するものであると考えられた。このことは、2 型糖尿病に対するセマグルチド皮下投与及びセマグルチド経口投与、セマグルチドの非臨床データならびに GLP-1 受容体作動薬に関する全般的な知見からも裏付けられている。

2.7.4.2.2.8　急性腎不全

2.7.4.2.2.8.1　背景及び評価方法

GLP-1 受容体作動薬による胃腸障害の副作用（悪心、下痢及び嘔吐）は、脱水や稀な例では急性腎疾患を引き起こす可能性がある。このため、急性腎不全を注目すべき安全性領域として事前に規定した。

すべての第 3 相試験において、ベースラインでの腎機能障害の程度を、KDIGO 2012[63]により定義された、Chronic Kidney Disease Epidemiology Collaboration（CKD-EPI）を用いてクレアチニンにより推算する eGFR に基づき分類した。

表 2.7.4.2-47　　腎機能分類

Category	Estimated glomerular filtration rate
Normal renal function	≥90 mL/min
Mild renal impairment	60 to < 90 mL/min
Moderate renal impairment	30 to < 60 mL/min
Severe renal impairment	15 to < 30 mL/min
Kidney failure	< 15 mL/min

すべての第 3 相試験において、腎不全は除外基準であった。いずれの第 3 相試験においても、以下の基準に合致する被験者が組み入れられた：

- 2 型糖尿病を有さない被験者を対象とした第 3 相試験（4373 及び 4382 試験の 2 型糖尿病を有さない被験者）
    - eGFR ≥15 mL/min

- 2 型糖尿病を有する被験者を対象とした第 3 相試験（4374 及び 4382 試験の 2 型糖尿病を有する被験者）
  - eGFR ≥30 mL/min
  - eGFR ≥60 ml/min ：SGLT2 阻害薬を投与している被験者が対象

日本人被験者が参加した 3 つの第 3 相試験の被験者におけるベースラインの腎機能については、2.7.4.1.3 項に示す。

急性腎不全のリスクは、事前に規定した急性腎不全に対する MedDRA 検索〔検索に含まれる用語は、4382 試験（Module 5.3.5.1）Appendix 16.1.9、4373 試験（Module 5.3.5.1）Appendix 16.1.9、4374 試験（Module 5.3.5.1）Appendix 16.1.9〕に基づき評価した。急性腎不全の診断基準は、eGFR の低下であり、糸球体濾過不良の診断基準はクレアチニンの上昇である。これら 2 つの腎機能パラメータ（eGFR 及びクレアチニン）の補足的な臨床検査評価は、注目すべき安全性領域である急性腎不全の評価の一部として検討した。4374 試験では UACR についても評価した。

急性腎不全及び腎機能パラメータは、on-treatment 観察期間に基づき評価した。

2.7.4.2.2.8.2　有害事象に基づく急性腎不全

日本人被験者が参加した 3 つの第 3 相臨床試験において、急性腎不全の発現件数は少なく（各投与群で 5 件以下）、当該事象の発現頻度及び単位時間あたりの発現件数について投与群間で明らかな違いはなく、用量反応性も認められなかった（表 2.7.4.2-48、表 2.7.4.2-49 及び表 2.7.4.2-50）。また、基本語の分布についても投与群間で明らかな違いは認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.48、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.46、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.46〕。

4382 及び 4373 試験では、すべての事象は非重篤であり、重度な事象はなかった。4373 試験の 1 例（被験者番号：913028）で「脱水」の事象がともに報告されたが、「大腸穿孔」の重篤な事象に関連するものであった〔4373 試験（Module 5.3.5.1）Section 12.5.9.1〕。

4374 試験では数件の重篤な有害事象（各投与群で 1～3 件）及び重度の有害事象（各投与群で 1～2 件）が報告された。計 9 件の急性腎不全の事象はいずれも、転帰は「回復」であり、他の原因を有していた。計 9 件の急性腎不全の事象のうち 7 件で、急性腎不全を引き起こす可能性のある有害事象（「胃炎」、「胃腸炎」、「脱水」又は感染症）が、急性腎不全の事象とともに報告された。「嘔吐」や「下痢」の事象がともに報告された重篤な急性腎不全の事象はなかった〔4374 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1、16.2.7.25、Section 14.3.3〕。

3 つの第 3 相試験において、治験責任医師による治験薬との因果関係の評価又は転帰について、投与群間で明らかな違いは認められなかった。治験薬投与の中止に至った急性腎不全の事象はなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.47、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.45、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.45〕

表 2.7.4.2-48　急性腎不全の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	100			199			101		
Patient years of exposure (PYE)	136.2			275.0			141.8		
Adverse Events	1	(1.0)	1 0.7	1	(0.5)	1 0.4	0		
SAEs	0			0			0		
Severe AEs	0			0					
Leading to Permanent treatment discontinuation	0			0			0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

表 2.7.4.2-49　急性腎不全の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg			Placebo		
	N	(%)	E R	N	(%)	E R
Number of subjects	1306			655		
Patient years of exposure (PYE)	1706.1			829.6		
Adverse Events	3	(0.2)	4 0.2	2	(0.3)	2 0.2
SAEs	0			0		
Severe AEs	0			0		
Leading to Permanent treatment discontinuation	0			0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

表 2.7.4.2-50　急性腎不全の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	402			403			402		
Patient years of exposure (PYE)	529.8			533.0			528.3		
Adverse Events	2 (0.5)	2	0.4	4 (1.0)	5	0.9	2 (0.5)	2	0.4
SAEs	2 (0.5)	2	0.4	2 (0.5)	3	0.6	1 (0.2)	1	0.2
Severe AEs	2 (0.5)	2	0.4	1 (0.2)	1	0.2	1 (0.2)	1	0.2
Leading to Permanent treatment discontinuation	0			0			0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R:Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.2.2.8.3　腎機能パラメータ

2.7.4.2.2.8.3.1　推算糸球体濾過量及びクレアチニン

平均値の経時推移

日本人被験者が参加した 3 つの第 3 相試験では、ベースライン時の eGFR 及びクレアチニンの平均値はすべての投与群間で同様であった（表 2.7.4.2-51、表 2.7.4.2-52 及び表 2.7.4.2-53）。

On-treatment 観察期間中に、いずれの試験でも、eGFR の平均値はすべてのセマグルチド群（1.0、1.7 及び 2.4 mg）で投与開始後の最初の 20 週間でわずかに減少し、その後ベースライン値に戻った。プラセボ群については、4373 及び 4374 試験ではセマグルチド群と同様の傾向がみられたが、4382 試験では eGFR の平均値は安定していた〔4328 試験（Module 5.3.5.1）EOT Figure 14.3.5.44、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.44、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.45〕。クレアチニンは、すべての試験において、いずれの投与群でも 20 週までわずかな増加が認められたが、68 週ではベースラインの値まで減少した〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.18、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.17、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.18〕。

個々の被験者における高値

eGFR については、3 つの試験において、ベースライン及び 68 週では大部分の被験者が正常腎機能又は軽度腎機能障害を有していた。ベースラインから 68 週までのカテゴリーの分布は、すべての投与群間で同様と考えられた（表 2.7.4.2-51、表 2.7.4.2-52 及び表 2.7.4.2-53）。eGFR の経時推移、ならびにベースライン以降の最低値と最高値を示す箱ひげ図〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.43、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.43、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.44〕に基づくと、いずれの投与群でも経時的な eGFR の値の分布に変化はなく、表 2.7.4.2-51、表 2.7.4.2-52 及び表 2.7.4.2-53 のカテゴリーの要約でみられた傾向が認められた。クレアチニンについては、クレアチニンの個々の高値に注目すると、3 つの試験において、ベースライン時に基準範囲上限を超える値を有する被験者の割合は、投与群間で同様であった（表 2.7.4.2-51、表 2.7.4.2-52 及び表 2.7.4.2-53）。4382 試験では、68 週にセマグルチド 1.7 mg 群で基準範囲上限を超える値を有した被験者の割合はわずかに高かったが、セマグルチド 2.4 mg 群とプラセボ群ではベースラインからの明らかな違いは認められなかった。4373 試験では、セマグルチド 2.4 mg 群でベースラインからのわずかな改善が認められたが、プラセボ群ではベースラインからの違いは認められなかった。4374 試験では、すべての投与群で、ベースラインからのわずかな改善が認められた。クレアチニンの経時推移、ならびにベースライン以降の最低値と最高値を示す箱ひげ図〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.17、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.16、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.17〕に基づくと、いずれの投与群でもクレアチニンの 20 週から 68 週の分布に変化はなく、平均の推移でみられた傾向が同様に認められた〔4382 試験（Module 5.3.5.1）EOT Figure 14.3.5.18、4373 試験（Module 5.3.5.1）EOT Figure 14.3.5.17、4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.18〕。ベースライン以降のいずれの時点において、クレアチニンが基準範囲上限の 3 倍を超えた被験者はいずれの投与群にもいなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.5.3、4373 試験（Module 5.3.5.1）EOT Table 14.3.5.3、4374 試験（Module 5.3.5.1）EOT Table 14.3.5.3〕。

表 2.7.4.2-51　eGFR 及びクレアチニンのベースライン値、68 週のベースラインに対する比ならびにベースライン及び 68 週のカテゴリーの要約－on-treatment 観察期間（4382 試験）

	Sema 1.7 mg	Sema 2.4 mg	Placebo
Number of subjects	100	199	101
eGFR (mL/min/1.73m²)			
Descriptive statistics (Geometric mean (CV))			
Baseline level	96.78 (15.6)	96.62 (17.0)	98.62 (13.8)
Ratio to baseline at week 68	0.98 (7.6)	0.99 (8.1)	0.99 (7.4)
Categorical summary (N (%))			
Visit 1 (week -1)			
N	100 (100)	199 (100)	101 (100)
Normal (>=90)	73 (73.0)	140 (70.4)	78 (77.2)
Mild RI (60-<90)	26 (26.0)	58 (29.1)	23 (22.8)
Moderate RI (30-<60)	1 (1.0)	1 (0.5)	0
Severe RI (15-<30)	0	0	0
End-stage renal disease (<15)	0	0	0
Visit 24 (week 68)			
N	93 (93.0)	186 (93.5)	98 (97.0)
Normal (>=90)	68 (73.1)	130 (69.9)	77 (78.6)
Mild RI (60-<90)	23 (24.7)	53 (28.5)	21 (21.4)
Moderate RI (30-<60)	2 (2.2)	3 (1.6)	0
Severe RI (15-<30)	0	0	0
End-stage renal disease (<15)	0	0	0
Creatinine (mg/dL)			
Descriptive statistics (Geometric mean (CV))			
Baseline level	0.8 (22.3)	0.8 (24.0)	0.8 (20.9)
Ratio to baseline at week 68	1.01 (9.9)	1.01 (11.0)	1.00 (11.6)
Categorical summary (N (%))			
Visit 1 (week -1)			
N	100 (100)	199 (100)	101 (100)
Low (<LLN)	10 (10.0)	40 (20.1)	11 (10.9)
Normal	88 (88.0)	153 (76.9)	87 (86.1)
High (>ULN)	2 (2.0)	6 (3.0)	3 (3.0)
Visit 24 (week 68)			
N	93 (93.0)	186 (93.5)	98 (97.0)
Low (<LLN)	10 (10.8)	33 (17.7)	15 (15.3)
Normal	77 (82.8)	149 (80.1)	82 (83.7)
High (>ULN)	6 (6.5)	4 (2.2)	1 (1.0)

eGFR: Estimated glomerular filtration rate.
CV: Coefficient of variation in %. N: Number of subjects with an observation at the visit, %: Percentages are based on subjects with an observation at the visit, LLN: Lower limit normal, ULN: Upper limit normal.
Observed data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.
eGFR calculated based on creatinine value using the CKD-EPI equation.

表 2.7.4.2-52　eGFR 及びクレアチニンのベースライン値、68 週のベースラインに対する比ならびにベースライン及び 68 週のカテゴリーの要約－on-treatment 観察期間（4373 試験）

	Sema 2.4 mg	Placebo
Number of subjects	1306	655
eGFR (mL/min/1.73m²)		
Descriptive statistics (Geometric mean (CV))		
Baseline level	96.28 (18.7)	95.87 (18.3)
Ratio to baseline at week 68	0.99 (10.0)	0.99 (10.0)
Categorical summary (N (%))		
Visit 1 (week -1)		
N	1306 (100)	655 (100)
Normal (>=90)	887 (67.9)	445 (67.9)
Mild RI (60-<90)	401 (30.7)	200 (30.5)
Moderate RI (30-<60)	18 (1.4)	10 (1.5)
Severe RI (15-<30)	0	0
End-stage renal disease (<15)	0	0
Visit 24 (week 68)		
N	1053 (80.6)	497 (75.9)
Normal (>=90)	720 (68.4)	323 (65.0)
Mild RI (60-<90)	316 (30.0)	168 (33.8)
Moderate RI (30-<60)	17 (1.6)	6 (1.2)
Severe RI (15-<30)	0	0
End-stage renal disease (<15)	0	0
Creatinine (mg/dL)		
Descriptive statistics (Geometric mean (CV))		
Baseline level	0.8 (19.5)	0.8 (19.8)
Ratio to baseline at week 68	1.00 (11.1)	0.99 (11.1)
Categorical summary (N (%))		
Visit 1 (week -1)		
N	1306 (100)	655 (100)
Low (<LLN)	78 (6.0)	37 (5.6)
Normal	1187 (90.9)	600 (91.6)
High (>ULN)	41 (3.1)	18 (2.7)
Visit 24 (week 68)		
N	1053 (80.6)	497 (75.9)
Low (<LLN)	63 (6.0)	31 (6.2)
Normal	963 (91.5)	452 (90.9)
High (>ULN)	27 (2.6)	14 (2.8)

eGFR: Estimated glomerular filtration rate.
CV: Coefficient of variation in %. N: Number of subjects with an observation at the visit, %: Percentages are based on subjects with an observation at the visit, LLN: Lower limit normal, ULN: Upper limit normal.
Observed data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.
eGFR calculated based on creatinine value using the CKD-EPI equation.

表 2.7.4.2-53　eGFR 及びクレアチニンのベースライン値、68 週のベースラインに対する比ならびにベースライン及び 68 週のカテゴリーの要約－on-treatment 観察期間（4374 試験）

	Sema 1.0 mg	Sema 2.4 mg	Placebo
Number of subjects	402	403	402
eGFR (mL/min/1.73m²)			
Descriptive statistics (Geometric mean (CV))			
Baseline level	93.46 (21.5)	94.22 (22.1)	92.48 (23.2)
Ratio to baseline at week 68	0.99 (10.3)	0.98 (10.8)	1.00 (10.6)
Categorical summary (N (%))			
Visit 1 (week -1)			
N	402 (100)	403 (100)	402 (100)
Normal (>=90)	265 (65.9)	270 (67.0)	259 (64.4)
Mild RI (60-<90)	120 (29.9)	114 (28.3)	120 (29.9)
Moderate RI (30-<60)	17 (4.2)	18 (4.5)	23 (5.7)
Severe RI (15-<30)	0	1 (0.2)	0
End-stage renal disease (<15)	0	0	0
Visit 24 (week 68)			
N	350 (87.1)	350 (86.8)	338 (84.1)
Normal (>=90)	232 (66.3)	236 (67.4)	215 (63.6)
Mild RI (60-<90)	105 (30.0)	100 (28.6)	108 (32.0)
Moderate RI (30-<60)	13 (3.7)	13 (3.7)	15 (4.4)
Severe RI (15-<30)	0	1 (0.3)	0
End-stage renal disease (<15)	0	0	0
Creatinine (mg/dL)			
Descriptive statistics (Geometric mean (CV))			
Baseline level	0.8 (26.1)	0.7 (26.0)	0.8 (27.3)
Ratio to baseline at week 68	1.01 (12.5)	1.02 (13.0)	0.98 (13.3)
Categorical summary (N (%))			
Visit 1 (week -1)			
N	402 (100)	403 (100)	402 (100)
Low (<LLN)	75 (18.7)	84 (20.8)	86 (21.4)
Normal	306 (76.1)	295 (73.2)	285 (70.9)
High (>ULN)	21 (5.2)	24 (6.0)	31 (7.7)
Visit 24 (week 68)			
N	350 (87.1)	350 (86.8)	338 (84.1)
Low (<LLN)	59 (16.9)	54 (15.4)	83 (24.6)
Normal	278 (79.4)	277 (79.1)	235 (69.5)
High (>ULN)	13 (3.7)	19 (5.4)	20 (5.9)

eGFR: Estimated glomerular filtration rate.
CV: Coefficient of variation in %. N: Number of subjects with an observation at the visit, %: Percentages are based on subjects with an observation at the visit, LLN: Lower limit normal, ULN: Upper limit normal.
Observed data from on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.
eGFR calculated based on creatinine value using the CKD-EPI equation.

2.7.4.2.2.8.3.2　尿中アルブミン／クレアチニン比

4374 試験では UACR を評価した。ベースラインにおいて、UACR の平均値は投与群間で同様であった。UACR は、ベースラインから 68 週までにセマグルチド 2.4 mg 群では 24%及びセマグルチド 1.0 mg 群では 13%減少し、プラセボ群では 17%増加した（表 2.7.4.2-54）。

UACR の個々の値に注目すると、ベースライン時に微量アルブミン尿及び顕性アルブミン尿を有する被験者の割合はすべての投与群で同様であった。68 週では、セマグルチド 2.4 mg 群とセマグルチド 1.0 mg 群ではわずかに減少し、プラセボ群ではわずかに増加した（表 2.7.4.2-54）。

UACR の経時推移、ならびにベースライン以降の最低値と最高値を示す箱ひげ図〔4374 試験（Module 5.3.5.1）EOT Figure 14.3.5.46〕に基づくと、ベースラインから投与終時（68 週）までに UACR の値の分布にわずかな変化がみられ、カテゴリーの要約でみられた傾向が同様に認められた（表 2.7.4.2-54）。

表 2.7.4.2-54　　UACR のベースライン値、68 週のベースラインに対する比ならびにベースライン及び 68 週のカテゴリーの要約－on-treatment 観察期間（4374 試験）

	Semaglutide 1.0 mg	**Semaglutide 2.4 mg**	**Placebo**
Number of subjects	402	403	402
Descriptive statistics (geometric mean (CV))			
Baseline	2.2 (211.9)	2.3 (225.7)	2.3 (190.9)
Ratio to baseline at week 68	0.87 (128.1)	0.76 (116.5)	1.17 (118.1)
Categorical summary (N (%))			
Visit 2 (week 0)			
Normal	306 (78.1)	319 (80.8)	315 (79.3)
Microalbuminuria	70 (17.9)	63 (15.9)	71 (17.9)
Macroalbuminuria	16 (4.1)	13 (3.3)	11 (2.8)
Visit 24 (week 68)			
Normal	289 (84.8)	301 (87.0)	247 (73.7)
Microalbuminuria	42 (12.3)	40 (11.6)	73 (21.8)
Macroalbuminuria	10 (2.9)	5 (1.4)	15 (4.5)

CV: coefficient of variation in %; N: number of subjects; UACR: urine albumin-to-creatinine ratio; %: percentages are based on subjects with an observation at the visit. Observed data from the on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 14 days.

2.7.4.2.2.8.4　　結論

事前に規定した MedDRA 検索により特定された急性腎不全の有害事象及び腎機能パラメータの評価から、セマグルチド 2.4 mg による急性腎不全のリスクの増加はみられなかった。

日本人被験者が参加した第 3 相試験（4382、4373 及び 4374 試験）において、MedDRA 検索により特定された急性腎不全に関連する有害事象の発現件数は少なかった（各投与群で 0～5 件）。「嘔吐」や「下痢」の有害事象と急性腎不全との間に関連性は認められなかった。しかしながら、他の GLP-1 受容体作動薬を用いた治療と同様に、胃腸障害の副作用が稀に脱水を起こし、腎機能に影響を及ぼすことがある。

2 型糖尿病に対するセマグルチド皮下投与及びセマグルチド経口投与で認められた所見と同様に、腎機能パラメータである eGFR 及びクレアチニンはセマグルチドの投与によって影響を受けなかった。

4374 試験で検討した UACR についてはセマグルチドの投与により改善が認められ、セマグルチド 2.4 mg 群では 24%及びセマグルチド 1.0 mg 群では 13%減少し、プラセボ群では 17%増加した。

2.7.4.2.2.9 低血糖

2.7.4.2.2.9.1 背景及び評価方法

GLP-1 受容体作動薬は、グルコース濃度依存的にインスリン分泌を促進する。血中グルコース濃度が上昇していないと、GLP-1 受容体作動薬はインスリン分泌に対してほとんど又は全く活性を示さないため、低血糖のリスクは低いと考えられている[64]。

2 型糖尿病を有する被験者では、低血糖の頻度及び単位時間あたりの発現件数は併用する糖尿病治療薬によって影響を受ける。特にインスリン及びスルホニルウレア薬は低血糖のリスクを増加させる可能性がある。2 型糖尿病に対するセマグルチド皮下投与[14]及びその他の GLP-1 受容体作動薬[23, 25, 26]は、インスリン又はスルホニルウレア薬と併用する場合、単独療法で使用する場合と比較して低血糖のリスクが増加する。さらに、体重減少はインスリン感受性を改善し、血糖コントロールが改善される可能性がある。そのため、血糖降下治療が適切に調整されない場合には、低血糖のリスクが増加する可能性がある。

2 型糖尿病を有さない被験者を対象とした第 3 相試験（4373 試験及び 4382 試験の 2 型糖尿病を有さない被験者）では、低血糖は、報告された低血糖の有害事象〔MedDRA 検索の詳細は 4382 試験（Module 5.3.5.1）Appendix 16.1.9、4373 試験（Module 5.3.5.1）Appendix 16.1.9 に示す〕に基づき、on-treatment 観察期間を用いて評価した。このような有害事象は、血糖の測定値が得られていることは稀であることから、低血糖の症状に基づいていた。被験者が試験中に 2 型糖尿病を発症した場合には、治験責任医師は各国のガイドラインに従って、被験者の治療をすることとした。

2 型糖尿病を有する被験者を対象とした第 3 相試験（4374 及び 4382 試験の 2 型糖尿病を有する被験者）では、低血糖は「hypoglycaemic episode form」により報告された。併用療法には、食事療法及び運動療法のみ、単独療法〔メトホルミン、スルホニルウレア薬、SGLT2 阻害薬又はグリタゾン（以下、チアゾリジン）による安定した治療〕又は各国の添付文書に基づき最大 3 種類までの経口糖尿病薬（メトホルミン、スルホニルウレア薬、SGLT2 阻害薬又はチアゾリジン）が含まれた。低血糖は on-treatment 観察期間に基づいて評価し、2018 年 ADA/2017 年 IHSG 分類により要約した[11, 12]。詳細については、2.7.4.1.1.8.4 項（安全性データの収集）2.7.4.1.1.9.5 項（統計手法）に示す。

また、4374 試験の被験者では、セマグルチドとスルホニルウレア薬の併用が低血糖に及ぼす影響も評価した。

2.7.4.2.2.9.2 2 型糖尿病を有さない被験者における低血糖の有害事象

4382 試験のスクリーニング時に 2 型糖尿病を有さない被験者において、低血糖の有害事象を発現した被験者はいなかった。

4373 試験では、低血糖の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は低く、セマグルチド 2.4 mg 群とプラセボ群で同様であった（表 2.7.4.2-55）。いずれの投与群においても、重篤な有害事象は報告されなかった。重症度が重度の有害事象もなく、治験薬投与の中止に至った有害

事象もなかった。被験者の大部分は事象から回復した〔4373 試験（Module 5.3.5.1）EOT Table 14.3.1.58〕。

表 2.7.4.2-55　　低血糖の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg N (%) E R	Placebo N (%) E R
Number of subjects	1306	655
Patient years of exposure (PYE)	1706.1	829.6
Adverse Events	8 (0.6) 15 0.9	5 (0.8) 7 0.8

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years. PYE: The duration of the on-treatment period in years. On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
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2.7.4.2.2.9.3　　2 型糖尿病を有する被験者における低血糖

4382 試験のスクリーニング時に 2 型糖尿病を有する被験者において、重大な又は血糖値確定症候性低血糖（ノボ ノルディスク社の分類）は、いずれの投与群においても報告されなかった（表 2.7.4.2-56）。4374 試験では、重大な又は血糖値確定症候性低血糖の発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群とセマグルチド 1.0 mg 群で多かった（表 2.7.4.2-57）。

2018 年 ADA/2017 年 IHSG 分類については、4382 試験では重大な低血糖（レベル 3）又は臨床的に問題となる低血糖（レベル 2）〔clinically significant hypoglycaemia (level 2)〕を発現した被験者はいなかった。4374 試験では、重大な低血糖（レベル 3）が 1 件報告された。本低血糖は、ベースライン時にメトホルミンの投与を受けていたセマグルチド 2.4 mg 群の被験者において、用量漸期間中に発現した。本事象は「慢性胆嚢炎」の重篤な有害事象のための入院に関連して発現した。入院時、56 mg/dL の血糖値が報告され、被験者は水分補給及びグルコースの静脈内投与を受けた。当該被験者はこの低血糖から回復した〔4374 試験（Module 5.3.5.1）Section 12.5.10、Section 14.3.3〕。臨床的に問題となる低血糖（レベル 2）は、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群でより多く報告された。これらの低血糖を発現した被験者の割合について、セマグルチド 2.4 mg 群とセマグルチド 1.0 mg 群の間に明らかな違いは認められず、臨床的に問題となる低血糖（レベル 2）において明らかな用量反応性も認められなかった。両試験において、低血糖の警告値（レベル 1）〔hypoglycaemia alert value (level 1)〕を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった。

両試験において、低血糖の重篤な有害事象は、いずれの投与群においても報告されなかった。

表 2.7.4.2-56　分類別の低血糖－on-treatment 観察期間－安全性解析対象集団（4382 試験、スクリーニング時に 2 型糖尿病を有する被験者）

	Sema 1.7 mg N	(%)	E	R	Sema 2.4 mg N	(%)	E	R	Placebo N	(%)	E	R
Number of subjects	25				49				25			
Patient years of exposure (PYE)	35.5				68.3				35.6			
Severe or BG-confirmed symptomatic hypoglycaemic episodes	0				0				0			
ADA 2013 classification												
Severe	0				0				0			
Documented symptomatic	0				2	(4.1)	3	4.4	0			
Asymptomatic	2	(8.0)	5	14.1	3	(6.1)	4	5.9	0			
Pseudo-hypoglycaemia	0				4	(8.2)	4	5.9	0			
Probable symptomatic	0				4	(8.2)	8	11.7	0			
Unclassifiable	0				0				0			
ADA 2018 classification												
Level 3 - Severe	0				0				0			
Level 2 - Clinically significant	0				0				0			
Level 1 - Alert value	2	(8.0)	5	14.1	5	(10.2)	7	10.3	0			
Not hypoglycaemia	0				5	(10.2)	12	17.6	0			
Level 2 or 3 hypoglycaemic episodes (ADA 2018 Classification)	0				0				0			

Episodes with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. PYE: The duration of the on-treatment period in years.
'BG-confirmed': hypoglycaemic episode with a plasma glucose value < 3.1 mmol/L (56 mg/dL), N: number of subjects with at least one episode, %: proportion of subjects with at least one episode, E: number of episodes, R: episodes per 100 years of exposure, ADA: American Diabetes Association.

表 2.7.4.2-57　　分類別の低血糖－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	402				403				402			
Patient years of exposure (PYE)	529.8				533.0				528.3			
Severe or BG-confirmed symptomatic hypoglycaemic episodes	22	(5.5)	29	5.5	23	(5.7)	51	9.6	12	(3.0)	18	3.4
ADA 2013 classification												
Severe	0				1	(0.2)	1	0.2	0			
Documented symptomatic	51	(12.7)	99	18.7	61	(15.1)	178	33.4	29	(7.2)	70	13.2
Asymptomatic	44	(10.9)	173	32.7	58	(14.4)	168	31.5	14	(3.5)	21	4.0
Pseudo-hypoglycaemia	11	(2.7)	12	2.3	8	(2.0)	15	2.8	12	(3.0)	15	2.8
Probable symptomatic	7	(1.7)	8	1.5	11	(2.7)	16	3.0	9	(2.2)	11	2.1
Unclassifiable	0				2	(0.5)	2	0.4	1	(0.2)	1	0.2
ADA 2018 classification												
Level 3 - Severe	0				1	(0.2)	1	0.2	0			
Level 2 - Clinically significant	27	(6.7)	38	7.2	25	(6.2)	57	10.7	10	(2.5)	17	3.2
Level 1 - Alert value	63	(15.7)	205	38.7	82	(20.3)	258	48.4	31	(7.7)	70	13.2
Not hypoglycaemia	35	(8.7)	49	9.2	35	(8.7)	64	12.0	24	(6.0)	31	5.9
Level 2 or 3 hypoglycaemic episodes (ADA 2018 Classification)	27	(6.7)	38	7.2	26	(6.5)	58	10.9	10	(2.5)	17	3.2

Episodes with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. PYE: The duration of the on-treatment period in years.; 'BG-confirmed': hypoglycaemic episode with a plasma glucose value < 3.1 mmol/L (56 mg/dL); N: number of subjects with at least one episode, %: proportion of subjects with at least one episode, E: number of episodes, R: episodes per 100 years of exposure, ADA: American Diabetes Association.

4374 試験において、レベル 2 とレベル 3 の低血糖が認められた被験者と認められなかった被験者との比較により、低血糖のリスク因子の概要を表 2.7.4.2-58 に示す。3 つの投与群のいずれについても、低血糖を発現しなかった被験者と比較して、低血糖を発現した被験者では全般的に糖尿病罹患期間が長く、年齢が高く（プラセボ群で最も顕著であった）、68 週の HbA1c の大幅な低下がみられた。ベースライン時に、3 つの投与群においてスルホニルウレア薬を使用していた被験者の割合は 22.7%であった〔4374 試験（Module 5.3.5.1）EOT Table 14.1.3〕。試験期間中、被験者はスルホニルウレア薬を開始することも終了することも可能であったことから、低血糖とスルホニルウレア薬の併用について低血糖の発現時に評価した。レベル 2 及びレベル 3 の低血糖の半数以上が、治験薬とスルホニルウレア薬との併用時に発現し、これは 3 つの投与群のすべてで認められた。低血糖に関するデータは、2 型糖尿病に対するセマグルチド皮下投与[14]及びセマグルチド経口投与[15]で認められたデータと同様である。

表 2.7.4.2-58　低血糖（ADA2018 分類のレベル 2 又はレベル 3）ー低血糖を発現した被験者と発現しなかった被験者のリスク因子ーon-treatment 観察期間（4374 試験）

	Subjects with episodes			Subjects without episodes		
	Sema 1.0 mg	Sema 2.4 mg	Placebo	Sema 1.0 mg	Sema 2.4 mg	Placebo
Number of subjects	27	26	10	375	377	392
Age (years)						
N	27	26	10	375	377	392
Mean (SD)	58 (8)	57 (12)	65 (5)	55 (10)	55 (11)	55 (10)
Median	59	60	65	56	55	55
Min ; Max	41 ; 71	30 ; 73	60 ; 73	20 ; 81	19 ; 84	20 ; 82
Diabetes duration (years)						
N	27	26	10	375	377	391
Mean (SD)	9.7 (7.6)	9.2 (5.5)	11.6 (5.0)	7.6 (5.8)	8.2 (6.2)	8.0 (6.2)
Median	9.7	9.6	12.3	6.3	6.7	6.7
Min ; Max	0.5 ; 34.4	1.6 ; 21.5	2.8 ; 17.6	0.5 ; 34.7	0.5 ; 37.7	0.6 ; 29.9
HbA1c (%) at baseline						
N	27	26	10	375	377	392
Mean (SD)	8.1 (0.9)	8.3 (0.8)	8.0 (0.7)	8.1 (0.8)	8.1 (0.8)	8.1 (0.8)
Median	8.0	8.3	7.7	8.0	7.9	8.0
Min ; Max	6.3 ; 10.1	7.2 ; 9.9	7.2 ; 9.2	5.8 ; 10.2	6.7 ; 10.6	5.7 ; 10.3
HbA1c (%) at Visit 24 (Week 68)						
N	26	25	8	324	325	329
Mean (SD)	6.2 (0.7)	6.0 (0.6)	7.3 (0.8)	6.5 (1.0)	6.3 (1.1)	7.8 (1.3)
Median	6.0	5.9	7.1	6.3	6.0	7.6
Min ; Max	5.2 ; 8.0	5.2 ; 7.6	6.4 ; 9.0	5.0 ; 10.9	4.8 ; 13.4	5.1 ; 11.8
SU at time of event(s)						
Yes, N (%) E	15 (55.6) 23	16 (61.5) 32	7 (70.0) 11			
No, N (%) E	13 (48.1) 15	13 (50.0) 26	4 (40.0) 6			

For 'SU at time of event(s)' subjects are able to contribute to both depending on their SU status at time of event.
ADA: American Diabetes Association, N: number of subjects, %: proportion of subjects, SU: Sulphonylurea.

2.7.4.2.2.9.4　結論

4382 試験においてスクリーニング時に 2 型糖尿病を有さない被験者では、低血糖の有害事象を発現した被験者はいなかった。4373 試験では、低血糖の有害事象を発現した被験者の割合は低く、セマグルチド 2.4 mg 群とプラセボ群で同様であった。すべての事象は非重篤であり、重度の有害事象はなかった。

4382 試験においてスクリーニング時に 2 型糖尿病を有する被験者では、重大な又は血糖値確定症候性低血糖を発現した被験者はいなかったが、4734 試験では重大な又は血糖値確定症候性低血糖の発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群で多かった。

4382 試験においてスクリーニング時に 2 型糖尿病を有する被験者では、重大な低血糖（レベル 3）又は臨床的に問題となる低血糖（レベル 2）を発現した被験者はいなかった。4374 試験では、臨床的に問題となる低血糖（レベル 2）を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群で高かった。低血糖の大部分は、セマグルチド 2.4 mg 及びセマグルチド 1.0 mg のスルホニルウレア薬との併用時に発現しており、これは 2 型糖尿病に対するセマグルチド皮下投与及びセマグルチド経口投与で認められた所見と同様である。重大な低血糖は、セマグルチド 2.4 mg の投与を受けた被験者で認められた 1 件のみであった。

2.7.4.2.2.10　網膜障害

2.7.4.2.2.10.1　背景及び評価方法

2 型糖尿病の診断時までに、患者の約 20%が糖尿病網膜症を有し、2 型糖尿病を発症後 10～20 年後には、患者の約半数以上が糖尿病網膜症を発症すると考えられている。このように、糖尿病網膜症はよく知られた糖尿病の細小血管合併症であり、コントロール不良な 2 型糖尿病に伴う慢性的な高血糖が一因となり引き起こされる。その他の要因としては、コントロール不良な高血圧や脂質異常症がある[65]。一部の患者（約 10%）では、糖尿病網膜症が視力を脅かすような病態に進展する[66]。糖尿病網膜症に加えて、糖尿病患者では緑内障、白内障及びその他の眼の障害もより早期に、高頻度で発現する[65]。

糖尿病網膜症の発症及び進展のリスク因子としては、糖尿病罹患期間の長期化、血糖コントロール不良及び高血圧や脂質異常症に対する不十分な治療などがある[66, 67, 68, 69, 70]。したがって、これらのリスク因子を低減させるための治療は、糖尿病網膜症の発症予防や進行を阻止する上で重要である。糖尿病網膜症の発症及び進行の予防及び／又は遅延のための厳格な血糖コントロールの有益な効果は、1 型糖尿病及び 2 型糖尿病のいずれにおいても十分に確立されている[71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81]。しかしながら、血糖コントロールの急速な改善が初期の糖尿病網膜症の悪化と関連する可能性がある[71, 74, 75, 76]。この逆転現象は、早期悪化（early worsening）と呼ばれ、インスリン治療ではよく知られており、インスリン製剤の製品情報にも記載されている。このリスクは、特に長期間にわたり糖尿病に罹患しており、血糖コントロール不良で、HbA1c が急激かつ大幅に低下し、糖尿病網膜症の既往歴を有している患者において認められている[71, 74, 75, 76]。時間の経過に伴い、糖尿病網膜症の早期悪化は、血糖の改善による網膜合併症の減少により相殺されると考えられている[71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81]。

2 型糖尿病患者を対象としたセマグルチド皮下投与の CVOT（NN9535-3744 試験）では、4 つの基準（硝子体出血、糖尿病に起因する失明、硝子体内注射による治療の必要性、光凝固による治療の必要

性）のうち 1 つ以上に合致する事象からなる糖尿病網膜症に関連する合併症に関するイベント判定委員会により確定された複合エンドポイントが含まれていた。この複合エンドポイントは「糖尿病網膜症に関連する合併症」と呼ばれ、本試験においてプラセボ群と比較してセマグルチド皮下投与群でこれらの事象のリスクが高いことが示された〔セマグルチド皮下投与群で 50 例（3.0%）、プラセボ群で 29 例（1.8%）であり、最初の糖尿病網膜症に関連する合併症を発現するまでの時間についてのハザード比は 1.76（95%信頼区間：1.11; 2.78）〕。このリスクの増加は、主にベースライン時に糖尿病網膜症の既往歴を有し、血糖コントロール不良で、インスリンによる治療を受けていた患者において認められた〔NN9535-3744 試験（Module 5.3.5.1）〕。事後解析では、プラセボと比較して、セマグルチド皮下投与によるリスクの増加の大部分は、セマグルチド皮下投与の投与開始後初期の 16 週間における HbA1c の急激かつ大幅な低下による可能性が示唆された[82]。絶対リスクは、糖尿病網膜症の既往歴を有さない被験者と比較して、糖尿病網膜症の既往歴を有する被験者で大きかった。このことから、4382 試験の 2 型糖尿病を有する被験者及び 4374 試験では、網膜障害を注目すべき安全性領域として含めることとした。

4382 試験及び 4374 試験の 2 型糖尿病を有する患者に対して、すべての網膜障害及び視力障害の事象を特定するために MedDRA 検索を用いた〔検索用語については、4382 試験（Module 5.3.5.1）Appendix 16.1.9、4374 試験（Module 5.3.5.1）Appendix 16.1.9〕。検索は、階層的 MedDRA 標準検索式（SMQ）（187 個の基本語から構成される）に基づいており、この手法により MedDRA のバージョンの更新時に検索を更新することが可能である。この MedDRA 検索は、2 型糖尿病に対するセマグルチド皮下投与及びセマグルチド経口投与で使用された、MedDRA Version 13.1 から選択した 35 個の基本語に基づく検索とは異なる。これらの基本語は MedDRA に含まれる階層構造〔器官別大分類、高位グループ語（HLGT）又は SMQ〕のいずれにも属しておらず、より新しい MedDRA version への検索の構造的な更新ができなかった。

6 つの基本語（「糖尿病性緑内障」、「硝子体混濁」、「視神経乳頭血管炎」、「糖尿病性眼病変」、「視神経乳頭浮腫」及び「糖尿病性ぶどう膜炎」）を除き、以前に使用した MedDRA 検索に含まれていたすべての基本語は、肥満症のためのセマグルチドの第 3 相試験プログラムにおいて使用された MedDRA 検索によって特定された。しかしながら、4382 及び 4374 試験において上記の 6 つの基本語は有害事象として報告されなかった。

網膜障害の有害事象及び眼の検査は、発現から診断までの時間が長くなる可能性があるため、in-trial 観察期間に基づき評価した。

2.7.4.2.2.10.2 有害事象に基づく網膜障害

2.7.4.2.2.10.2.1 事前に規定した MedDRA 検索

ベースライン時に、糖尿病網膜症の既往歴を有する被験者の割合は、4382 試験の 2 型糖尿病を有する患者集団及び 4374 試験の全集団でそれぞれ 18.2%及び 10.2%であった〔4382 試験（Module 5.3.5.1）EOT Table 14.1.21、4374 試験（Module 5.3.5.1）EOT Table 14.1.18〕。

網膜障害の有害事象を発現した被験者の割合は、4382 試験ではセマグルチド 1.7 mg 群及びプラセボ群と比較して、セマグルチド 2.4 mg 群で高く（表 2.7.4.2-59）、4374 試験では、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群で高かった（表 2.7.4.2-60）。

いずれの投与群でも重篤な有害事象は報告されなかった。両試験において、網膜障害の有害事象の大部分は、軽度であり、治験責任医師により治験薬との因果関係は「なし」と判定された〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.60、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.58〕。

4382 試験では、治験薬の投与への対応を行った事象はなかった。4374 試験では、1 例が治験薬の投与を中止し、1 例が治験薬の投与量を減量した。これらの被験者はいずれも、セマグルチド 1.0 mg の投与を受けていた。前者は発現した事象に対する治療は行わずに経過観察のみを継続したが、事象から回復しなかった。後者は、事象から回復し、セマグルチドの投与を完了した〔詳細は 4374 試験（Module 5.3.5.1）Section 12.5.14 に示す〕。

両試験において、大部分の網膜障害の事象（基本語）が「糖尿病網膜症」であった。この基本語について、4382 試験では事象を発現した被験者の割合及び単位時間あたりの発現件数に投与群間で明らかな違いはみられなかったが〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.61〕、4374 試験では、セマグルチド 1.0 mg 群及びプラセボ群と比較して、セマグルチド 2.4 mg 群でより多くの事象が報告された〔4374 試験（Module 5.3.5.1）EOT Table 14.3.1.59〕。また、4374 試験では、事象を発現した被験者の割合はセマグルチド 1.0 mg 群とプラセボ群の間で同様であったことから、セマグルチドによる明らかな用量反応性は認められなかった。両試験において、残りの網膜障害の事象は、複数の基本語に分布しており、各基本語内での発現件数が少なく、セマグルチド群（1.0、1.7 及び 2.4 mg）とプラセボ群の間で明確な傾向は認められず、セマグルチドによる明らかな用量反応性も認められなかった。

表 2.7.4.2-59　網膜障害の有害事象－MedDRA 検索－in-trial 観察期間－安全性解析対象集団（4382 試験、スクリーニング時に 2 型糖尿病を有する被験者）

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	25				49				25			
Patient years of observation (PYO)	36.1				70.7				36.0			
Adverse Events	2	(8.0)	3	8.3	7	(14.3)	7	9.9	2	(8.0)	2	5.6
SAEs	0				0				0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYO: The duration of the in-trial period in years.
MedDRA version 23.1

表 2.7.4.2-60　網膜障害の有害事象－MedDRA 検索－in-trial 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	402				403				402			
Patient years of observation (PYO)	569.1				572.8				566.6			
Adverse Events	25	(6.2)	30	5.3	28	(6.9)	36	6.3	17	(4.2)	19	3.4
SAEs	0				0				0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYO: The duration of the in-trial period in years.
MedDRA version 22.1

2.7.4.2.2.10.2.2　追加データの収集

治験責任医師が、糖尿病網膜症の新規発症又は悪化によるものと判断した有害事象については、追加データを収集することとした（2.7.4.1.1.8.2.2 項）。このため、事前に規定された MedDRA 検索により特定された事象と追加データが収集された有害事象は 1：1 ではない。追加情報には、事象の特定方法、治療を必要とした事象かどうかが含まれており、糖尿病網膜症の事象をより包括的に評価することが可能であった。

4382 試験では 7 件、4374 試験では 45 件の有害事象について追加データの収集が行われた。これらの事象は治験責任医師により糖尿病網膜症の新規発症又は悪化であると評価されたことを意味する〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.65、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.63〕。4382 試験のすべての事象及び 4374 試験の大部分の事象（基本語）は、「糖尿病網膜症」として報告され、両試験において投与群間の発現状況に傾向は認められなかった。4374 試験の残りの事象は、5 つの基本語に分布していた：「非増殖性網膜症」、「黄斑浮腫」、「網膜出血」、「網膜症」及び「眼出血」。4374 試験のプラセボ群で 1 件の「眼出血」（基本語）が報告されたが、この事象は事前に規定した MedDRA 検索には含まれなかった。

予想されたとおり、4382 試験のすべての事象及び 4374 試験の大部分の事象が、52 週及び 68 週に予定されていた 2 回の眼の検査時、又は他の定期検査時に特定され、眼に関連する症状の発現に基づくものではなかった〔詳細は、4382 試験（Module 5.3.5.1）Section 12.5.13.1、4374 試験（Module 5.3.5.1）Section 12.5.14.1〕。4374 試験では、計 3 件の事象（いずれもセマグルチド 1.0 mg 群）は症状があったために特定された。4382 試験のすべての事象及び 4374 試験の大部分の事象が、事象に対する治療は必要ないと判断され、経過観察のみであった。

糖尿病網膜症の事象に関連する追加情報は、4382 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.24、4374 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.24 に示す。

2.7.4.2.2.10.2.3　糖尿病網膜症のリスク因子

糖尿病網膜症の発症又は悪化のリスク因子には、糖尿病網膜症の既往、2 型糖尿病罹患期間の長期化、ベースライン時の HbA1c の高値、HbA1c の急速な改善、セマグルチドとインスリンとの併用が含まれる [71, 74, 75, 76, 82]。

追加データの収集が行われた事象（すなわち、治験責任医師により糖尿病網膜症の新規発症又は悪化と判断された事象）と事前に規定した MedDRA 検索で特定した事象において重複している事象を表 2.7.4.2-61 及び表 2.7.4.2-62 に示し、さらにこれらの事象を発現した被験者の割合及び発現しなかった被験者の割合を示した。4374 試験では、セマグルチド 2.4 mg 群、セマグルチド 1.0 mg 群及びプラセボ群において、ベースライン時に網膜症の既往歴を有していた被験者の割合は、事象を発現しなかった被験者と比較して事象を発現した被験者で高かったが、4382 試験では同様の傾向はみられなかった。残りのリスク因子について明確な傾向は認められず、一部の投与群（4382 試験のセマグルチド 2.4 mg 群及び 4374 試験のセマグルチド 1.0 mg 群とプラセボ群）では、事象を発現した被験者において、糖尿病罹患期間が長く、ベースライン時の HbA1c の中央値が高かったが、両試験のこのほかの投与群では認められなかった。4374 試験では、セマグルチド 2.4 mg 群において 68 週の HbA1c の低下が事象を発現した被験者でわずかに大きかったが、セマグルチド 1.0 mg 群とプラセボ群では認められなかった。

表 2.7.4.2-61　糖尿病網膜症－糖尿病網膜症の新規発症又は悪化の有害事象を発現した被験者と発現しなかった被験者におけるリスク因子－in-trial 観察期間－安全性解析対象集団（4382 試験、スクリーニング時に 2 型糖尿病を有する被験者）

	Subjects with events			Subjects without events		
	Sema 1.7 mg	Sema 2.4 mg	Placebo	Sema 1.7 mg	Sema 2.4 mg	Placebo
Number of subjects	1	3	2	24	46	23
History of diabetic retinopathy						
No, N (%)	1 (100)	2 (66.7)	2 (100)	21 (87.5)	37 (80.4)	18 (78.3)
Yes, N (%)	0	1 (33.3)	0	3 (12.5)	9 (19.6)	5 (21.7)
Age (years)						
N	1	3	2	24	46	23
Mean (SD)	61 (.)	49 (5)	43 (6)	53 (8)	54 (10)	52 (7)
Median	61	47	43	53	55	51
Min ; Max	61 ; 61	46 ; 55	39 ; 47	35 ; 69	32 ; 78	38 ; 68
Diabetes duration (years)						
N	1	3	2	24	46	23
Mean (SD)	6.1 (.)	9.9 (5.4)	6.6 (6.5)	7.9 (5.7)	7.6 (5.5)	8.1 (3.9)
Median	6.1	9.8	6.6	7.1	6.1	7.6
Min ; Max	6.1 ; 6.1	4.5 ; 15.3	2.0 ; 11.2	0.5 ; 22.9	0.7 ; 23.1	1.2 ; 19.2
HbA1c (%) at baseline						
N	1	3	2	24	46	23
Mean (SD)	8.4 (.)	9.4 (0.5)	8.3 (0.5)	8.2 (0.7)	8.3 (0.8)	8.1 (0.8)
Median	8.4	9.5	8.3	8.2	8.1	7.9
Min ; Max	8.4 ; 8.4	8.9 ; 9.8	7.9 ; 8.6	7.1 ; 9.5	6.8 ; 10.3	7.1 ; 10.1
HbA1c (%) change at Visit 24 (Week 68)						
N	1	3	2	24	46	23
Mean (SD)	-0.5 (.)	-2.8 (1.1)	-0.4 (0.7)	-2.2 (0.6)	-2.2 (1.1)	0.3 (1.5)
Median	-0.5	-2.5	-0.4	-2.1	-2.2	0.1
Min ; Max	-0.5 ; -0.5	-4.0 ; -1.9	-0.9 ; 0.1	-3.2 ; -1.3	-4.5 ; 1.2	-1.2 ; 5.8

The table summarises diabetic retinopathy risk factors in subjects with AEs of new onset or worsening of diabetic retinopathy with additional data collection versus subjects without these AEs. Events that are also captured by the pre-defined MedDRA search are included covering the preferred term 'Diabetic retinopathy'.
AE: Adverse event, N: number of subjects, %: proportion of subjects.

表 2.7.4.2-62　糖尿病網膜症－糖尿病網膜症の新規発症又は悪化の有害事象を発現した被験者と発現しなかった被験者におけるリスク因子－in-trial 観察期間－安全性解析対象集団（4374 試験）

	Subjects with events			Subjects without events		
	Sema 1.0 mg	Sema 2.4 mg	Placebo	Sema 1.0 mg	Sema 2.4 mg	Placebo
Number of subjects	12	19	11	390	384	391
History of diabetic retinopathy						
No, N (%)	5 (41.7)	14 (73.7)	8 (72.7)	356 (91.3)	344 (89.6)	357 (91.3)
Yes, N (%)	7 (58.3)	5 (26.3)	3 (27.3)	34 (8.7)	40 (10.4)	34 (8.7)
Age (years)						
N	12	19	11	390	384	391
Mean (SD)	53 (12)	55 (11)	57 (7)	56 (10)	55 (11)	55 (11)
Median	53	55	54	56	56	56
Min ; Max	35 ; 71	32 ; 74	50 ; 72	20 ; 81	19 ; 84	20 ; 82
Diabetes duration (years)						
N	12	19	11	390	384	390
Mean (SD)	8.8 (5.7)	7.1 (5.6)	10.3 (7.8)	7.7 (5.9)	8.3 (6.2)	8.1 (6.1)
Median	7.6	4.6	8.8	6.5	6.9	6.7
Min ; Max	1.9 ; 23.4	0.5 ; 17.6	0.6 ; 29.9	0.5 ; 34.7	0.5 ; 37.7	0.6 ; 29.6
HbA1c (%) at baseline						
N	12	19	11	390	384	391
Mean (SD)	8.4 (0.8)	8.3 (1.0)	8.2 (1.0)	8.1 (0.8)	8.1 (0.8)	8.1 (0.8)
Median	8.5	7.7	8.4	8.0	8.0	8.0
Min ; Max	7.2 ; 9.4	7.2 ; 10.4	6.6 ; 9.7	5.8 ; 10.2	6.7 ; 10.6	5.7 ; 10.3
HbA1c (%) change at Visit 24 (Week 68)						
N	12	19	10	363	362	363
Mean (SD)	-1.3 (1.8)	-2.0 (1.2)	-0.2 (1.3)	-1.6 (1.1)	-1.7 (1.2)	-0.3 (1.3)
Median	-1.6	-2.0	-0.2	-1.7	-1.7	-0.3
Min ; Max	-3.7 ; 3.5	-4.5 ; 1.1	-2.1 ; 1.6	-4.7 ; 2.8	-4.9 ; 5.4	-3.8 ; 6.1

The table summarises diabetic retinopathy risk factors in subjects with AEs of new onset or worsening of diabetic retinopathy with additional data collection versus subjects without these AEs. Events that are also captured by the pre-defined MedDRA search are included covering the following 5 preferred terms: 'Diabetic retinopathy', 'Non-proliferative retinopathy', 'Retinal haemorrhage', 'Retinopathy' and 'Macular oedema'.
AE: Adverse event, N: number of subjects, %: proportion of subjects.

2.7.4.2.2.10.3 眼の検査

ベースライン、52 週及び投与終了時（68 週）に眼の検査（眼底写真又は散瞳眼底検査）を実施した。

4382 及び 4374 試験では、ベースライン及び 68 週の眼の検査結果に、投与群間で明らかな違いは認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.6.8、4374 試験（Module 5.3.5.1）EOT Table 14.3.6.8〕。ベースラインから 68 週の変化に基づくと、各投与群の数例の被験者において、眼の検査の結果がベースライン時に「正常」又は「異常、臨床的に問題なし」から 68 週に「異常、臨床的に問題あり」に変化した。同様の結果が、ベースラインから 52 週の変化でもみられた〔4382 試験（Module 5.3.5.1）EOT Table 14.3.6.9、4374 試験（Module 5.3.5.1）EOT Table 14.3.6.9〕。

個々の被験者の眼の検査の結果は、4382 試験（Module 5.3.5.1）EOT Listing 14.3.7.4 及び 4374 試験（Module 5.3.5.1）EOT Listing 14.3.7.4 に示す。

2.7.4.2.2.10.4 結論

網膜障害の有害事象を発現した被験者の割合は、4382 試験ではセマグルチド 1.7 mg 群及びプラセボ群と比較してセマグルチド 2.4 mg 群で高く、4374 試験ではプラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群で高かった。有害事象の大部分は「糖尿病網膜症」（基本語）として報告された。この「糖尿病網膜症」について、4382 試験では事象を発現した被験者の割合及び単位時間あたりの発現件数に投与群間で違いは認められなかったが、4374 試験ではセマグルチド 1.0 mg 群及びプラセボ群と比較してセマグルチド 2.4 mg 群でより多くの被験者が事象を発現した。重篤な網膜障害の有害事象は認められず、大部分の事象が軽度であり、治験責任医師により治験薬との因果関係は「なし」と判定された。

治験責任医師により糖尿病網膜症の新規発症又は悪化と判断された事象（基本語）は、主に「糖尿病網膜症」であり、両試験において投与群間の発現状況に特定の傾向は認められなかった。大部分の事象が、試験において予定されていた 2 回の眼の検査（又は他の定期検査）で特定され、眼に関連する症状の発現に基づくものではなかった。また大部分の事象では、事象に対する治療は必要ないと判断され、経過観察のみであった。4374 試験では、いずれの投与群でも、ベースラインにおいて糖尿病網膜症の既往歴を有していた被験者の割合は、事象を発現しなかった被験者と比較して事象を発現した被験者で高かったが、4382 試験では同様の傾向はみられなかった。

ベースライン及び 68 週の眼の検査の結果に、投与群間で明らかな違いはみられなかった。

以上の結果は、2 型糖尿病に対するセマグルチド皮下投与（オゼンピック皮下注）での現在の知見と同様であった。

2.7.4.2.2.11 免疫原性

2.7.4.2.2.11.1 背景及び評価方法

タンパク製剤として、セマグルチドは局所又は全身の免疫原性に関連する有害事象あるいは抗セマグルチド抗体の産生を引き起こす潜在的リスクがある。そのため、免疫原性に関連する有害事象をセマグルチドの注目すべき安全性領域とした。

アレルギー反応又は注射部位反応に関連する可能性がある事象を特定し、要約するために、すべての有害事象に対して MedDRA 検索を実施した〔検索用語については、4382 試験（Module 5.3.5.1）Appendix 16.1.9、4373 試験（Module 5.3.5.1）Appendix 16.1.9、4374 試験（Module 5.3.5.1）Appendix 16.1.9〕。

免疫原性は、さらに抗セマグルチド抗体の測定により評価した。日本人被験者が参加した 3 つの第 3 相試験では、治験期間を通して抗体産生を定期的に評価した。

2.7.4.2.2.11.2 アレルギー反応

日本人被験者が参加した 3 つの第 3 相試験では、アレルギー反応の有害事象を報告した被験者の割合はいずれの投与群でも同様であった（表 2.7.4.2-63、表 2.7.4.2-64 及び表 2.7.4.2-65）。これらの事象の大部分が、器官別大分類「皮膚および皮下組織障害」に含まれる事象であり、いずれの投与群でも明らかな発現傾向は認められなかった。最も高頻度で報告された基本語は、4382 試験では「湿疹」であり、4373 と 4374 試験では「発疹」であった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.39、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.39、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.39〕。

4373 試験のプラセボ群の 1 件（「過敏症」）と 4374 試験のセマグルチド 1.0 mg 群で発現した 1 件（「ショック」）を除き、すべての有害事象が非重篤であった。重篤な有害事象は治験終了時までに回復した。事象の大部分が軽度又は中等度であり、治験責任医師により、治験薬との因果関係は「なし」と判定された。4373 試験の 4 例（セマグルチド 2.4 mg 群の 2 例とプラセボ群の 2 例）ならびに 4374 試験の 3 例（セマグルチド 2.4 mg 群の 1 例及びプラセボ群の 2 例）は、治験薬の投与を中止した。

4373 試験のセマグルチド 2.4 mg で 1 件の「アナフィラキシー性輸血反応」が報告されたが、治験薬の投与とは関連がなかった〔4373 試験（Module 5.3.5.1）Appendix 16.2.7, Listing 16.2.7.1〕。3 つの第 3 相試験では、この他のアナフィラキシー反応の事象の報告はなかった。

表 2.7.4.2-63　アレルギー反応の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	100			199			101		
Patient years of exposure (PYE)	136.2			275.0			141.8		
Adverse Events	11 (11.0)	13	9.5	18 (9.0)	21	7.6	9 (8.9)	10	7.1
SAEs	0			0			0		
Severe AEs	0			0			0		
Leading to Permanent treatment discontinuation	0			0			0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 23.1

表 2.7.4.2-64　アレルギー反応の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R
Number of subjects	1306			655		
Patient years of exposure (PYE)	1706.1			829.6		
Adverse Events	96 (7.4)	108	6.3	54 (8.2)	63	7.6
SAEs	0			1 (0.2)	1	0.1
Severe AEs	5 (0.4)	6	0.4	2 (0.3)	2	0.2
Leading to Permanent treatment discontinuation	2 (0.2)	2	0.1	2 (0.3)	2	0.2

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

表 2.7.4.2-65　　アレルギー反応の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	402				403				402			
Patient years of exposure (PYE)	529.8				533.0				528.3			
Adverse Events	22	(5.5)	24	4.5	26	(6.5)	29	5.4	18	(4.5)	21	4.0
SAEs	1	(0.2)	1	0.2	0				0			
Severe AEs	1	(0.2)	1	0.2	0				0			
Leading to Permanent treatment discontinuation	0				1	(0.2)	1	0.2	2	(0.5)	2	0.4

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

2.7.4.2.2.11.3 注射部位反応

4382 試験では、注射部位反応の有害事象はセマグルチド 2.4 mg 群のみで報告された（4 例 15 件）（表 2.7.4.2-66）。4373 及び 4374 試験では、注射部位反応の有害事象を報告した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド群（1.0 mg 及び 2.4 mg）で同様又は低かった（表 2.7.4.2-67 及び表 2.7.4.2-68）。4382 と 4374 試験においてセマグルチドの用量の増量に伴う一貫した用量反応性はみられなかった。高頻度で報告された基本語は、4382 試験では「注射部位紅斑」、4373 及び 4374 試験では「注射部位疼痛」及び「注射部位内出血」であった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.37、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.37、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.3〕。

3 つの第 3 相試験において、すべての事象が非重篤であり、4374 試験のセマグルチド 1.0 mg 群で発現した 1 件を除き、すべての事象が軽度又は中等度であった。事象の大部分の転帰が「回復」であった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.36、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.36、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.36〕。治験薬投与の中止に至った注射部位反応の有害事象は認められなかった。

表 2.7.4.2-66　注射部位反応の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	100			199			101		
Patient years of exposure (PYE)	136.2			275.0			141.8		
Adverse Events	0			4	(2.0)	15 5.5	0		
SAEs	0			0			0		
Severe AEs	0			0			0		
Leading to Permanent treatment discontinuation	0			0			0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 23.1

表 2.7.4.2-67　注射部位反応の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg			Placebo		
	N	(%)	E R	N	(%)	E R
Number of subjects	1306			655		
Patient years of exposure (PYE)	1706.1			829.6		
Adverse Events	65	(5.0)	99 5.8	44	(6.7)	82 9.9
SAEs	0			0		
Severe AEs	0			0		
Leading to Permanent treatment discontinuation	0			0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

表 2.7.4.2-68　注射部位反応の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	402			403			402		
Patient years of exposure (PYE)	529.8			533.0			528.3		
Adverse Events	6 (1.5)	7	1.3	12 (3.0)	18	3.4	10 (2.5)	18	3.4
SAEs	0			0			0		
Severe AEs	1 (0.2)	1	0.2	0			0		
Leading to Permanent treatment discontinuation	0			0			0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

2.7.4.2.2.11.4 抗体

日本人被験者が参加した 3 つの第 3 相試験において、試験期間を通して特定の来院時及び事後調査（治験終了）来院で、抗セマグルチド抗体を測定した。

いずれの試験においても、ベースライン以降のいずれかの時点で抗セマグルチド抗体陽性であった被験者の割合は低かった（セマグルチド 2.4 mg 群で 2.9～3.0%、セマグルチド 1.7 mg 群で 1.0%、セマグルチド 1.0 mg 群で 1.0%）〔4382 試験（Module 5.3.5.1）EOT table 14.3.5.45、4373 試験（Module 5.3.5.1）EOT table 14.3.5.45、4374 試験（Module 5.3.5.1）EOT Table 14.3.5.47〕。

4382 試験では、セマグルチド 1.7 mg 群の 1 例（セマグルチド 1.7 mg に無作為割り付けされたすべての被験者の 1.0%に相当）は投与前から抗体が存在しており、ベースライン、4、8、12、28 週に抗セマグルチド抗体陽性であったが、52、68 及び 75 週では陰性であった。抗セマグルチド抗体価は、ベースラインが最も高く、ベースライン以降は低下したことから〔4382 試験（Module 5.3.5.1）EOT Listing 14.3.4.2〕、セマグルチドの投与によって投与前に存在していた抗体が上昇することはなかった。セマグルチド 2.4 mg 群では、6 例（3%）がベースライン以降の 1 回以上の時点で投与により産生された抗体が認められた。このうち、5 例（2.5%）が内因性 GLP-1 に対する交叉反応性を有する抗体も陽性であった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.5.45〕。また、このうち 1 例は 1 回の来院（来院 14、28 週）で一時的に抗体が陽性であったが、残りの 5 例は持続的に抗体が認められた。抗体反応の程度は低かった。セマグルチド 2.4 mg 群において抗体反応が持続した 5 例のうち、4 例は事後調査来院時にも抗セマグルチド抗体陽性が認められ、いずれも試験の 1 時点以上前の時点で抗セマグルチド抗体が認められた。*In vitro* で中和作用を有する抗セマグルチド抗体又は *in vitro* で中和作用を有する抗 GLP-1 抗体が陽性であった検体はなかった。

4373 試験では、セマグルチド 2.4 mg 群で、1 例（セマグルチド 2.4 mg に無作為割り付けされたすべての被験者の 1.0%未満）においてベースライン時に抗セマグルチド抗体が認められたが、ベースライン以降のすべての来院では抗体が陰性であった〔4373 試験（Module 5.3.5.1）EOT Listing 14.3.4.2〕。したがって、抗体がセマグルチド 2.4 mg 投与後に上昇しなかった。ベースライン以降の 1 回以上の時点で抗セマグルチド抗体が認められた 38 例（2.9%）のうち、20 例（1.5%）が内因性 GLP-1 に対する交叉反応性を有する抗体も陽性であった〔4373 試験（Module 5.3.5.1）EOT Table 14.3.5.45〕。多くの被験者が試験期間中の 1 回の来院のみで抗体が陽性であり、16 例が事後調査来院時に抗セマグルチド抗体が認められた。抗体反応の程度は低かった。*In vitro* で中和作用を有する抗セマグルチド抗体又は *in vitro* で中和作用を有する抗 GLP-1 抗体が陽性であった検体はなかった。

4374 試験では、セマグルチド 2.4 mg 群の 12 例（3.0%）及びセマグルチド 1.0 mg 群の 4 例（1.0%）において、ベースライン以降の 1 回以上の来院で抗セマグルチド抗体が認められた。このうち、セマグルチド 2.4 mg 群の 7 例（1.7%）及びセマグルチド 1.0 mg 群の 4 例（1.0%）が内因性 GLP-1 に対する交叉反応性を有する抗体も陽性であった〔4374 試験（Module 5.3.5.1）EOT Table 14.3.5.47〕。多くの被験者が試験期間中の 1 回の来院のみで抗体が陽性であり〔4374 試験（Module 5.3.5.1）EOT Table 14.3.4.2〕、4 例が事後調査来院時に抗セマグルチド抗体が認められた。抗体反応の程度は低かった。*In vitro* で中和作用を有する抗セマグルチド抗体又は *in vitro* で中和作用を有する抗 GLP-1 抗体が陽性であった検体はなかった。

抗セマグルチド抗体が陽性であった被験者の詳細については、各治験総括報告書〔4382 試験（Module 5.3.5.1）Section 12.5.10.3、EOT Listing 14.3.4.2、4373 試験（Module 5.3.5.1）Section 12.5.11.3、EOT Listing 14.3.4.2、4374 試験（Module 5.3.5.1）Section 12.5.11.3、EOT Listing 14.3.4.2〕に示す。

2.7.4.2.2.11.5 結論

日本人被験者が参加した 3 つの第 3 相試験（4382、4373 及び 4374 試験）すべてにおいて、アレルギー反応の有害事象を発現した被験者の割合は投与群間で同様であった。4374 試験のセマグルチド 1.0 mg 群及び 4373 試験のプラセボ群の各 1 例を除き、すべての事象が非重篤であった。発現した事象（基本語）の種類の発現状況に投与群間で明らかな違いは認められなかった。3 つの試験において、治験薬の投与に関連するアナフィラキシー反応の事象は認められなかった。

4382 試験では、セマグルチド 2.4 mg 群においてのみ注射部位反応の有害事象が報告された。4373 及び 4374 試験では、注射部位反応の有害事象を発現した被験者の割合は、プラセボ群と比較してセマグルチド群（1.0 mg 及び 2.4 mg）で同様又は低かった。4382 及び 4374 試験においてセマグルチドの用量の増加に伴う一貫した用量反応性は認められなかった。すべての注射部位反応の有害事象が非重篤であった。

3 つの試験において、ベースライン以降の 1 時点以上で抗セマグルチド抗体が陽性であった被験者の割合は低かった。2 例において、ベースラインで投与前から存在していた抗体が認められた。4373 試験のセマグルチド 2.4 mg 群の 1 例は、ベースライン以外のすべての検体の抗体が陰性であった。4382 試験のセマグルチド 1.7 mg の 1 例は、28 週まで抗体が陽性であったが、その後の来院では抗体は陰性であった。*In vitro* で中和作用を有する抗セマグルチド抗体又は *in vitro* で中和作用を有する抗 GLP-1 抗体が陽性であった検体はなかった。

全体として、セマグルチドで認められた免疫原性は低く、この結果は 2 型糖尿病に対するセマグルチド皮下投与（オゼンピック皮下注）及びセマグルチド経口投与（リベルサス錠）の開発プログラムで報告されたことと同様である。

2.7.4.2.2.12 精神障害

2.7.4.2.2.12.1 背景及び評価方法

中枢作用性の体重管理薬については、近年、メンタルヘルスに影響を及ぼす可能性を検討することが重要視されている。過体重又は肥満被験者の大部分は、精神障害、特にうつ病や不安症などの気分関連障害の既往歴を有する。肥満と精神障害の何らかの因果関係については依然として明確になっていない[83, 84, 85]。肥満男性と比較して肥満女性はうつ病の発現率が高いことから、性別が重要な因子であることが考えられる[83, 84, 86]。

2 型糖尿病に対するセマグルチド皮下投与及びセマグルチド経口投与の開発プログラムでは、セマグルチドと気分関連障害、自殺念慮又は自殺行為との関連性は認められていない。

On-treatment 観察期間を用いて精神障害の有害事象に対する事前に規定された MedDRA 検索に基づき、精神障害のリスクは広く評価された〔検索用語については、4382 試験（Module 5.3.5.1）Appendix 16.1.9、4373 試験（Module 5.3.5.1）Appendix 16.1.9、4374 試験（Module 5.3.5.1）Appendix 16.1.9〕。さ

らに、肥満症のためのセマグルチドの臨床開発プログラムでは、C-SSRS と PHQ-9 の 2 つのメンタルヘルス質問票を用いた。C-SSRS は自殺行為及び自殺念慮を評価する詳細な質問票であり、治験責任医師又は資格を有する代理人との面談として実施した。PHQ-9 は、精神障害の評価に用いられる自己記入式の診断ツールである患者健康質問票の 9 項目のうつ病モジュールである。C-SSRS と PHQ-9 の結果は、in-trial 観察期間に基づき評価した。これらの質問票に基づく評価に in-trial 観察期間を用いたのは、C-SSRS の質問は最終評価時からの期間に対応するものであり、評価に on-treatment 観察期間を使用した場合、多くの評価が除外される可能性があったためである。

被験者の福祉を保護し、被験者が試験を完了する可能性を高めるために、以下の除外基準を適用し、重度な精神障害を有する又は過去に有していた被験者は第 3 相試験への組み入れから除外した。

- スクリーニング前 2 年以内に大うつ病性障害の既往を有する被験者
- その他の重大な精神障害（統合失調症、双極性障害など）と診断された被験者
- スクリーニング時の PHQ-9 のスコアが 15 点以上の被験者
- これまでに自殺企図の既往を有する被験者
- スクリーニング前の 30 日以内に自殺行為のあった被験者
- スクリーニング前の 30 日以内に C-SSRS の 4 型又は 5 型に該当する自殺念慮を有する被験者

第 3 相試験では、スクリーニング時に精神障害に関する詳細な既往歴を体系的に収集した（2.7.4.1.1.8.1 項）。

2.7.4.2.2.12.2 精神障害の既往歴

日本人被験者が参加した 3 つの第 3 相試験では、精神障害の既往歴を有する被験者の割合について投与群間で明らかな違いはみられなかった。精神障害の既往歴に関するデータは、各治験総括報告書（4382 試験（Module 5.3.5.1）EOT Table 14.1.15、4373 試験（Module 5.3.5.1）EOT Table 14.1.16、4374 試験（Module 5.3.5.1）EOT Table 14.1.13）に示す。

2.7.4.2.2.12.3 有害事象に基づく精神障害

4382 試験では、いずれの投与群でも精神障害の有害事象の報告件数は少なかった（各投与群で 6 件以下）（表 2.7.4.2-69）。4373 試験では、精神障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群で低い傾向がみられたが（表 2.7.4.2-70）、4374 試験では、精神障害の有害事象を報告した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド 1.0 mg 群及びセマグルチド 2.4 mg 群で高い傾向がみられた（表 2.7.4.2-71）。4382 及び 4374 試験において、用量反応性はみられなかった。3 つのいずれの試験でも、基本語レベルについては投与群間で明らかな違いは認められなかった。4382 試験において最も高頻度で報告された精神障害の有害事象は、「不眠症」であり、1 例以上で報告された基本語はこの事象のみであった。4373 及び 4374 試験において高頻度で報告された事象（基本語）は、「不安」、「不眠症」、「うつ病」及び「抑うつ気分」であった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.59、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.57、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.57〕。

4382 及び 4374 試験では、すべての精神障害の事象が非重篤で、軽度又は中等度であった。4373 試験では、大部分の事象が、非重篤であり、軽度又は中等度であった。器官別大分類「精神障害」に含ま

れる重篤な有害事象は、セマグルチド 2.4 mg 群で 3 件（「自殺念慮」、「急性ストレス反応」及び「不安」が各 1 件）ならびにプラセボ群で 1 件「自殺企図」が報告された。4 件の重篤な有害事象のすべてが、治験責任医師により治験薬との因果関係は「なし」と判定され、転帰は「回復」であった〔4373 試験（Module 5.3.5.1）EOT Listing 14.3.2.1〕。3 つの試験において、治験薬との因果関係及び転帰に投与群間で明らかな違いは認められなかった。いずれの試験においても、治験薬投与の中止に至った精神障害の有害事象を発現した被験者の割合は少なく、投与群間で明らかな違いも認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.58、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.56、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.56〕。

表 2.7.4.2-69　精神障害の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	100			199			101		
Patient years of exposure (PYE)	136.2			275.0			141.8		
Adverse Events	4 (4.0)	4	2.9	6 (3.0)	6	2.2	1 (1.0)	1	0.7
SAEs	0			0			0		
Severe AEs	0			0			0		
Leading to Permanent treatment discontinuation	0			0			0		

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 23.1

表 2.7.4.2-70　精神障害の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R
Number of subjects	1306			655		
Patient years of exposure (PYE)	1706.1			829.6		
Adverse Events	124 (9.5)	160	9.4	83 (12.7)	113	13.6
SAEs	3 (0.2)	3	0.2	1 (0.2)	1	0.1
Severe AEs	3 (0.2)	5	0.3	4 (0.6)	5	0.6
Leading to Permanent treatment discontinuation	7 (0.5)	7	0.4	3 (0.5)	4	0.5

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

表 2.7.4.2-71　精神障害の有害事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	402			403			402		
Patient years of exposure (PYE)	529.8			533.0			528.3		
Adverse Events	23 (5.7)	28	5.3	24 (6.0)	29	5.4	15 (3.7)	16	3.0
SAEs	0			0			0		
Severe	0			0			0		
Leading to Permanent treatment discontinuation	1 (0.2)	1	0.2	0			1 (0.2)	1	0.2

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years. PYE: The duration of the on-treatment period in years.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

2.7.4.2.2.12.4 メンタルヘルス評価

日本人被験者が参加した 3 つの第 3 相試験において、スクリーニング時、無作為割り付け時、12、20、36、52 及び 68 週（治験薬の投与終了時）の 7 回の来院においてメンタルヘルスの評価を実施した。

2.7.4.2.2.12.4.1 コロンビア自殺評価スケール（C-SSRS）

ベースラインにおいて、4373 試験のプラセボ群の 2 例のみに自殺念慮が認められた。いずれの試験及び投与群においても、自殺行為が認められた被験者はいなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.6.10、4373 試験（Module 5.3.5.1）EOT Table 14.3.6.8、4374 試験（Module 5.3.5.1）EOT Table 14.3.6.10〕。

ベースライン後では、いずれの試験においても自殺念慮が認められた被験者は少なく（各投与群で 6 例以下）、投与群間で明らかな違いは認められなかった。これらの被験者のうち、4374 試験のセマグルチド 2.4 mg の 1 例に自殺行為が認められた。

2.7.4.2.2.12.4.2 患者さんの健康に関する質問票-9（PHQ-9）

ベースラインにおいて、4382 及び 4373 試験では、PHQ-9 スコアが 10～14 点（中等度うつ症状）であった被験者の割合は投与群間で同様であったが、4374 試験では、PHQ-9 スコアが 10～14 点であった被験者数はプラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群で多い傾向が認められた。除外基準に規定したように、PHQ-9 スコアが 15 点以上の被験者はいなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.6.11、4373 試験（Module 5.3.5.1）EOT Table 14.3.6.9、4374 試験（Module 5.3.5.1）EOT Table 14.3.6.11〕。

ベースライン後では、4382 試験において、PHQ-9 スコアが 10～14 点（中等度うつ症状）及び 15～19 点（中等度～重度うつ症状）であった被験者の割合は、すべての投与群で低く、同様であった。試験期間のいずれかの時点に、PHQ-9 スコアが 20 点以上であった被験者はいなかった。4373 試験では、PHQ-9 スコアが 10 点以上〔すなわち、10～14 点、15～19 点又は 20 点以上（重度うつ症状）〕であった被験者の割合は、プラセボ群と比較してセマグルチド 2.4 mg 群でわずかに低かった。4374 試験では、PHQ-9 スコアが 15 点以上（すなわち、15～19 点又は 20 点以上）であった被験者が、プラセボ群と比較してセマグルチド 1.0 mg 群及びセマグルチド 2.4 mg 群で多い傾向が認められた。

いずれの試験においても、無作為割り付け以降に、質問項目 9「死んだ方がましだ、あるいは自分を何らかの方法で傷つけようと思ったことがある」に「はい」と回答した被験者の割合に投与群間で明らかな違いは認められなかった。

2.7.4.2.2.12.5 結論

4382 及び 4373 試験では、プラセボ群と比較してセマグルチド群（1.7 及び 2.4 mg）において精神障害の有害事象の発現件数の明らかな増加は認められなかったが、4374 試験では、プラセボ群と比較して、セマグルチド群（1.0 及び 2.4 mg）で非重篤な精神障害の有害事象がより多く発現した。4382 及び 4374 試験において、用量反応性は認められなかった。さらに、プラセボ群と比較してセマグルチド群

（1.0、1.7 及び 2.4 mg）で質問票に基づく自殺念慮、自殺行為又は抑うつ症状のリスクの増加することは認められなかった。

これらの結果は、2 型糖尿病に対するセマグルチド皮下投与及びセマグルチド経口投与の臨床開発プログラムにおいて有害事象報告に基づいて得られた結果と同様であった。以上のことから、肥満症のためのセマグルチド 2.4 mg の臨床開発プログラムにおいて実施した有害事象報告及び質問票に基づくより詳細な評価は、2 型糖尿病に対する臨床開発プログラムから得られた知見を支持するものであると考えられた。

2.7.4.2.2.13　稀な事象

2.7.4.2.2.13.1　背景及び評価方法

いずれの医薬品の臨床開発でも、発現頻度は少ないが薬物により発現する可能性のある事象が確実に評価され、治験薬との因果関係が判定されるように稀な事象は注目すべき安全性領域として定義される[87]。したがって、稀な事象をセマグルチド 2.4 mg の特に注目すべき安全性領域として、on-treatment 観察期間を用いて評価した。該当する事象は事前に規定した MedDRA 検索に基づき特定した〔4382 試験（Module 5.3.5.1）Appendix 16.1.9、4373 試験（Module 5.3.5.1）Appendix 16.1.9、4374 試験（Module 5.3.5.1）Appendix 16.1.9〕。他の安全性領域の MedDRA 検索で特定される基本語は除外した。これらの事象の種類は多岐にわたることから、発現した事象の総数を比較することは重要ではないため、評価は器官別大分類及び基本語、ならびに叙述の症例評価に基づき実施した。

2.7.4.2.2.13.2　有害事象に基づく稀な事象

日本人被験者が参加した 3 つのいずれの第 3 相試験でも、MedDRA 検索により特定された稀な事象の発現件数は少なく、報告された有害事象の発現頻度について投与群間で違いはみられなかった（表 2.7.4.2-72、表 2.7.4.2-73 及び表 2.7.4.2-74）。事象は複数の器官別大分類に分布しており、特定の基本語が多く発現することはなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.55、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.53、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.53〕。

事象の大部分が、非重篤で、軽度又は中等度であり、治験責任医師により治験薬との因果関係は「なし」と判定された。4382 試験のセマグルチド 2.4 mg 群の 1 件（「メッケル憩室炎」）及び 4373 試験のプラセボ群の 1 件（「好中球減少性敗血症」）が重篤な有害事象として報告された。これらの有害事象は、治験責任医師により因果関係は「なし」と判定された。「メッケル憩室炎」については、治験薬の投与を一時的に中断したが、「好中球減少性敗血症」は、治験薬の投与の変更には至らなかった〔Trial 4382 試験（Module 5.3.5.1）Appendix 16.2.7, Listing 16.2.7.1、4373 試験（Module 5.3.5.1）Appendix 16.2.7, Listing 16.2.7.1〕。

表 2.7.4.2-72　稀な事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg N	(%)	E	R	Sema 2.4 mg N	(%)	E	R	Placebo N	(%)	E	R
Number of subjects	100				199				101			
Patient years of exposure (PYE)	136.2				275.0				141.8			
Events	1	(1.0)	1	0.7	2	(1.0)	2	0.7	0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years, PYE: The duration of the on-treatment period in years.
Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 23.1

表 2.7.4.2-73　稀な事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg N	(%)	E	R	Placebo N	(%)	E	R
Number of subjects	1306				655			
Patient years of exposure (PYE)	1706.1				829.6			
Events	7	(0.5)	7	0.4	5	(0.8)	6	0.7

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years, PYE: The duration of the on-treatment period in years.
Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

表 2.7.4.2-74　稀な事象－MedDRA 検索－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	402				403				402			
Patient years of exposure (PYE)	529.8				533.0				528.3			
Events	4	(1.0)	4	0.8	3	(0.7)	3	0.6	2	(0.5)	2	0.4

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events,
R: Event rate per 100 years, PYE: The duration of the on-treatment period in years.
Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

2.7.4.2.2.13.3　　結論

日本人被験者が参加した 3 つの第 3 相試験（4382、4373 及び 4374 試験）において、稀な事象の MedDRA 検索で特定された事象は、複数の基本語にわたっており、特定の事象が多く報告されることはなかった。重篤な有害事象の報告は少なかった（4382 試験のセマグルチド 2.4 mg 群で 1 件及び 4373 試験のプラセボ群で 1 件）。得られたデータにより、稀な事象のいずれについてもセマグルチドによるリスクの増加は示唆されなかった。

2.7.4.2.3　国際共同第 3 相試験の併合データにおける有害事象

2.7.4.2.3.1 背景及び評価方法

肥満症のためのセマグルチド 2.4 mg の安全性の集約的な評価を支持し、潜在的な安全性のシグナル、特に発現件数が少ない安全性領域の安全性シグナルを検出する可能性を高めるために、国際共同第 3 相試験の併合データを本概要に提示する。国際共同第 3 相試験併合データには 4 つの第 3 相試験（4373、4374、4375 及び 4376 試験）が含まれ、セマグルチド 2.4 mg とプラセボを比較する。

国際共同第 3 相試験併合データに含まれる 4 つの第 3 相試験のデザインの特徴を 2.7.4.1.1.3.2 項に示す。各試験のデザインの詳細については各治験総括報告書（Module 5.3.5.1）Section 9 に示す。

国際共同第 3 相試験併合データに含まれる各試験の被験者の内訳、人口統計学的特性及び他のベースライン特性については、各治験総括報告書〔4373 試験（Module 5.3.5.1）Section 10.1、Section 10.2、4374 試験（Module 5.3.5.1）Section 10.1、Section 10.2、4375 試験（Module 5.3.5.1）Section 10.1、Section 10.2、4376 試験（Module 5.3.5.1）Section 10.1、Section 10.2〕に示す。国際共同第 3 相併合データに基づく被験者の内訳、人口統計学的特性及び他のベースライン特性は Global summary of safety（Module 5.3.5.3）Appendix 7.1 に示し、被験者の内訳は Table 7.1.1、ベースライン特性は Table 7.1.8 及び Table 7.1.9、既往歴は Table 7.1.10～Table 7.1.14、スクリーニング時の合併症は Table 7.1.15～Table 7.1.19、併用薬剤は Table 7.1.20 にそれぞれ示す。

個々の試験及び国際共同第 3 相試験併合データの安全性データの収集方法については 2.7.4.1.1.8 項、統計手法については2.7.4.1.1.9 項に示す。

2.7.4.2.3.2 有害事象の概要

有害事象

第 3 相試験併合データでは、プラセボ併合群と比較してセマグルチド 2.4 mg 併合群でより多くの有害事象が報告された（表 2.7.4.2-75）。この違いは主に胃腸障害の有害事象によるものであった。これらの事象の大部分は、非重篤で、軽度又は中等度であり、大部分の被験者が試験終了時までに事象から回復した。第 3 相試験併合データでは、重篤な有害事象及び重大な有害事象を発現した被験者の割合も、プラセボ併合群と比較してセマグルチド 2.4 mg 併合群でわずかに高かった。治験薬投与の中止に至った有害事象を発現した被験者の割合は、両併合群で少なかったが、プラセボ併合群と比較してセマグルチド 2.4 mg 併合群で高かった。この違いは胃腸障害の有害事象によるものであった。

表 2.7.4.2-75　有害事象－on-treatment 観察期間－安全性解析対象集団（第 3 相試験併合データ）

	Sema 2.4 mg N	(Adj.%)	E	Adj.R	Placebo N	(Adj.%)	E	Adj.R
Number of subjects	2650				1529			
Patient years of exposure (PYE)	3309.5				1885.4			
All events	2348	(88.5)	17774	521.0	1272	(83.6)	6794	365.2
SAEs	246	(9.3)	341	10.5	100	(6.4)	132	6.8
Severity								
Severe	269	(9.9)	459	13.4	105	(6.9)	148	8.0
Moderate	1381	(51.5)	4878	141.2	654	(43.7)	1778	97.3
Mild	2180	(82.2)	12437	366.4	1143	(75.1)	4868	259.9
Relationship to trial product								
Probable	1048	(39.7)	3603	105.1	282	(18.7)	579	31.0
Possible	1371	(51.3)	4863	140.6	464	(30.9)	1032	55.7
Unlikely	2095	(78.7)	9266	274.0	1205	(79.3)	5164	277.6
Missing	36	(1.4)	42	1.3	17	(1.1)	19	0.9
Outcome								
Fatal	2	(<0.1)	2	<0.1	3	(0.2)	3	0.2
Recovered	2257	(85.0)	15396	449.4	1206	(79.4)	5455	293.6
Recovering	143	(5.3)	222	6.7	75	(5.0)	112	6.4
Recovered With Sequelae	20	(0.8)	30	0.9	7	(0.5)	8	0.4
Not Recovered	1034	(39.1)	2109	63.4	605	(39.6)	1211	64.4
Unknown	8	(0.4)	15	0.5	5	(0.3)	5	0.2
Missing	0				0			
Leading to Permanent treatment discontinuation	149	(5.7)	200	5.9	47	(3.0)	57	3.0

Phase 3a pool: STEP 1-4 data from subjects randomised to Sema 2.4 mg or Placebo during the controlled periods of the trials.
Adverse events with onset prior to randomisation are not included.
N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure, Adj.: Adjusted
The % and R are adjusted using the Cochran-Mantel-Haenszel method to account for differences between trials.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

死亡及びその他の重篤な有害事象

第 3 相試験併合データでは、in-trial 観察期間において、6 例に計 11 件の転帰「死亡」の有害事象（セマグルチド 2.4 mg 併合群で 3 例 3 件、プラセボ併合群で 3 例 8 件）が報告された。転帰「死亡」の有害事象及び死亡例の発現については、セマグルチド 2.4 mg 併合群とプラセボ併合群は同様であった。セマグルチド 2.4 mg 併合群及びプラセボ併合群で、転帰「死亡」の有害事象を発現した被験者の割合は少なく、同様であった（表 2.7.4.2-76）。転帰「死亡」の有害事象は複数の器官別大分類及び基本語に分布していた。セマグルチド 2.4 mg 併合群については、転帰「死亡」の有害事象は、器官別大分類「一般・全身障害および投与部位の状態」（2 例 2 件）及び「心臓障害」（1 件）に含まれるものであった〔Global summary of safety（Module 5.3.5.3）Appendix 7.2、Table 7.2.19〕。

第 3 相試験併合データにおいて、計 6 件の事象がイベント判定委員会に送付され、確定された〔Global summary of safety（Module 5.3.5.3）Appendix 7.3、Table 7.3.74〕。この 6 例は、表 2.7.4.2-76 に提示した in-trial 観察期間に転帰「死亡」の有害事象を発現した 6 例と同じ被験者であった。セマグルチド 2.4 mg 併合群の 3 件の死亡は、死因が特定されなかった 1 件の死亡を含み、心血管死に分類された。プラセボ併合群の 3 件の死亡は、すべて悪性腫瘍による死亡と分類された〔Global summary of safety（Module 5.3.5.3）Appendix 7.3、Table 7.3.75〕。第 3 相試験併合データで報告された死亡に加えて、体重管理のためのセマグルチド 2.4 mg の臨床開発プログラムでは 2 例の死亡が報告された。4374 試験のセマグルチド 1.0 mg の 1 例の死亡は原因不明の死亡と分類され、4153 試験のセマグルチド 0.4 mg の 1 日 1 回投与（急速用量漸増）群の 1 例の死亡は、悪性腫瘍による死亡に分類された。

表 2.7.4.2-76　　転帰「死亡」の有害事象－in-trial 観察期間（第 3 相試験併合データ）

System organ class Preferred term	Sema 2.4 mg N (Adj.%) E Adj.R	Placebo N (Adj.%) E Adj.R
Number of subjects	2650	1529
Patient years of observation (PYO)	3556.8	2048.9
Events	3 (0.1) 3 <0.1	3 (0.2) 8 0.4

Phase 3a pool: STEP 1-4 data from subjects randomised to Sema 2.4 mg or Placebo during the controlled periods of the trials.
Adverse events with onset prior to randomisation are not included.
N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of observation, Adj.: Adjusted.
The % and R are adjusted using the Cochran-Mantel-Haenszel method to account for differences between trials.

重篤な有害事象を発現した被験者の割合は、プラセボ併合群と比較してセマグルチド 2.4 mg 併合群でわずかに高く、この違いは胆嚢障害（主に 4375 試験で認められた）及び胃腸障害の有害事象によるものであった。重篤な有害事象を発現した被験者の大部分は試験終了時に回復した。重篤な有害事象の転帰が「未回復」、「回復したが後遺症あり」及び「死亡」と報告された被験者の割合は、セマグルチド 2.4 mg 併合群とプラセボ併合群で同様であった。重篤な有害事象の大部分は治験責任医師により治験薬との因果関係は「なし」と判定された。治験薬投与の中止に至った重篤な有害事象を発現した被験者の割合は、セマグルチド 2.4 mg 併合群とプラセボ併合群で同様であった〔Global summary of safety（Module 5.3.5.3）Appendix 7.2、Table 7.2.20〕。

2.7.4.2.3.3　注目すべき安全性領域

結果の概要

胃腸障害が GLP-1 受容体作動薬の副作用としてよく知られていることと一致して、用量漸増を含む第 3 相試験併合データにおいて胃腸障害の有害事象を発現した被験者の割合は、プラセボ併合群と比較してセマグルチド 2.4 mg 併合群で高かった（表 2.7.4.2-77）。胃腸障害の重篤な有害事象、重度の有害事象及び治験薬投与の中止に至った有害事象を発現した被験者の割合は、プラセボ併合群と比較してセマグルチド 2.4 mg 併合群で高かった〔Global summary of safety（Module 5.3.5.3）Appendix 7.3、Table 7.3.1〕。

第 3 相試験併合データにおいて、胆嚢関連障害を発現した被験者の割合は低かったが、プラセボ併合群と比較してセマグルチド 2.4 mg 併合群でより多くの事象が報告された（表 2.7.4.2-77）。また、胆嚢関連障害の重篤な有害事象及び重大な有害事象の発現頻度及び単位時間あたりの発現件数は、プラセボ併合群と比較してセマグルチド 2.4 mg 併合群で高かった。胆嚢関連障害の有害事象のため治験薬の投与を中止した被験者の割合は、セマグルチド 2.4 mg 併合群とプラセボ併合群で同様であった〔Global summary of safety（Module 5.3.5.3）Appendix 7.3、Table 7.3.1〕。

精神障害、心血管障害／心血管事象、新生物（悪性新生物を含む）、アレルギー反応、注射部位反応、肝障害、稀な事象、急性腎不全、膵炎（急性）及び低血糖（2 型糖尿病を有さない患者を含む第 3 相試験併合データに基づく）について、セマグルチド 2.4 mg 群に好ましくない投与群間の違いは示唆されなかった（表 2.7.4.2-77）。

2 型糖尿病を有する被験者を含む第 3 相試験（4374 試験）を用いて評価した網膜障害及び 2018 年 ADA/2017 年 IHSG 分類に基づく低血糖については、それぞれ 2.7.4.2.2.10 項及び 2.7.4.2.2.9.3 項に示す。

国際共同第 3 相試験の併合データの詳細な評価に基づき、いずれの注目すべき安全性領域においても、プラセボと比較してセマグルチド 2.4 mg で新たな予測されない安全性所見は認められなかった。

表 2.7.4.2-77　　安全性領域の概要（第 3 相試験併合データ、用量漸増を含む第 3 相試験併合データ、2 型糖尿病有さない被験者を含む第 3 相試験併合データ）

	Sema 2.4 mg N	(Adj.%)	E	Adj.R	Placebo N	(Adj.%)	E	Adj.R
Global phase 3a dose escalation group								
Number of subjects	2116				1261			
Patient years of exposure (PYE)	2765.3				1619.3			
Safety focus areas								
Gastrointestinal disorders - OT								
MedDRA search	1562	(72.9)	6993	246.3	581	(47.1)	1334	85.5
Global phase 3a pool								
Number of subjects	2650				1529			
Patient years of exposure (PYE)	3309.5				1885.4			
Patient years of observation (PYO)	3556.8				2048.9			
Safety focus areas								
Gallbladder-related disorders – OT								
MedDRA search	70	(2.5)	85	2.4	24	(1.6)	26	1.5
Acute pancreatitis – OT								
MedDRA search	3	(0.1)	3	<0.1	1	(<0.1)	1	<0.1
EAC-confirmed events	4	(0.2)	5	0.2	1	(<0.1)	1	<0.1
Cardiovascular disorders – IT								
MedDRA search	223	(8.7)	288	8.3	166	(10.9)	218	10.9
EAC-confirmed events	15	(0.6)	17	0.5	11	(0.7)	15	0.7
Neoplasms – IT								
MedDRA search	187	(6.9)	227	6.3	108	(7.1)	126	6.2
Malignant neoplasms – IT								
MedDRA search	28	(1.1)	29	0.8	17	(1.1)	19	0.9
Hepatic disorders – OT								
MedDRA search	60	(2.3)	70	2.1	42	(2.7)	54	2.7
Acute renal failure – OT								
MedDRA search	8	(0.4)	10	0.3	5	(0.3)	5	0.3
Allergic reactions – OT								
MedDRA search	183	(6.9)	207	6.2	102	(6.8)	115	6.2
Injection site reactions - OT								
MedDRA search	113	(4.2)	163	4.7	72	(4.9)	122	6.5
Psychiatric disorders – OT								
MedDRA search	254	(9.3)	341	10.0	157	(10.7)	210	12.1
Rare events - OT								
MedDRA search	21	(0.8)	22	0.7	9	(0.6)	11	0.6
Global phase 3a without T2D group								
Number of subjects	2247				1127			
Patient years of exposure (PYE)	2776.4				1357.0			
Safety focus areas								
Hypoglycaemia – OT								
MedDRA search	13	(0.6)	20	0.7	8	(0.7)	10	0.8

Phase 3a dose escalation group: STEP 1-3 data from subjects randomised to Sema 2.4 mg or Placebo during the controlled periods of the trials.
Phase 3a pool: STEP 1-4 data from subjects randomised to Sema 2.4 mg or Placebo during the controlled periods of the trials.
Phase 3a without T2D group: STEP 1, 3 and 4 data from subjects randomised to Sema 2.4 mg or Placebo during the controlled periods of the trials.
AEs with onset prior to randomisation are not included.
EAC: Event adjudication committee, N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure,
Adj.: Adjusted.
The % and R are adjusted using the Cochran-Mantel-Haenszel method to account for differences between trials. Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1.

2.7.4.2.3.4　結論

国際共同第 3 相試験の併合データにおいて、肥満症のためのセマグルチド 2.4 mg の全般的な有害事象プロファイルは、2 型糖尿病を対象としたセマグルチド皮下投与（オゼンピック皮下注）[14] を含む他の GLP-1 受容体作動薬と同様であった。プラセボ併合群と比較して、セマグルチド 2.4 mg 併合群でより多くの有害事象が報告され、この違いは非重篤で軽度な胃腸障害の有害事象によるものであった。

転帰「死亡」の有害事象及び死亡例の発現について、セマグルチド 2.4 mg 併合群はプラセボ併合群と同様であった。転帰「死亡」の有害事象を発現した被験者の割合は、セマグルチド 2.4 mg 併合群及びプラセボ併合群で低く、同様であった。

国際共同第 3 相試験の併合データの評価において、いずれの安全性領域においても、プラセボ併合群と比較してセマグルチド 2.4 mg 併合群で新たな予測されない安全性所見は認められなかった。胃腸障害と胆嚢関連障害を発現した被験者は、プラセボ併合群と比較してセマグルチド 2.4 mg 併合群で多かった。

2.7.4.2.4　個別有害事象の文章による説明

完了した試験で報告されたすべての被験者における有害事象の叙述は各治験総括報告書（Module 5）Section 14.3.3 に示す。

2.7.4.3　臨床検査値の評価

2.7.4.3.1　背景及び評価方法

関連する血液学的検査及び血液生化学的検査について、臨床検査評価を行った（表 2.7.4.1-4）。これらの項目については、ベースライン、20、52 及び 68 週（投与終了時）の来院で検体を採取した。

試験実施期間中、継続的な観察を目的として、中央検査機関は治験責任医師に対して臨床検査結果を提供することとした。臨床検査結果には、基準値範囲、警告及び外れ値についての情報が含まれた。治験実施計画書で事前に規定した cut-off 値を上回る値又は下回る値（2.7.4.1.1.8.3 項）は、臨床検査の外れ値として「Laboratory outlier form」により報告することとした（詳細は治験実施計画書の Appendix 2 に示す）。臨床検査所見が治験責任医師により臨床的に問題がある所見（すなわち疾患及び／又は臓器毒性を示唆し、治験責任医師による処置を必要とする重症度の異常所見）であると評価された場合、当該所見は有害事象として報告されることとした。

一部の血液生化学的検査項目は、関連する注目すべき安全性領域に関連して提示した：

- eGFR、UACR 及びクレアチニン：2.7.4.2.2.8.3 項（注目すべき安全性領域：急性腎不全）
- AST、ALT、アルカリホスファターゼ、総ビリルビン及び GGT：2.7.4.2.2.7.3 項（注目すべき安全性領域：肝障害）
- アミラーゼ及びリパーゼ：2.7.4.2.2.4.4.1 項（注目すべき安全性領域：急性膵炎）
- カルシトニン：2.7.4.2.2.6.4 項（注目すべき安全性領域：新生物）

臨床検査項目は、on-treatment 観察期間に基づき評価する：

- 平均値（中心化傾向）
- 異常、臨床的に問題ありと判定された個々の値（有害事象として報告）
- 事前に規定された臨床検査の外れ値の基準を満たす個々の値

2.7.4.3.2　血液学的検査

血液学的検査パラメータ〔ヘマトクリット、ヘモグロビン、血小板、赤血球、白血球及び白血球分画（好塩基球、好酸球、好中球、リンパ球、単球）〕の評価を以下に示す。

日本人被験者が参加した 3 つの第 3 相試験では、ベースラインから 68 週の変化量、平均値のプロット及び箱ひげ図に基づくと、いずれの血液学的検査パラメータについても試験期間において注目すべき平均値の変化は認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.5.27、14.3.5.28、EOT Figure 14.3.5.30～14.3.5.39、4373 試験（Module 5.3.5.1）EOT Table 14.3.5.27、14.3.5.28 及び EOT Figure 14.3.5.30～14.3.5.39、4374 試験（Module 5.3.5.1）EOT Table 14.3.5.28、14.3.5.29 及び EOT Figure 14.3.5.31～14.3.5.40〕。

すべての血液学的検査パラメータについて、試験期間中に基準範囲外の値を示した被験者の割合に注目すべき変化は認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.5.29、4373 試験（Module 5.3.5.1） EOT Table 14.3.5.29、4374 試験（Module 5.3.5.1）EOT Table 14.3.5.30〕。血液学的検査パラメータについて事前に規定された臨床検査の外れ値の基準に合致する被験者も認められなかった。

全体的に、血液学的検査パラメータにおいて、セマグルチドの用量増加に伴う用量反応性は認められなかった。

血液学的検査の詳細は、各治験総括報告書〔4382 試験（Module 5.3.5.1）Section 12.6.3、4373 試験（Module 5.3.5.1）Section 12.6.3、Trial 4374 試験（Module 5.3.5.1）Section 12.6.3〕に示す。

2.7.4.3.3　血液生化学的検査

安全性領域の一部として評価した項目を除く、血液生化学的検査パラメータ〔アルブミン、カルシウム（アルブミン補正）、クレアチンキナーゼ、カリウム、ナトリウム、TSH、尿素、重炭酸（4382 試験の 2 型糖尿病を有する被験者と 4374 試験）〕の評価を以下に示す。

日本人被験者が参加した 3 つの第 3 相試験では、68 週のベースラインに対する比、平均値のプロット及び箱ひげ図に基づくと、安全性領域で検討した項目以外の、いずれの血液生化学的検査パラメータについても試験期間において注目すべき平均値の変化は認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.5.1、14.3.5.2、EOT Figure 14.3.5.6、14.3.5.7、14.3.5.13、14.3.5.16～14.3.5.18、14.3.5.21～14.3.5.24 及び 14.3.5.26、4373 試験（Module 5.3.5.1）EOT Tables 14.3.5.1、14.3.5.2、EOT Figure 14.3.5.6、14.3.5.7、14.3.5.15～14.3.5.18、14.3.5.21～14.3.5.24、14.3.5.26、4374 試験（Module 5.3.5.1）EOT Table 14.3.5.1、14.3.5.2、EOT Figure 14.3.5.6、14.3.5.7、14.3.5.13、14.3.5.16～14.3.5.19、14.3.5.22～14.3.5.25、14.3.5.27〕。

安全性領域で検討した項目以外のすべての血液生化学的検査パラメータについて、試験期間中に基準範囲外の値を示した被験者の割合に注目すべき変化は認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.5.3、4373 試験（Module 5.3.5.1）EOT Table 14.3.5.3、4374 試験（Module 5.3.5.1）EOT Table 14.3.5.3〕。

いずれの試験でも、試験期間中にクレアチンキナーゼ、カリウム、ナトリウムについて基準範囲外の値を示した被験者は少なく、投与群間で明らかな違いは認められなかった。

全体的に、血液生化学的検査パラメータにおいて、セマグルチドの用量増加に伴う用量反応性は認められなかった。

血液生化学的検査の詳細は、各治験総括報告書〔4382 試験（Module 5.3.5.1）Section 12.6.2、4373 試験（Module 5.3.5.1）Section 12.6.2、4374 試験（Module 5.3.5.1）Section 12.6.2〕に示す。

2.7.4.4　バイタルサイン、身体的所見及び安全性に関連する他の観察項目

2.7.4.4.1　背景及び評価方法

GLP-1 受容体作動薬は脈拍数を増加させることが知られている[88]。また 2 型糖尿病に対するセマグルチド皮下投与 [14] 及びセマグルチド経口投与 [15] を含む一部の GLP-1 受容体作動薬 [88] は収縮期血圧を低下させる。

本項では、on-treatment 観察期間に得られた身体所見のデータを提示する（2.7.4.4.2 項）。血圧は Module 2.7.3.3.4.1 及び Module 2.7.3.3.4.2 に示す。脈拍数と心電図は、心血管障害の安全性領域の一部として評価し、それぞれ 2.7.4.2.2.5.4 項及び 2.7.4.2.2.5.5 項に提示する。

2.7.4.4.2　身体所見

身体所見はスクリーニング時及び投与終了時に実施した。詳細は 2.7.4.1.1.8.11 項及び 2.7.4.1.1.9.8 項に示す。

日本人被験者が参加した 3 つの第 3 相試験では、すべての身体所見の項目について、被験者の大部分ですべての来院における身体所見の結果が「正常」であった。すべての来院において身体所見の結果が「異常、臨床的に問題あり」であった被験者の割合は低く、-1 週（スクリーニング）から 68 週の「異常、臨床的に問題あり」への変化において投与群間で明らかな違いは認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.6.7、EOT Listing 14.3.7.3、4373 試験（Module 5.3.5.1）EOT Table 14.3.6.7、EOT Listing 14.3.7.3、4374 試験（Module 5.3.5.1）EOT Table 14.3.6.7、EOT Listing 14.3.7.3〕。

2.7.4.5　特別な患者集団及び状況下における安全性

2.7.4.5.1　日本人集団と全集団における結果の一貫性の検討

2.7.4.5.1.1　背景及び評価方法

本項では、日本人被験者が参加した 3 つの第 3 相試験（4382、4373 及び 4374 試験）における、日本人集団と全集団の主な安全性の結果（治験薬投与の中止に至った有害事象及び胃腸障害の有害事象を含む有害事象）の一貫性を検討した。主な有効性パラメータに関する一貫性の検討については Module 2.7.3.3.9.3 に示す。

上述の検討の前に、3 つの第 3 相試験について、日本人集団と全集団におけるベースライン及び被験者背景（ベースラインの内因性要因及び外因性民族的要因）の類似性の検討を行った。その結果、4373 及び 4374 試験において日本人集団と全集団との間でいくつかの違いがみられた（Module 2.7.3.3.9.2）。しかしながら、2 つの集団のベースラインでみられた内因性民族的要因の違いが、試験結果の評価において臨床的に意味のある影響を及ぼすとは考えられなかった。これらの評価の詳細については、Evaluation on the consistency of efficacy and safety results in the Japanese population and the entire population for trials 4373, 4374 and 4382（Module 5.3.5.4）に示す。

2.7.4.5.1.2　日本人集団と全集団における結果の一貫性；被験者の内訳及び曝露

Module 2.7.3.3.9.1 に示す。

2.7.4.5.1.3　日本人集団と全集団における結果の一貫性；有害事象

4382 試験

日本人集団及び全集団において、on-treatment 観察期間に有害事象を発現した被験者の割合は、セマグルチド 2.4 mg 群、セマグルチド 1.7 mg 群及びプラセボ群で同様であったが、有害事象の単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.7 mg 群で多かった（表 2.7.4.5-1）。

両集団において、重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は低く、投与群間で同様であった。死亡例は認められなかった。両集団において、いずれの投与群でも有害事象の大部分が軽度又は中等度であり、転帰は「回復」であった。事象の重症度及び転帰について 2 つの集団間で明らかな違いは認められなかった。両集団において、治験責任医師により治験薬との因果関係が「あり」又は「可能性あり」と判定された有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.7 mg 群で高かった。両集団において、治験薬投与の中止に至った有害事象を発現した被験者の割合及び単位時間あたりの発現件数は低かったが、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.7 mg 群でわずかに高かった。

両集団において、胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群とセマグルチド 1.7 mg 群で高かった。セマグルチド群において治験薬投与の中止に至った胃腸障害の有害事象の発現件数は少なく、プラセボ群では治験薬投与の中止に至った胃腸障害の有害事象は認められなかった。両集団において、最も高頻度で報告され

た胃腸障害の有害事象は、セマグルチド 2.4 mg 群で「便秘」、セマグルチド 1.7 mg 群で「下痢」であった。両集団において、セマグルチド 1.7 mg 群と比較して、セマグルチド 2.4 mg 群で胃腸障害の有害事象の発現件数が増加することは示唆されなかった。

表 2.7.4.5-1　有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験、日本人集団及び全集団）

	Japanese Population								Entire Trial Population							
	Sema 1.7 mg				Sema 2.4 mg				Placebo				Sema 1.7 mg				Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	91				179				89				100				199				101			
Patient years of exposure (PYE)	125.0				247.1				124.8				136.2				275.0				141.8			
Adverse Events	74	(81.3)	324	259.2	153	(85.5)	719	290.9	70	(78.7)	190	152.3	82	(82.0)	483	354.6	171	(85.9)	834	303.3	80	(79.2)	235	165.7
Serious																								
Yes	4	(4.4)	4	3.2	9	(5.0)	11	4.5	7	(7.9)	7	5.6	7	(7.0)	10	7.3	10	(5.0)	12	4.4	7	(6.9)	7	4.9
No	74	(81.3)	320	256.0	152	(84.9)	708	286.5	68	(76.4)	183	146.7	82	(82.0)	473	347.3	170	(85.4)	822	298.9	78	(77.2)	228	160.8
Severity																								
Severe	2	(2.2)	2	1.6	3	(1.7)	4	1.6	4	(4.5)	4	3.2	3	(3.0)	3	2.2	3	(1.5)	4	1.5	5	(5.0)	5	3.5
Moderate	9	(9.9)	10	8.0	18	(10.1)	23	9.3	5	(5.6)	5	4.0	14	(14.0)	63	46.3	25	(12.6)	42	15.3	11	(10.9)	13	9.2
Mild	73	(80.2)	312	249.6	151	(84.4)	692	280.0	68	(76.4)	181	145.1	79	(79.0)	417	306.1	168	(84.4)	788	286.5	76	(75.2)	217	153.0
Relationship to trial product																								
Probable	20	(22.0)	33	26.4	45	(25.1)	123	49.8	9	(10.1)	12	9.6	25	(25.0)	61	44.8	55	(27.6)	158	57.5	10	(9.9)	16	11.3
Possible	51	(56.0)	88	70.4	77	(43.0)	172	69.6	9	(10.1)	15	12.0	55	(55.0)	190	139.5	84	(42.2)	206	74.9	10	(9.9)	17	12.0
Unlikely	67	(73.6)	203	162.4	136	(76.0)	423	171.2	64	(71.9)	163	130.6	73	(73.0)	232	170.3	152	(76.4)	469	170.5	74	(73.3)	202	142.4
Missing	0				1	(0.6)	1	0.4	0				0				1	(0.5)	1	0.4	0			
Outcome																								
Fatal	0				0				0				0				0				0			
Recovered	70	(76.9)	257	205.6	147	(82.1)	619	250.5	65	(73.0)	150	120.2	78	(78.0)	409	300.3	164	(82.4)	729	265.1	75	(74.3)	186	131.1
Recovering	9	(9.9)	16	12.8	16	(8.9)	21	8.5	5	(5.6)	5	4.0	9	(9.0)	16	11.7	16	(8.0)	21	7.6	5	(5.0)	5	3.5
Recovered With Sequelae	0				0				0				0				0				0			
Not Recovered	33	(36.3)	51	40.8	50	(27.9)	79	32.0	20	(22.5)	35	28.1	35	(35.0)	58	42.6	54	(27.1)	84	30.5	26	(25.7)	44	31.0
Unknown	0				0				0				0				0				0			
Leading to Permanent treatment discontinuation	2	(2.2)	2	1.6	5	(2.8)	9	3.6	1	(1.1)	1	0.8	3	(3.0)	6	4.4	5	(2.5)	9	3.3	1	(1.0)	1	0.7
GIAEs	58	(63.7)	127	101.6	105	(58.7)	280	113.3	25	(28.1)	33	26.5	64	(64.0)	256	187.9	118	(59.3)	343	124.7	30	(29.7)	43	30.3
GIAEs Leading to Permanent treatment discontinuation	1	(1.1)	1	0.8	4	(2.2)	5	2.0	0				2	(2.0)	5	3.7	4	(2.0)	5	1.8	0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years. PYE: The duration of the on-treatment period in years. GIAEs: Gastrointestinal adverse events.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 23.1

4373 試験

日本人集団及び全集団において、on-treatment 観察期間に有害事象を発現した被験者の割合は、セマグルチド 2.4 mg 群とプラセボ群で同様であったが、有害事象の単位時間あたりの発現件数は、プラセボ群と比較して、セマグルチド 2.4 mg 群で多かった（表 2.7.4.5-2）。

日本人集団では、重篤な有害事象を発現した被験者は各投与群で 2 例のみであった。全集団では、重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数はプラセボ群と比較してセマグルチド 2.4 mg 群で高かった。日本人集団では死亡例は認められなかった。両集団において、いずれの投与群でも、有害事象の大部分が軽度又は中等度であり、転帰は「回復」であった。事象の重症度及び転帰について 2 つの集団間で明らかな違いは認められなかった。両集団において、治験責任医師により治験薬との因果関係が「あり」又は「可能性あり」と判定された有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群で高かった。日本人集団では、治験薬投与の中止に至った有害事象を発現した被験者は各投与群で少なかった（セマグルチド 2.4 mg 群で 2 例及びプラセボ群で 1 例）。全集団では、治験薬投与の中止に至った有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群で高かった。

日本人集団では、胃腸障害の有害事象を発現した被験者の割合は、セマグルチド 2.4 mg 群とプラセボ群で同様であったが、全集団ではプラセボ群と比較してセマグルチド 2.4 mg 群で高かった。両集団において、胃腸障害の有害事象の単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群で多かった。日本人集団では、セマグルチド 2.4 mg 群の 1 例で治験薬投与の中止に至った胃腸障害の有害事象が認められた。全集団では、プラセボ群と比較してセマグルチド 2.4 mg 群でより多くの被験者が治験薬投与の中止に至った胃腸障害の有害事象を発現した。両集団において、セマグルチド 2.4 mg 群で最も高頻度で認められた胃腸障害の有害事象は「悪心」であった。

表 2.7.4.5-2　有害事象－on-treatment 観察期間－安全性解析対象集団（4373 試験、日本人集団及び全集団）

	Japanese Population						Entire Trial Population					
	Sema 2.4 mg			Placebo			Sema 2.4 mg			Placebo		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	67			33			1306			655		
Patient years of exposure (PYE)	93.5			45.3			1706.1			829.6		
Adverse Events	59	(88.1)	256 273.8	30	(90.9)	96 211.8	1171	(89.7)	9658 566.1	566	(86.4)	3302 398.0
Serious												
Yes	2	(3.0)	2 2.1	2	(6.1)	2 4.4	128	(9.8)	164 9.6	42	(6.4)	53 6.4
No	59	(88.1)	254 271.6	30	(90.9)	94 207.4	1169	(89.5)	9494 556.5	560	(85.5)	3249 391.7
Severity												
Severe	0			1	(3.0)	1 2.2	143	(10.9)	242 14.2	44	(6.7)	68 8.2
Moderate	4	(6.0)	7 7.5	3	(9.1)	5 11.0	723	(55.4)	2612 153.1	311	(47.5)	863 104.0
Mild	58	(86.6)	249 266.3	28	(84.8)	90 198.5	1079	(82.6)	6804 398.8	507	(77.4)	2371 285.8
Relationship to trial product												
Probable	13	(19.4)	20 21.4	3	(9.1)	4 8.8	571	(43.7)	2148 125.9	147	(22.4)	330 39.8
Possible	29	(43.3)	65 69.5	8	(24.2)	11 24.3	726	(55.6)	2700 158.3	223	(34.0)	555 66.9
Unlikely	52	(77.6)	171 182.9	27	(81.8)	79 174.3	1032	(79.0)	4780 280.2	536	(81.8)	2409 290.4
Missing	0			1	(3.0)	2 4.4	24	(1.8)	30 1.8	7	(1.1)	8 1.0
Outcome												
Fatal	0			0			0			1	(0.2)	1 0.1
Recovered	57	(85.1)	231 247.1	29	(87.9)	78 172.1	1140	(87.3)	8439 494.6	545	(83.2)	2710 326.7
Recovering	3	(4.5)	3 3.2	3	(9.1)	4 8.8	59	(4.5)	91 5.3	25	(3.8)	37 4.5
Recovered With Sequelae	0			0			11	(0.8)	19 1.1	4	(0.6)	5 0.6
Not Recovered	15	(22.4)	22 23.5	11	(33.3)	14 30.9	513	(39.3)	1106 64.8	265	(40.5)	548 66.1
Unknown	0			0			2	(0.2)	3 0.2	1	(0.2)	1 0.1
Leading to Permanent treatment discontinuation	2	(3.0)	2 2.1	1	(3.0)	1 2.2	92	(7.0)	123 7.2	20	(3.1)	23 2.8
GIAEs	35	(52.2)	93 99.5	17	(51.5)	26 57.4	969	(74.2)	4309 252.6	314	(47.9)	739 89.1
GIAEs Leading to Permanent treatment discontinuation	1	(1.5)	1 1.1	0			59	(4.5)	78 4.6	5	(0.8)	5 0.6

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years. PYE: The duration of the on-treatment period in years. GIAEs: Gastrointestinal adverse events.

On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

4374 試験

日本人集団では、on-treatment 観察期間に有害事象を発現した被験者の割合は、セマグルチド 2.4 mg 群はプラセボ群と同様であり、セマグルチド 1.0 mg 群はプラセボ群と比較して高かったが、全集団では、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群で高かった。両集団において、有害事象の単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群で多かった（表 2.7.4.5-3）。

日本人集団では、重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較して 2 つのセマグルチド群（1.0 mg 及び 2.4 mg）で低かった。全集団では、重篤な有害事象を発現した被験者の割合は投与群間で同様であったが、単位時間あたりの発現件数はセマグルチド 1.0 mg 群及びプラセボ群と比較してセマグルチド 2.4 mg 群でわずかに多かった。日本人集団では死亡例は認められなかった。両集団において、いずれの投与群でも、有害事象の大部分が軽度又は中等度であり、転帰は「回復」であった。事象の重症度及び転帰について 2 つの集団間で明らかな違いは認められなかった。両集団において、治験責任医師により治験薬との因果関係が「あり」又は「可能性あり」と判定された有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較して 2 つのセマグルチド群（1.0 mg 及び 2.4 mg）で高かった。日本人集団では、治験薬投与の中止に至った有害事象を発現した被験者は各投与群で少なかった（セマグルチド 2.4 mg 群で 1 例及びプラセボ群で 1 例）。全集団では、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群でより多くの被験者が有害事象により治験薬の投与を中止した。

両集団において、胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群で高かった。胃腸障害の有害事象により治験薬の投与を中止した日本人被験者は認められなかった。全集団では、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群でより多くの被験者が胃腸障害の有害事象により治験薬の投与を中止した。セマグルチド 2.4 mg 群で最も高頻度で発現した胃腸障害の有害事象は、日本人集団では「便秘」であったが、全集団では「悪心」であった。「悪心」は日本人集団で 3 番目に多く発現した事象であった。セマグルチド 1.0 mg 群で最も高頻度で発現した胃腸障害の有害事象は、両集団で「悪心」であった。日本人集団では、胃腸障害の有害事象を発現した被験者の割合は、セマグルチド 1.0 mg 群と比較してセマグルチド 2.4 mg 群で低かったが、全集団ではセマグルチド 1.0 mg 群と比較してセマグルチド 2.4 mg 群で高かった。両集団において、胃腸障害の有害事象の単位時間あたりの発現件数は、セマグルチド 1.0 mg 群と比較してセマグルチド 2.4 mg 群で多かった。

表 2.7.4.5-3　有害事象－on-treatment 観察期間－安全性解析対象集団（4374 試験、日本人集団及び全集団）

	Japanese Population									Entire Trial Population								
	Sema 1.0 mg				Sema 2.4 mg				Placebo				Sema 1.0 mg				Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R	N (%)	E	R		N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	36				42				47				402				403				402			
Patient years of exposure (PYE)	50.2				58.6				66.5				529.8				533.0				528.3			
Adverse Events	33	(91.7)	152	302.7	35	(83.3)	205	349.9	38 (80.9)	178	267.5		329	(81.8)	1859	350.9	353	(87.6)	2197	412.2	309	(76.9)	1388	262.7
Serious																								
Yes	1	(2.8)	1	2.0	3	(7.1)	4	6.8	5 (10.6)	7	10.5		31	(7.7)	53	10.0	40	(9.9)	71	13.3	37	(9.2)	53	10.0
No	33	(91.7)	151	300.8	35	(83.3)	201	343.1	37 (78.7)	171	257.0		326	(81.1)	1806	340.9	352	(87.3)	2126	398.8	307	(76.4)	1335	252.7
Severity																								
Severe	0				1	(2.4)	1	1.7	3 (6.4)	4	6.0		22	(5.5)	43	8.1	27	(6.7)	51	9.6	28	(7.0)	39	7.4
Moderate	1	(2.8)	1	2.0	6	(14.3)	7	11.9	3 (6.4)	4	6.0		135	(33.6)	315	59.5	173	(42.9)	508	95.3	118	(29.4)	264	50.0
Mild	33	(91.7)	151	300.8	35	(83.3)	197	336.3	37 (78.7)	170	255.5		306	(76.1)	1501	283.3	328	(81.4)	1638	307.3	279	(69.4)	1085	205.4
Relationship to trial product																								
Probable	12	(33.3)	19	37.8	11	(26.2)	28	47.8	6 (12.8)	7	10.5		133	(33.1)	344	64.9	169	(41.9)	456	85.5	62	(15.4)	100	18.9
Possible	11	(30.6)	20	39.8	16	(38.1)	30	51.2	12 (25.5)	15	22.5		153	(38.1)	407	76.8	182	(45.2)	534	100.2	93	(23.1)	170	32.2
Unlikely	32	(88.9)	113	225.1	34	(81.0)	146	249.2	38 (80.9)	156	234.5		296	(73.6)	1097	207.1	301	(74.7)	1197	224.6	289	(71.9)	1111	210.3
Missing	0				1	(2.4)	1	1.7	0				10	(2.5)	11	2.1	10	(2.5)	10	1.9	6	(1.5)	7	1.3
Outcome																								
Fatal	0				0				0				0				1	(0.2)	1	0.2	1	(0.2)	1	0.2
Recovered	32	(88.9)	119	237.0	34	(81.0)	143	244.1	34 (72.3)	130	195.4		315	(78.4)	1503	283.7	333	(82.6)	1812	339.9	285	(70.9)	1054	199.5
Recovering	0				4	(9.5)	7	11.9	4 (8.5)	4	6.0		19	(4.7)	32	6.0	17	(4.2)	26	4.9	17	(4.2)	19	3.6
Recovered With Sequelae	0				0				0				5	(1.2)	5	0.9	5	(1.2)	5	0.9	1	(0.2)	1	0.2
Not Recovered	17	(47.2)	33	65.7	23	(54.8)	55	93.9	23 (48.9)	44	66.1		147	(36.6)	319	60.2	163	(40.4)	345	64.7	156	(38.8)	310	58.7
Unknown	0				0				0				0				4	(1.0)	8	1.5	3	(0.7)	3	0.6
Leading to Permanent treatment discontinuation	0				1	(2.4)	1	1.7	1 (2.1)	1	1.5		20	(5.0)	23	4.3	25	(6.2)	34	6.4	14	(3.5)	18	3.4
GIAEs	22	(61.1)	42	83.7	23	(54.8)	58	99.0	22 (46.8)	44	66.1		231	(57.5)	724	136.7	256	(63.5)	924	173.3	138	(34.3)	262	49.6
GIAEs Leading to Permanent treatment discontinuation	0				0				0				14	(3.5)	16	3.0	17	(4.2)	24	4.5	4	(1.0)	6	1.1

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years. PYE: The duration of the on-treatment period in years. GIAEs: Gastrointestinal adverse events.

On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. MedDRA version 22.1

2.7.4.5.1.4　日本人集団と全集団における安全性に関する結果の一貫性の結論

4382、4373 及び 4374 試験の検討において、日本人集団と全集団の安全性プロファイルに一貫性が認められた。

2.7.4.5.2　内因性民族的要因

2.7.4.5.2.1 背景及び評価方法

日本人被験者が参加した 3 つの第 3 相試験（4382、4373 及び 4374 試験）の全集団から得られたデータに基づき、セマグルチドの安全性プロファイルに対する様々な内因性民族的要因（ベースラインの人口統計学的特性及び疾患特性）の影響を評価した。すべての評価に on-treatment 観察期間を用いた。評価した内因性民族的要因は、性別、ベースラインの年齢、ベースラインの体重、ベースラインの BMI、ベースラインの腎機能、ベースラインの糖代謝、ベースラインの脂質異常症の有無及びベースラインの高血圧の有無であった。すべてのサブグループの一覧は 2.7.4.1.1.9.4 項に示す。サブグループの定義の詳細は、各項（2.7.4.5.2.2.1 項～2.7.4.5.2.2.8 項）に示す。

セマグルチドの安全性プロファイルに対する内因性民族的要因の影響は、サブグループ別の有害事象、重篤な有害事象及び胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数におけるセマグルチドとプラセボ間での違いを比較することにより評価した。

試験対象集団全体に対して各投与群への無作為化が行われているが、サブグループ内では無作為化は行われていない。さらに一部のサブグループでは被験者数が少なく、偶然の所見（chance finding）が得られる可能性が高くなる。したがって、サブグループ間の結果は慎重に解釈すべきである。

3 つの第 3 相試験（4382、4373 及び 4374 試験）から得られたデータに基づき、母集団薬物動態解析を実施した。この解析では、様々な共変量（性別、年齢、人種、民族、体重、腎機能、注射部位及び糖代謝）によるセマグルチドの曝露量に対する影響について検討した。体重がセマグルチドの曝露量に対して最も重要な共変量であり、体重が重いほど曝露量が小さくなることが示された。詳細は Module 2.7.2 に示す。

2.7.4.5.2.2 内因性民族的要因別の有害事象

2.7.4.5.2.2.1　性別

日本人被験者が参加した 3 つの第 3 相試験における性別別の有害事象の概要（すべての有害事象、重篤な有害事象及び胃腸障害の有害事象）を表 2.7.4.5-4、表 2.7.4.5-5 及び表 2.7.4.5-6 に示す。

3 つの第 3 相試験において、男性及び女性のいずれにおいても、有害事象を発現した被験者の割合は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で同様又は高かったが、有害事象の単位時間あたりの発現件数は、男性及び女性のいずれにおいても、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で多い傾向がみられた。重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、4382 及び 4374 試験では、男性及び女性のいずれについても投与群間で概ね同程度であったが、4373 試験では、男性及び女性のいずれについても、重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数はプラセボ群と比較してセマグルチド 2.4 mg 群で高い傾向がみられた。3 つの試験において、胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの

発現件数は、男性及び女性のいずれについても、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった。

有害事象及び胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、男性と比較して女性で高い傾向が認められたが、投与群間の違いは男性及び女性の間で同程度であった。

4382 及び 4374 試験において、有害事象、重篤な有害事象及び胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数を考慮すると、女性及び男性のいずれについても、セマグルチド 1.0 mg 群又はセマグルチド 1.7 mg 群と比較してセマグルチド 2.4 mg 群で有害事象、重篤な有害事象及び胃腸障害の有害事象の発現が増加することは示唆されなかった。

表 2.7.4.5-4　　性別別の有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N		PYE		N		PYE		N		PYE	
Female	36		49.7		85		120.1		26		37.1	
Male	64		86.5		114		154.9		75		104.8	
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
Female	31	(86.1)	175	352.2	78	(91.8)	425	353.9	22	(84.6)	74	199.7
Male	51	(79.7)	308	356.0	93	(81.6)	409	264.0	58	(77.3)	161	153.7
SAEs												
Female	2	(5.6)	2	4.0	5	(5.9)	6	5.0	0			
Male	5	(7.8)	8	9.2	5	(4.4)	6	3.9	7	(9.3)	7	6.7
GIAEs												
Female	28	(77.8)	70	140.9	54	(63.5)	171	142.4	10	(38.5)	11	29.7
Male	36	(56.3)	186	215.0	64	(56.1)	172	111.0	20	(26.7)	32	30.5

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

表 2.7.4.5-5　性別別の有害事象－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
Female	955	1240.8			498	624.7		
Male	351	465.3			157	204.9		
Subjects with events	N	(%)	E	R	N	(%)	E	R
All events								
Female	866	(90.7)	7607	613.1	431	(86.5)	2723	435.9
Male	305	(86.9)	2051	440.8	135	(86.0)	579	282.6
SAEs								
Female	95	(9.9)	124	10.0	30	(6.0)	41	6.6
Male	33	(9.4)	40	8.6	12	(7.6)	12	5.9
GIAEs								
Female	731	(76.5)	3395	273.6	264	(53.0)	646	103.4
Male	238	(67.8)	914	196.4	50	(31.8)	93	45.4

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

表 2.7.4.5-6　性別別の有害事象－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
Female	202	268.3			222	297.0			190	253.9		
Male	200	261.5			181	236.1			212	274.4		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
Female	167	(82.7)	1047	390.3	204	(91.9)	1313	442.1	150	(78.9)	775	305.2
Male	162	(81.0)	812	310.5	149	(82.3)	884	374.5	159	(75.0)	613	223.4
SAEs												
Female	12	(5.9)	17	6.3	22	(9.9)	45	15.2	13	(6.8)	18	7.1
Male	19	(9.5)	36	13.8	18	(9.9)	26	11.0	24	(11.3)	35	12.8
GIAEs												
Female	132	(65.3)	446	166.2	155	(69.8)	554	186.5	72	(37.9)	154	60.7
Male	99	(49.5)	278	106.3	101	(55.8)	370	156.7	66	(31.1)	108	39.4

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.5.2.2.2　ベースラインの年齢

以下のベースラインの年齢（歳）の分類に基づき評価した：

- <65
- ≥65

日本人被験者が参加した 3 つの第 3 相試験における年齢別の有害事象の概要（すべての有害事象、重篤な有害事象及び胃腸障害の有害事象）を表 2.7.4.5-7、表 2.7.4.5-8 及び表 2.7.4.5-9 に示す。

4382 試験では、セマグルチド 1.7 mg 群及びプラセボ群において 65 歳以上の被験者が少なかった。そのため、これらの結果は慎重に解釈すべきである。

3 つの第 3 相試験では、両年齢サブグループにおいて、有害事象を発現した被験者の割合はプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で同様又は高かったが、単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で多かった。重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、4382 及び 4374 試験では、両年齢サブグループにおいて投与群間で概ね同程度であったが、4373 試験では、両年齢サブグループにおいてプラセボ群と比較してセマグルチド 2.4 mg 群で高い傾向が認められた。3 つの試験において、胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、両年齢サブグループにおいてプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった。

いずれの試験及び投与群においても、有害事象、重篤な有害事象及び胃腸障害の有害事象の発現状況に、年齢サブグループによる明らかな一貫した傾向は認められなかった。

4374 試験では、両年齢サブグループにおいて、有害事象及び胃腸障害の発現がセマグルチド 1.0 mg 群と比較してセマグルチド 2.4 mg で多い傾向がみられたが、4382 試験ではセマグルチド 2.4 mg 群とセマグルチド 1.7 mg 群の比較において同様の傾向は認められなかった。

表 2.7.4.5-7　　ベースラインの年齢別の有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
<65	90	122.4			166	229.0			95	133.3		
>=65	10	13.8			33	46.0			6	8.6		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
<65	73	(81.1)	422	344.8	142	(85.5)	692	302.2	75	(78.9)	224	168.1
>=65	9	(90.0)	61	441.6	29	(87.9)	142	308.5	5	(83.3)	11	128.2
SAEs												
<65	6	(6.7)	9	7.4	8	(4.8)	10	4.4	5	(5.3)	5	3.8
>=65	1	(10.0)	1	7.2	2	(6.1)	2	4.3	2	(33.3)	2	23.3
Gastrointestinal disorders												
<65	56	(62.2)	230	187.9	95	(57.2)	284	124.0	29	(30.5)	41	30.8
>=65	8	(80.0)	26	188.2	23	(69.7)	59	128.2	1	(16.7)	2	23.3

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

表 2.7.4.5-8　　ベースラインの年齢別の有害事象－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
<65	1198	1562.8			607	766.3		
>=65	108	143.3			48	63.2		
Subjects with events	N	(%)	E	R	N	(%)	E	R
All events								
<65	1074	(89.6)	8943	572.3	524	(86.3)	3016	393.6
>=65	97	(89.8)	715	498.9	42	(87.5)	286	452.4
SAEs								
<65	109	(9.1)	136	8.7	37	(6.1)	48	6.3
>=65	19	(17.6)	28	19.5	5	(10.4)	5	7.9
GIAEs								
<65	889	(74.2)	4027	257.7	291	(47.9)	690	90.0
>=65	80	(74.1)	282	196.8	23	(47.9)	49	77.5

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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表 2.7.4.5-9　ベースラインの年齢別の有害事象－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
<65	319	420.5			315	422.2			317	422.6		
>=65	83	109.3			88	110.9			85	105.7		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
<65	256	(80.3)	1449	344.6	270	(85.7)	1593	377.3	243	(76.7)	1098	259.8
>=65	73	(88.0)	410	375.3	83	(94.3)	604	544.7	66	(77.6)	290	274.4
SAEs												
<65	21	(6.6)	33	7.8	33	(10.5)	45	10.7	24	(7.6)	36	8.5
>=65	10	(12.0)	20	18.3	7	(8.0)	26	23.4	13	(15.3)	17	16.1
GIAEs												
<65	186	(58.3)	576	137.0	196	(62.2)	698	165.3	108	(34.1)	202	47.8
>=65	45	(54.2)	148	135.5	60	(68.2)	226	203.8	30	(35.3)	60	56.8

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.5.2.2.3　ベースラインの体重

以下のベースラインの体重（kg）の分類に基づき評価した：

- 4382 試験
  - <80
  - ≥80～ <90
  - ≥90～<100
  - ≥100
- 4373 及び 4374 試験
  - <90
  - ≥90～<100
  - ≥100～<115
  - ≥115

日本人被験者が参加した 3 つの第 3 相試験における体重別の有害事象の概要（すべての有害事象、重篤な有害事象及び胃腸障害の有害事象）を表 2.7.4.5-10、表 2.7.4.5-11 及び表 2.7.4.5-12 に示す。

3 つの第 3 相試験では、体重サブグループのいずれにおいても、有害事象を発現した被験者の割合は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で同様又は高かったが、有害事象の単位時間あたりの発現件数はプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で多かった。重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、4382 と 4374 試験では、いずれの体重サブグループでも投与群間で概ね同様であったが、4373 試験では、いずれの体重サブグループでもプラセボ群と比較してセマグルチド 2.4 mg で高い傾向が認められた。3 つの試験において、胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、いずれの体重サブグループでもプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった。

いずれの試験及び投与群においても、有害事象、重篤な有害事象及び胃腸障害の有害事象の発現状況に、体重サブグループによる明らかに一貫した傾向は認められなかった。

4382 及び 4374 試験において、有害事象、重篤な有害事象及び胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数を考慮すると、いずれの体重サブグループでも、セマグルチド 1.0 mg 群又はセマグルチド 1.7 mg 群と比較してセマグルチド 2.4 mg 群で有害事象、重篤な有害事象及び胃腸障害の有害事象の発現が増加することは示唆されなかった。

表 2.7.4.5-10　　ベースラインの体重別の有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
<80	31	43.7			73	101.6			24	33.2		
80-<90	37	49.0			63	87.6			36	50.3		
90-<100	17	23.3			28	38.9			23	32.7		
>=100	15	20.3			35	46.9			18	25.7		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
<80	25	(80.6)	123	281.7	64	(87.7)	330	324.8	19	(79.2)	52	156.8
80-<90	30	(81.1)	118	241.1	54	(85.7)	259	295.8	29	(80.6)	94	187.0
90-<100	12	(70.6)	67	287.1	23	(82.1)	89	228.7	16	(69.6)	53	161.9
>=100	15	(100)	175	863.8	30	(85.7)	156	332.4	16	(88.9)	36	140.3
SAEs												
<80	2	(6.5)	2	4.6	4	(5.5)	5	4.9	1	(4.2)	1	3.0
80-<90	2	(5.4)	2	4.1	3	(4.8)	4	4.6	4	(11.1)	4	8.0
90-<100	2	(11.8)	2	8.6	1	(3.6)	1	2.6	1	(4.3)	1	3.1
>=100	1	(6.7)	4	19.7	2	(5.7)	2	4.3	1	(5.6)	1	3.9
GIAEs												
<80	23	(74.2)	47	107.6	44	(60.3)	132	129.9	9	(37.5)	14	42.2
80-<90	19	(51.4)	49	100.1	37	(58.7)	109	124.5	10	(27.8)	12	23.9
90-<100	8	(47.1)	21	90.0	16	(57.1)	34	87.4	4	(17.4)	5	15.3
>=100	14	(93.3)	139	686.1	21	(60.0)	68	144.9	7	(38.9)	12	46.8

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

表 2.7.4.5-11　　ベースラインの体重別の有害事象－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
<90	339	440.9			162	208.3		
90-<100	267	352.7			151	190.2		
100-<115	331	429.8			163	211.0		
>=115	369	482.7			179	220.1		
Subjects with events	N	(%)	E	R	N	(%)	E	R
All events								
<90	311	(91.7)	2600	589.7	129	(79.6)	783	375.9
90-<100	232	(86.9)	1871	530.4	130	(86.1)	689	362.3
100-<115	299	(90.3)	2379	553.5	149	(91.4)	908	430.3
>=115	329	(89.2)	2808	581.8	158	(88.3)	922	419.0
SAEs								
<90	30	(8.8)	39	8.8	10	(6.2)	13	6.2
90-<100	29	(10.9)	35	9.9	9	(6.0)	9	4.7
100-<115	28	(8.5)	35	8.1	11	(6.7)	13	6.2
>=115	41	(11.1)	55	11.4	12	(6.7)	18	8.2
Gastrointestinal disorders								
<90	249	(73.5)	1163	263.8	77	(47.5)	173	83.0
90-<100	187	(70.0)	830	235.3	67	(44.4)	149	78.3
100-<115	251	(75.8)	1069	248.7	84	(51.5)	218	103.3
>=115	282	(76.4)	1247	258.4	86	(48.0)	199	90.4

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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表 2.7.4.5-12　ベースラインの体重別の有害事象－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
<90	150	196.0			147	194.9			141	184.1		
90-<100	85	111.5			77	100.4			78	103.3		
100-<115	81	103.1			91	118.8			94	128.3		
>=115	86	119.1			88	119.0			89	112.6		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
<90	127	(84.7)	649	331.1	133	(90.5)	835	428.5	104	(73.8)	416	225.9
90-<100	64	(75.3)	414	371.3	64	(83.1)	383	381.5	60	(76.9)	257	248.7
100-<115	66	(81.5)	362	351.0	81	(89.0)	525	441.9	75	(79.8)	363	283.0
>=115	72	(83.7)	434	364.3	75	(85.2)	454	381.5	70	(78.7)	352	312.7
SAEs												
<90	10	(6.7)	16	8.2	15	(10.2)	22	11.3	10	(7.1)	13	7.1
90-<100	5	(5.9)	13	11.7	6	(7.8)	9	9.0	7	(9.0)	9	8.7
100-<115	7	(8.6)	9	8.7	6	(6.6)	23	19.4	8	(8.5)	12	9.4
>=115	9	(10.5)	15	12.6	13	(14.8)	17	14.3	12	(13.5)	19	16.9
GIAE												
<90	98	(65.3)	260	132.7	102	(69.4)	365	187.3	48	(34.0)	98	53.2
90-<100	48	(56.5)	186	166.8	44	(57.1)	162	161.4	21	(26.9)	38	36.8
100-<115	43	(53.1)	152	147.4	59	(64.8)	213	179.3	36	(38.3)	66	51.5
>=115	42	(48.8)	126	105.8	51	(58.0)	184	154.6	33	(37.1)	60	53.3

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.5.2.2.4　ベースラインの BMI

以下のベースラインの BMI の分類に基づき評価した：

- <30
- ≥30～<35
- ≥35～<40
- ≥40

日本人被験者が参加した 3 つの第 3 相試験における BMI 別の有害事象の概要（すべての有害事象、重篤な有害事象及び胃腸障害の有害事象）を表 2.7.4.5-13、表 2.7.4.5-14 及び表 2.7.4.5-15 に示す。

4382 試験では、セマグルチド 1.7 mg 群及びプラセボ群において 40 以上の BMI を有する被験者が少なかった。そのため、これらの結果は慎重に解釈すべきである。

有害事象を発現した被験者の割合がプラセボ群と比較してセマグルチド 2.4 mg で低い傾向がみられた 4382 試験の BMI が≥35～<40 kg/m^2 のサブグループを除き、3 つの第 3 相試験では、BMI サブグループのいずれにおいても、有害事象を発現した被験者の割合はプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で同様又は高かった。有害事象の単位時間あたりの発現件数は、すべての試験において、BMI サブグループのいずれにおいても、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった。重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、4382 と 4374 試験では、BMI サブグループのいずれにおいても投与群間で概ね同様であったが、4373 試験では、いずれの BMI サブグループでもプラセボ群と比較してセマグルチド 2.4 mg で高い傾向が認められた。胃腸障害の有害事象を発現した被験者の割合がプラセボ群と比較してセマグルチド 2.4 mg 群で低い傾向がみられた 4382 試験の BMI が≥35～<40 kg/m^2 のサブグループを除き、3 つの試験では、BMI サブグループのいずれにおいても、胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった。

いずれの試験及び投与群においても、有害事象、重篤な有害事象及び胃腸障害の有害事象の発現状況に、BMI サブグループによる明らかに一貫した傾向は認められなかった。

4382 及び 4374 試験において、有害事象、重篤な有害事象及び胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数、ならびに一部のサブグループに含まれる被験者数が少なかったことを考慮すると、いずれの BMI サブグループでも、セマグルチド 1.0 mg 群又はセマグルチド 1.7 mg 群と比較してセマグルチド 2.4 mg 群で有害事象、重篤な有害事象及び胃腸障害の有害事象の発現が増加することは示唆されなかった。

表 2.7.4.5-13　　ベースラインの BMI 別の有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N		PYE		N		PYE		N		PYE	
<30	46		62.5		86		118.2		38		52.0	
30-<35	35		47.7		75		105.8		44		62.7	
35-<40	17		23.1		21		27.2		12		17.1	
>=40	2		2.8		17		23.8		7		10.0	
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Events												
<30	36	(78.3)	142	227.1	71	(82.6)	363	307.1	28	(73.7)	86	165.3
30-<35	29	(82.9)	246	515.5	69	(92.0)	307	290.2	35	(79.5)	98	156.2
35-<40	15	(88.2)	80	345.9	16	(76.2)	84	308.8	11	(91.7)	36	210.1
>=40	2	(100)	15	527.8	15	(88.2)	80	335.7	6	(85.7)	15	150.5
Serious												
Yes												
<30	2	(4.3)	2	3.2	4	(4.7)	6	5.1	5	(13.2)	5	9.6
30-<35	5	(14.3)	8	16.8	3	(4.0)	3	2.8	1	(2.3)	1	1.6
35-<40	0				2	(9.5)	2	7.4	0			
>=40	0				1	(5.9)	1	4.2	1	(14.3)	1	10.0
Gastrointestinal disorders												
<30	25	(54.3)	48	76.8	49	(57.0)	146	123.5	11	(28.9)	14	26.9
30-<35	22	(62.9)	164	343.7	48	(64.0)	125	118.1	10	(22.7)	15	23.9
35-<40	15	(88.2)	39	168.6	11	(52.4)	39	143.4	7	(58.3)	12	70.0
>=40	2	(100)	5	175.9	10	(58.8)	33	138.5	2	(28.6)	2	20.1

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

表 2.7.4.5-14　　ベースラインの BMI 別の有害事象－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
<30	81	106.8			36	47.8		
30-<35	436	576.9			207	269.8		
35-<40	406	525.5			208	257.0		
>=40	383	496.9			204	255.0		
Subjects with events	N	(%)	E	R	N	(%)	E	R
All events								
<30	70	(86.4)	439	410.9	30	(83.3)	124	259.3
30-<35	392	(89.9)	3079	533.7	170	(82.1)	1001	371.1
35-<40	372	(91.6)	3087	587.4	187	(89.9)	1073	417.5
>=40	337	(88.0)	3053	614.4	179	(87.7)	1104	433.0
SAEs								
<30	6	(7.4)	8	7.5	1	(2.8)	1	2.1
30-<35	41	(9.4)	50	8.7	11	(5.3)	14	5.2
35-<40	37	(9.1)	50	9.5	16	(7.7)	18	7.0
>=40	44	(11.5)	56	11.3	14	(6.9)	20	7.8
Gastrointestinal disorders								
<30	51	(63.0)	207	193.8	13	(36.1)	27	56.5
30-<35	316	(72.5)	1340	232.3	92	(44.4)	200	74.1
35-<40	310	(76.4)	1350	256.9	104	(50.0)	260	101.2
>=40	292	(76.2)	1412	284.2	105	(51.5)	252	98.8

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

表 2.7.4.5-15　　ベースラインの BMI 別の有害事象－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
<30	66	82.8			68	91.0			77	97.8		
30-<35	163	214.0			139	177.2			135	179.2		
35-<40	99	131.0			103	140.6			97	129.1		
>=40	74	102.0			93	124.2			93	122.3		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
<30	58	(87.9)	255	307.9	62	(91.2)	397	436.0	55	(71.4)	208	212.7
30-<35	132	(81.0)	720	336.5	118	(84.9)	761	429.6	107	(79.3)	462	257.9
35-<40	77	(77.8)	495	378.0	89	(86.4)	521	370.4	76	(78.4)	348	269.6
>=40	62	(83.8)	389	381.2	84	(90.3)	518	417.1	71	(76.3)	370	302.6
SAEs												
<30	5	(7.6)	5	6.0	6	(8.8)	6	6.6	7	(9.1)	8	8.2
30-<35	11	(6.7)	26	12.2	16	(11.5)	25	14.1	13	(9.6)	22	12.3
35-<40	10	(10.1)	16	12.2	6	(5.8)	12	8.5	11	(11.3)	17	13.2
>=40	5	(6.8)	6	5.9	12	(12.9)	28	22.5	6	(6.5)	6	4.9
GIAEs												
<30	42	(63.6)	105	126.8	41	(60.3)	145	159.3	24	(31.2)	37	37.8
30-<35	100	(61.3)	294	137.4	89	(64.0)	362	204.3	46	(34.1)	91	50.8
35-<40	46	(46.5)	184	140.5	68	(66.0)	207	147.2	30	(30.9)	66	51.1
>=40	43	(58.1)	141	138.2	58	(62.4)	210	169.1	38	(40.9)	68	55.6

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.5.2.2.5　ベースラインの腎機能

以下のベースラインの腎機能サブグループの分類〔eGFR（中央検査機関が KDIGO 2021[63] により定義された CKD-EPI を用いてクレアチニンにより算出）に基づく〕により評価した：

- 正常（≥90 mL/min/1.73 m^2）
- 軽度腎機能障害（≥60～<90 mL/min/1.73 m^2）
- 中等度腎機能障害（≥30～<60 mL/min/1.73 m^2）
- 重度腎機能障害（15～<30 mL/min/1.73 m^2）

4382（2 型糖尿病を有さない被験者のみ）及び 4373 試験では、スクリーニング時に末期腎疾患（eGFR<15 mL/min/1.73 m^2）を有する被験者は除外された。4382（2 型糖尿病を有する被験者のみ）及び 4374 試験では、スクリーニング時に重度腎機能障害を有する被験者は除外され、さらに SGLT2 阻害薬を使用している中等度腎機能障害を有する被験者も除外された。

日本人被験者が参加した 3 つの第 3 相試験における腎機能別の有害事象の概要（すべての有害事象、重篤な有害事象及び胃腸障害の有害事象）を表 2.7.4.5-16、表 2.7.4.5-17 及び表 2.7.4.5-18 に示す。

4374 試験ではベースライン時に 1 例が重度腎機能障害（15～<30 mL/min/1.73 m^2）を有していたが、当該被験者のデータについて本項では評価は行わない。中等度腎機能障害を有する被験者も少なかったことから、これらの結果は慎重に解釈すべきである。

3 つの第 3 相試験において、腎機能サブグループのいずれにおいても、有害事象を発現した被験者の割合はプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で同様又は高かった。有害事象の単位時間あたりの発現件数については、プラセボ群とセマグルチド 1.0 mg 群で同様であった 4374 試験の中等度腎機能障害のサブグループを除き、腎機能サブグループのいずれにおいてもプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で多かった。重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、4382 と 4374 試験では、腎機能サブグループのいずれにおいても投与群間で概ね同程度であったが、4373 試験では、腎機能サブグループのいずれにおいても、プラセボ群と比較してセマグルチド 2.4 mg 群で高い傾向がみられた。3 つの試験において、胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、腎機能サブグループのいずれにおいてもプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった。

いずれの試験及び投与群においても、有害事象、重篤な有害事象及び胃腸障害の有害事象の発現状況に、腎機能サブグループによる明らかに一貫した傾向は認められなかった。

有害事象及び胃腸障害の有害事象の発現が、4374 試験では、腎機能サブグループのいずれにおいてもセマグルチド 1.0 mg 群と比較してセマグルチド 2.4 mg 群で多い傾向が認められたが、4382 試験ではセマグルチド 2.4 mg 群とセマグルチド 1.7 mg 群の比較において同様の傾向は認められなかった。

表 2.7.4.5-16　　ベースラインの腎機能別の有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
Normal (>=90)	73	100.2			140	194.2			78	110.1		
Mild RI (60-<90)	26	34.6			58	79.4			23	31.8		
Moderate RI (30-<60)	1	1.4			1	1.4						
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
Normal (>=90)	64	(87.7)	383	382.3	121	(86.4)	618	318.3	65	(83.3)	195	177.2
Mild RI (60-<90)	17	(65.4)	90	260.0	49	(84.5)	214	269.4	15	(65.2)	40	125.9
Moderate RI (30-<60)	1	(100)	10	703.8	1	(100)	2	140.8				
SAEs												
Normal (>=90)	6	(8.2)	9	9.0	5	(3.6)	5	2.6	5	(6.4)	5	4.5
Mild RI (60-<90)	1	(3.8)	1	2.9	5	(8.6)	7	8.8	2	(8.7)	2	6.3
Moderate RI (30-<60)	0				0							
GIAEs												
Normal (>=90)	49	(67.1)	215	214.6	81	(57.9)	254	130.8	23	(29.5)	33	30.0
Mild RI (60-<90)	14	(53.8)	34	98.2	36	(62.1)	88	110.8	7	(30.4)	10	31.5
Moderate RI (30-<60)	1	(100)	7	492.6	1	(100)	1	70.4	0			

Adverse events with onset prior to randomisation are not included.
RI: Renal impairment
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

表 2.7.4.5-17　　ベースラインの腎機能別の有害事象－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
Normal (>=90)	887	1159.8			445	559.3		
Mild RI (60-<90)	401	523.0			200	256.9		
Moderate RI (30-<60)	18	23.2			10	13.4		
Subjects with events	N	(%)	E	R	N	(%)	E	R
Events								
Normal (>=90)	783	(88.3)	6540	563.9	382	(85.8)	2143	383.1
Mild RI (60-<90)	373	(93.0)	2943	562.7	174	(87.0)	1104	429.8
Moderate RI (30-<60)	15	(83.3)	175	753.2	10	(100)	55	411.6
Serious								
Yes								
Normal (>=90)	80	(9.0)	105	9.1	28	(6.3)	30	5.4
Mild RI (60-<90)	42	(10.5)	50	9.6	14	(7.0)	23	9.0
Moderate RI (30-<60)	6	(33.3)	9	38.7	0			
Gastrointestinal disorders								
Normal (>=90)	642	(72.4)	2964	255.6	223	(50.1)	511	91.4
Mild RI (60-<90)	313	(78.1)	1296	247.8	86	(43.0)	219	85.3
Moderate RI (30-<60)	14	(77.8)	49	210.9	5	(50.0)	9	67.3

Adverse events with onset prior to randomisation are not included.
RI: Renal impairment
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

表 2.7.4.5-18　ベースラインの腎機能別の有害事象－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
Normal (>=90)	265	350.8			270	364.2			259	346.0		
Mild RI (60-<90)	120	157.2			114	149.3			120	153.9		
Moderate RI (30-<60)	17	21.8			18	18.1			23	28.4		
Severe RI (15-<30)					1	1.4						
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All Events												
Normal (>=90)	216	(81.5)	1218	347.2	233	(86.3)	1293	355.1	196	(75.7)	833	240.7
Mild RI (60-<90)	100	(83.3)	561	356.9	103	(90.4)	787	527.1	96	(80.0)	443	287.9
Moderate RI (30-<60)	13	(76.5)	80	366.4	16	(88.9)	115	633.7	17	(73.9)	112	394.1
Severe RI (15-<30)					1	(100)	2	140.8				
SAEs												
Normal (>=90)	17	(6.4)	29	8.3	22	(8.1)	25	6.9	22	(8.5)	30	8.7
Mild RI (60-<90)	14	(11.7)	24	15.3	12	(10.5)	24	16.1	10	(8.3)	17	11.0
Moderate RI (30-<60)	0				6	(33.3)	22	121.2	5	(21.7)	6	21.1
Severe RI (15-<30)					0							
GIAEs												
Normal (>=90)	150	(56.6)	480	136.8	164	(60.7)	548	150.5	92	(35.5)	175	50.6
Mild RI (60-<90)	72	(60.0)	211	134.2	80	(70.2)	342	229.1	38	(31.7)	68	44.2
Moderate RI (30-<60)	9	(52.9)	33	151.1	12	(66.7)	34	187.4	8	(34.8)	19	66.9
Severe RI (15-<30)					0				0			

Adverse events with onset prior to randomisation are not included.
RI: Renal impairment
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.5.2.2.6　ベースラインの糖代謝

4382 及び 4373 試験について、以下のベースラインの糖代謝の分類（治験責任医師による報告に基づく）により評価した：

- 正常血糖
- pre-diabetes
- 2 型糖尿病（4382 試験のみ）

4382 及び 4373 試験におけるベースラインの糖代謝別の有害事象の概要（すべての有害事象、重篤な有害事象及び胃腸障害の有害事象）を表 2.7.4.5-19 及び表 2.7.4.5-20 に示す。

両試験において、糖代謝サブグループのいずれについても、有害事象を発現した被験者の割合はプラセボ群と比較してセマグルチド群（1.7 及び 2.4 mg）で同様又は高かったが、単位時間あたりの発現件数はプラセボ群と比較してセマグルチド群（1.7 及び 2.4 mg）で多かった。重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、糖代謝グループのいずれについても概ね同程度であった。胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、糖代謝サブグループのいずれにおいても、プラセボ群と比較してセマグルチド群（1.7 及び 2.4 mg）で高かった。

いずれの試験及び投与群においても、有害事象、重篤な有害事象及び胃腸障害の有害事象の発現状況に、糖代謝サブグループによる明らかに一貫した傾向は認められなかった。

4382 試験において、有害事象及び胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数を考慮すると、いずれの糖代謝サブグループでも、セマグルチド 1.7 mg 群と比較してセマグルチド 2.4 mg 群で有害事象及び胃腸障害の有害事象の発現が増加することは示唆されなかった。

表 2.7.4.5-19　ベースラインの糖代謝別の有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
Normo-glycaemia	55	74.1			106	145.7			51	71.3		
Pre-diabetes	20	26.6			44	61.1			25	34.9		
T2D	25	35.5			49	68.3			25	35.6		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
Normo-glycaemia	45	(81.8)	203	274.0	93	(87.7)	430	295.2	40	(78.4)	138	193.5
Pre-diabetes	15	(75.0)	192	722.4	40	(90.9)	156	255.4	20	(80.0)	45	129.0
T2D	22	(88.0)	88	247.6	38	(77.6)	248	363.3	20	(80.0)	52	146.0
SAEs												
Normo-glycaemia	5	(9.1)	5	6.7	7	(6.6)	9	6.2	4	(7.8)	4	5.6
Pre-diabetes	2	(10.0)	5	18.8	1	(2.3)	1	1.6	1	(4.0)	1	2.9
T2D	0				2	(4.1)	2	2.9	2	(8.0)	2	5.6
GIAEs												
Normo-glycaemia	35	(63.6)	89	120.1	61	(57.5)	185	127.0	18	(35.3)	29	40.7
Pre-diabetes	14	(70.0)	138	519.3	25	(56.8)	66	108.1	5	(20.0)	6	17.2
T2D	15	(60.0)	29	81.6	32	(65.3)	92	134.8	7	(28.0)	8	22.5

Adverse events with onset prior to randomisation are not included.
T2D: Type 2 diabetes
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

表 2.7.4.5-20　ベースラインの糖代謝別の有害事象－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
Normo-glycaemia	713	931.6			392	495.5		
Pre-diabetes	593	774.5			263	334.1		
Subjects with events	N	(%)	E	R	N	(%)	E	R
All events								
Normo-glycaemia	640	(89.8)	5230	561.4	330	(84.2)	1861	375.6
Pre-diabetes	531	(89.5)	4428	571.8	236	(89.7)	1441	431.3
SAEs								
Normo-glycaemia	62	(8.7)	81	8.7	18	(4.6)	19	3.8
Pre-diabetes	66	(11.1)	83	10.7	24	(9.1)	34	10.2
GIAEs								
Normo-glycaemia	534	(74.9)	2363	253.6	180	(45.9)	399	80.5
Pre-diabetes	435	(73.4)	1946	251.3	134	(51.0)	340	101.8

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.5.2.2.7　ベースラインの脂質異常症の有無

以下のベースラインの脂質異常症の有無（治験責任医師による報告による）に基づくサブグループにより評価した：

- 脂質異常症「あり」
- 脂質異常症「なし」

日本人被験者が参加した 3 つの第 3 相試験における脂質異常症の有無別の有害事象の概要（すべての有害事象、重篤な有害事象及び胃腸障害の有害事象）を表 2.7.4.5-21、表 2.7.4.5-22 及び表 2.7.4.5-23 に示す。

3 つの第 3 相試験では、脂質異常症の両サブグループにおいて、有害事象を発現した被験者の割合は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で同様又は高かったが、有害事象の単位時間あたりの発現件数はプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で多かった。重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、4382 試験と 4374 試験では、脂質異常症の両サブグループにおいて投与群間で概ね同程度であったが、4373 試験では、脂質異常症の両サブグループにおいてプラセボ群と比較してセマグルチド 2.4 mg 群で高い傾向がみられた。3 つの試験において、胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、脂質異常症の両サブグループにおいて、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった。

いずれの試験及び投与群においても、有害事象、重篤な有害事象及び胃腸障害の有害事象の発現状況に、脂質異常症の有無による明らかに一貫した傾向は認められなかった。

4374 試験では、脂質異常症の両サブグループにおいて、有害事象及び胃腸障害の有害事象の発現がセマグルチド 1.0 mg 群と比較してセマグルチド 2.4 mg で多い傾向がみられたが、4382 試験ではセマグルチド 2.4 mg 群とセマグルチド 1.7 mg 群の比較において同様の傾向は認められなかった。

表 2.7.4.5-21　ベースラインの脂質異常症の有無別の有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
Yes	87	118.1			178	245.5			80	112.7		
No	13	18.1			21	29.5			21	29.1		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
Yes	70	(80.5)	433	366.6	152	(85.4)	747	304.3	62	(77.5)	178	157.9
No	12	(92.3)	50	276.1	19	(90.5)	87	294.9	18	(85.7)	57	195.7
SAEs												
Yes	7	(8.0)	10	8.5	8	(4.5)	9	3.7	5	(6.3)	5	4.4
No	0				2	(9.5)	3	10.2	2	(9.5)	2	6.9
GIAEs												
Yes	53	(60.9)	236	199.8	104	(58.4)	303	123.4	23	(28.8)	30	26.6
No	11	(84.6)	20	110.4	14	(66.7)	40	135.6	7	(33.3)	13	44.6

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

表 2.7.4.5-22　ベースラインの脂質異常症の有無別の有害事象－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
Yes	499	668.3			226	294.9		
No	807	1037.8			429	534.7		
Subjects with events	N	(%)	E	R	N	(%)	E	R
All events								
Yes	450	(90.2)	3509	525.0	193	(85.4)	1124	381.2
No	721	(89.3)	6149	592.5	373	(86.9)	2178	407.3
SAEs								
Yes	59	(11.8)	71	10.6	17	(7.5)	21	7.1
No	69	(8.6)	93	9.0	25	(5.8)	32	6.0
GIAEs								
Yes	349	(69.9)	1466	219.4	102	(45.1)	232	78.7
No	620	(76.8)	2843	274.0	212	(49.4)	507	94.8

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

表 2.7.4.5-23　　ベースラインの脂質異常症の有無別の有害事象－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
Yes	276	364.6			265	348.1			284	375.0		
No	126	165.1			138	185.0			118	153.3		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
Yes	233	(84.4)	1331	365.0	238	(89.8)	1531	439.9	225	(79.2)	1034	275.7
No	96	(76.2)	528	319.7	115	(83.3)	666	360.0	84	(71.2)	354	230.9
SAEs												
Yes	23	(8.3)	40	11.0	28	(10.6)	58	16.7	33	(11.6)	48	12.8
No	8	(6.3)	13	7.9	12	(8.7)	13	7.0	4	(3.4)	5	3.3
GIAEs												
Yes	165	(59.8)	502	137.7	175	(66.0)	602	173.0	98	(34.5)	187	49.9
No	66	(52.4)	222	134.4	81	(58.7)	322	174.1	40	(33.9)	75	48.9

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.5.2.2.8　ベースラインの高血圧の有無

以下のベースラインの高血圧の有無（治験責任医師による報告による）に基づくサブグループにより評価した。

- 高血圧「あり」
- 高血圧「なし」

日本人被験者が参加した 3 つの第 3 相試験における高血圧の有無の有害事象の概要（すべての有害事象、重篤な有害事象及び胃腸障害の有害事象）を表 2.7.4.5-24、表 2.7.4.5-25 及び表 2.7.4.5-26 に示す。

3 つの第 3 相試験では、高血圧の両サブグループにおいて、有害事象を発現した被験者の割合はプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で同様又は高かったが、有害事象の単位時間あたりの発現件数はプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で多かった。重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、4382 試験と 4374 試験では、高血圧の両サブグループにおいて投与群間で概ね同程度であったが、4373 試験では、高血圧の両サブグループにおいてプラセボ群と比較してセマグルチド 2.4 mg 群で高い傾向がみられた。3 つの試験において、胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、高血圧の両サブグループにおいて、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった。

いずれの試験及び投与群においても、有害事象、重篤な有害事象及び胃腸障害の有害事象の発現状況に、高血圧の有無による明らかに一貫した傾向は認められなかった。

4382 及び 4374 試験において、有害事象及び胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数を考慮すると、高血圧の両サブグループでも、セマグルチド 1.0 mg 群又はセマグルチド 1.7 mg 群と比較してセマグルチド 2.4 mg 群で有害事象及び胃腸障害の有害事象の発現が増加することは示唆されなかった。

表 2.7.4.5-24　　ベースラインの高血圧の有無別の有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
Yes	73	102.9			152	208.9			73	101.9		
No	27	33.3			47	66.1			28	39.9		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
Yes	60	(82.2)	377	366.5	130	(85.5)	613	293.4	56	(76.7)	156	153.0
No	22	(81.5)	106	318.0	41	(87.2)	221	334.2	24	(85.7)	79	198.0
SAEs												
Yes	4	(5.5)	7	6.8	10	(6.6)	12	5.7	7	(9.6)	7	6.9
No	3	(11.1)	3	9.0	0				0			
GIAEs												
Yes	48	(65.8)	215	209.0	90	(59.2)	242	115.8	21	(28.8)	33	32.4
No	16	(59.3)	41	123.0	28	(59.6)	101	152.7	9	(32.1)	10	25.1

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

表 2.7.4.5-25　ベースラインの高血圧の有無別の有害事象－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
Yes	472	631.8			234	304.3		
No	834	1074.3			421	525.3		
Subjects with events	N	(%)	E	R	N	(%)	E	R
All events								
Yes	427	(90.5)	3223	510.2	205	(87.6)	1170	384.5
No	744	(89.2)	6435	599.0	361	(85.7)	2132	405.9
SAEs								
Yes	59	(12.5)	77	12.2	19	(8.1)	27	8.9
No	69	(8.3)	87	8.1	23	(5.5)	26	5.0
GIAEs								
Yes	327	(69.3)	1381	218.6	104	(44.4)	215	70.7
No	642	(77.0)	2928	272.5	210	(49.9)	524	99.8

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

表 2.7.4.5-26　　ベースラインの高血圧の有無別の有害事象－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
Yes	284	377.4			275	362.3			286	373.4		
No	118	152.4			128	170.8			116	154.9		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
Yes	230	(81.0)	1324	350.9	250	(90.9)	1516	418.5	219	(76.6)	1013	271.3
No	99	(83.9)	535	351.0	103	(80.5)	681	398.8	90	(77.6)	375	242.0
SAEs												
Yes	25	(8.8)	43	11.4	31	(11.3)	62	17.1	30	(10.5)	45	12.1
No	6	(5.1)	10	6.6	9	(7.0)	9	5.3	7	(6.0)	8	5.2
GIAEs												
Yes	154	(54.2)	495	131.2	176	(64.0)	599	165.3	89	(31.1)	166	44.5
No	77	(65.3)	229	150.2	80	(62.5)	325	190.3	49	(42.2)	96	62.0

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.5.2.2.9　結論

全体として、日本人被験者が参加した 3 つの試験において、提示した内因性民族的要因についてサブグループに分けて検討した結果、セマグルチドとプラセボの比較における有害事象プロファイルに明らかな違いは認められなかった。

サブグループの評価から、セマグルチドに関する新たな安全性の懸念は示されなかった。3 つの第 3 相試験において、サブグループ間でわずかな違いが認められた。すべての有害事象、ならびにセマグルチド及び GLP-1 受容体作動薬で最も一般的な有害事象である胃腸障害の有害事象[14, 15, 16, 23, 24, 25, 26]は、女性被験者においてより多く報告される傾向があったが、投与群間の違いは女性と男性の間で同程度であった。

以上のことから、肥満症のためのセマグルチド 2.4 mg の臨床開発プログラムにおいて、セマグルチドと内因性民族的要因との間に予測できない臨床的に問題となる関連性は認められなかった。したがって、選択したいずれの患者においても用量調節は必要ないと考えられる。

2.7.4.5.3　外因性民族的要因

2.7.4.5.3.1　背景及び評価方法

4382（2 型糖尿病を有する被験者のみ）及び 4374 試験の全集団から得られたデータに基づき、セマグルチドの安全性プロファイルに対する外因性民族的要因の影響を評価した。すべての評価に on-treatment 観察期間を用いた。評価した外因性民族的要因は、併用する糖尿病治療薬であった。事前に規定したサブグループの一覧は 2.7.4.1.1.9.4 項に示す。サブグループの定義の詳細は、2.7.4.5.3.2.1 項に示す。

セマグルチドの安全性プロファイルに対する外因性民族的要因の影響は、サブグループ別の有害事象、重篤な有害事象及び胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数におけるセマグルチドとプラセボの間の違いを比較することにより評価した。

試験対象集団全体に対して各投与群への無作為化が行われているが、サブグループ内では無作為化は行われていない。さらに一部のサブグループでは被験者数が少なく、偶然の所見（chance finding）が得られる可能性が高くなる。したがってサブグループ間の結果は慎重に解釈すべきである。

2.7.4.5.3.2 外因性民族的要因別の有害事象

2.7.4.5.3.2.1　糖尿病の基礎治療薬

4382（2 型糖尿病を有する被験者のみ）及び 4374 試験について、以下の糖尿病の基礎治療薬に基づくサブグループにより評価した。

- グループ 1：食事療法・運動療法のみ又は 1 剤の経口糖尿病薬（メトホルミン又は SGLT2 阻害薬）
- グループ 2：1 剤の経口糖尿病薬（スルホニルウレア薬又はチアゾリジン）あるいは 2～3 剤の経口糖尿病薬（メトホルミン、スルホニルウレア薬、SGLT2 阻害薬又はチアゾリジン）

グループ 1 には、2 型糖尿病の治療の必要性が限定的であり、体重を増加させることはないと考えられる経口糖尿病薬（メトホルミン又は SGLT-2 阻害薬）の単独療法を受けている被験者を含めた。グル

ープ 2 には、2 型糖尿病の治療をより必要とし、体重増加を引き起こす可能性があると考えられる経口糖尿病薬（スルホニルウレア薬又はチアゾリジン）による治療を受けている被験者を含めた。4374 試験では、糖尿病の基礎治療及びベースライン時の HbA1c 値による層別化を行った。

4382 及び 4374 試験における併用する糖尿病の基礎治療薬サブグループ別の有害事象の概要（すべての有害事象、重篤な有害事象及び胃腸障害の有害事象）を表 2.7.4.5-27 及び表 2.7.4.5-28 に示す。

糖尿病の基礎治療薬のグループ 1 に含まれる被験者において、有害事象を発現した被験者の割合は、4382 試験ではプラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.7 mg 群で低かったが、4374 試験では投与群間で同程度であった。糖尿病の基礎治療薬のグループ 2 に含まれる被験者では、両試験において、有害事象を発現した被験者の割合はプラセボと比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった。単位時間あたりの有害事象の発現件数については、いずれの試験においても、糖尿病の基礎治療薬の両グループにおいて、プラセボと比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で多い傾向が認められた。

4382 試験では、糖尿病の基礎治療薬のグループ 1 の 2 例（セマグルチド 2.4 mg 群とプラセボ群で各 1 例）に重篤な有害事象が認められたが、糖尿病の基礎治療薬のグループ 2 では重篤な有害事象は認められなかった。4374 試験では、糖尿病の基礎治療薬のグループ 1 において、重篤な有害事象を発現した被験者の割合及び単位時間あたりの発現件数は投与群間で概ね同程度であった。糖尿病の基礎治療薬のグループ 2 については、重篤な有害事象を発現した被験者の割合は投与群間で同程度であったが、重篤な有害事象の単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド 2.4 mg 群及びセマグルチド 1.0 mg 群で多い傾向が認められた。

いずれの試験及び糖尿病の基礎治療薬のグループでも、胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は、プラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）で高かった。

4374 試験では、すべての有害事象及び胃腸障害の有害事象における投与群間の差が、糖尿病の基礎治療薬のグループ 1 の被験者と比較してグループ 2 の被験者でより顕著であったが、この傾向は 4382 試験では認められなかった。

4374 試験では、糖尿病の基礎治療薬のグループのいずれにおいても、有害事象の発現がセマグルチド 1.0 mg 群と比較してセマグルチド 2.4 mg で多い傾向が認められたが、4382 試験では同様の傾向は認められなかった。胃腸障害の有害事象の発現は、4382 及び 4374 試験において、いずれの糖尿病の基礎治療薬のグループでも、セマグルチド 1.7 mg 群及びセマグルチド 1.0 mg 群と比較してセマグルチド 2.4 mg 群で多い傾向が認められた。

表 2.7.4.5-27　糖尿病の基礎治療別の有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験、スクリーニング時に 2 型糖尿病を有する被験者）

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
Diabetes treatment group 1	9	12.8			27	37.2			12	17.1		
Diabetes treatment group 2	16	22.7			22	31.1			13	18.5		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
Diabetes treatment group 1	7	(77.8)	28	218.3	18	(66.7)	129	346.9	11	(91.7)	27	157.8
Diabetes treatment group 2	15	(93.8)	60	264.2	20	(90.9)	119	382.9	9	(69.2)	25	135.0
SAEs												
Diabetes treatment group 1	0				2	(7.4)	2	5.4	2	(16.7)	2	11.7
Diabetes treatment group 2	0				0				0			
GIAEs												
Diabetes treatment group 1	5	(55.6)	11	85.8	16	(59.3)	49	131.8	2	(16.7)	2	11.7
Diabetes treatment group 2	10	(62.5)	18	79.3	16	(72.7)	43	138.4	5	(38.5)	6	32.4

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

表 2.7.4.5-28　糖尿病の基礎治療別の有害事象－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
Diabetes treatment group 1	243	317.3			231	306.7			230	303.0		
Diabetes treatment group 2	159	212.5			172	226.3			172	225.3		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
Diabetes treatment group 1	194	(79.8)	1033	325.6	194	(84.0)	1165	379.8	184	(80.0)	856	282.5
Diabetes treatment group 2	135	(84.9)	826	388.7	159	(92.4)	1032	456.0	125	(72.7)	532	236.1
SAEs												
Diabetes treatment group 1	17	(7.0)	21	6.6	21	(9.1)	28	9.1	20	(8.7)	33	10.9
Diabetes treatment group 2	14	(8.8)	32	15.1	19	(11.0)	43	19.0	17	(9.9)	20	8.9
GIAEs												
Diabetes treatment group 1	142	(58.4)	392	123.6	137	(59.3)	457	149.0	78	(33.9)	143	47.2
Diabetes treatment group 2	89	(56.0)	332	156.2	119	(69.2)	467	206.4	60	(34.9)	119	52.8

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.5.3.2.2　結論

全体として、日本人被験者が参加した第 3 相試験では、糖尿病の基礎治療薬によるサブグループに分けて検討した結果において、セマグルチドとプラセボの間の有害事象プロファイルの違いが大きくなることはなかった。

4374 試験では、糖尿病の基礎治療薬サブグループ間ですべての有害事象と胃腸障害の有害事象の報告にわずかな違いが認められたが、4382 試験では同様の傾向は認められなかった。

以上のことから、肥満症のためのセマグルチド 2.4 mg の臨床開発プログラムでは、セマグルチドと外因性民族的要因との間に予測できない臨床的に問題となる関連性は認められなかった。したがって、選択したいずれの患者においても用量調節は必要ないと考えられる。

2.7.4.5.4　体重減少

2.7.4.5.4.1　背景及び評価方法

セマグルチドの投与を受け、投与終了時（68 週）に最も大きい体重減少（20%以上）が認められた被験者における安全性プロファイルについて、on-treatment 観察期間から得られたデータに基づき評価した。これは、体重減少の程度に関連した予測できない有害な影響の可能性を評価するために実施した。

評価においては、セマグルチド群（1.0、1.7 及び 2.4 mg）で報告された有害事象に注目し、有害事象を発現した被験者の割合と単位時間あたりの発現件数を、20%以上の体重減少が認められた被験者と体重減少が 20%未満であった被験者との間で比較した。このサブグループの評価は、無作為割り付け前には存在しなかった要因に基づくものであることから、因果関係の可能性を明確に確立することができないため、結果は慎重に解釈すべきである。

2.7.4.5.4.2　体重減少別の有害事象

日本人被験者が参加した第 3 相試験において、以下の 68 週の体重減少の分類に基づき評価した。

- 20%以上の体重減少
- 20%未満の体重減少

日本人被験者が参加した 3 つの第 3 相試験における体重減少率別の有害事象の概要（すべての有害事象、重篤な有害事象及び胃腸障害の有害事象）を表 2.7.4.5-29、表 2.7.4.5-30 及び表 2.7.4.5-31 に示す。

4382 試験の 10 例、4373 試験の 172 例、4374 試験の 65 例が 68 週の体重の評価を実施しなかったことから表中では「Missing」として集計されている。留意すべき点として、プラセボ群では 20%以上の体重減少が認められた被験者が少なかったことがある。セマグルチドの投与を受けた被験者において、体重減少が 20%未満であった被験者と比較して 20%以上の体重減少が認められた被験者でより高頻度に報告された有害事象について以下に示す。

日本人被験者が参加した 3 つの第 3 相試験では、すべての試験及び投与群について、有害事象、重篤な有害事象及び胃腸障害の有害事象の発現状況に、ベースラインから 68 週の体重減少が 20%以上だった被験者と 20%未満だった被験者の間で明らかに一貫した傾向は認められなかった。

4382 と 4374 試験において、有害事象、重篤な有害事象及び胃腸障害の有害事象を発現した被験者の割合及び単位時間あたりの発現件数を考慮すると、いずれの体重減少のサブグループでも、セマグルチド 1.0 mg 群又はセマグルチド 1.7 mg 群と比較してセマグルチド 2.4 mg 群で有害事象、重篤な有害事象及び胃腸障害の有害事象の発現が増加することは示唆されなかった。

表 2.7.4.5-29　68 週時の体重減少（率）別の有害事象－on-treatment 観察期間－安全性解析対象集団（4382 試験）

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
>= 20% Weight loss	11	15.7			38	53.7			2	2.8		
< 20% Weight loss	86	119.4			155	216.1			98	137.9		
Missing	3	1.2			6	5.2			1	1.1		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
>= 20% Weight loss	8	(72.7)	36	229.2	36	(94.7)	153	284.8	2	(100)	4	140.8
< 20% Weight loss	72	(83.7)	444	372.0	130	(83.9)	666	308.2	77	(78.6)	230	166.8
Missing	2	(66.7)	3	260.3	5	(83.3)	15	288.4	1	(100)	1	89.7
SAEs												
>= 20% Weight loss	0				2	(5.3)	3	5.6	0			
< 20% Weight loss	7	(8.1)	10	8.4	7	(4.5)	8	3.7	6	(6.1)	6	4.4
Missing	0				1	(16.7)	1	19.2	1	(100)	1	89.7
GIAEs												
>= 20% Weight loss	7	(63.6)	14	89.1	23	(60.5)	64	119.1	1	(50.0)	1	35.2
< 20% Weight loss	56	(65.1)	241	201.9	92	(59.4)	271	125.4	28	(28.6)	41	29.7
Missing	1	(33.3)	1	86.8	3	(50.0)	8	153.8	1	(100)	1	89.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

表 2.7.4.5-30　　68 週時の体重減少（率）別の有害事象－on-treatment 観察期間－安全性解析対象集団（4373 試験）

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
>= 20% Weight loss	388	549.1			10	14.2		
< 20% Weight loss	824	1092.6			567	761.4		
Missing	94	64.5			78	54.0		
Subjects with events	N	(%)	E	R	N	(%)	E	R
All events								
>= 20% Weight loss	350	(90.2)	3129	569.9	10	(100)	47	331.5
< 20% Weight loss	743	(90.2)	6021	551.1	496	(87.5)	3027	397.5
Missing	78	(83.0)	508	788.0	60	(76.9)	228	422.6
SAEs								
>= 20% Weight loss	37	(9.5)	53	9.7	0			
< 20% Weight loss	85	(10.3)	104	9.5	36	(6.3)	47	6.2
Missing	6	(6.4)	7	10.9	6	(7.7)	6	11.1
GIAEs								
>= 20% Weight loss	297	(76.5)	1394	253.9	5	(50.0)	11	77.6
< 20% Weight loss	610	(74.0)	2654	242.9	276	(48.7)	665	87.3
Missing	62	(66.0)	261	404.9	33	(42.3)	63	116.8

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

表 2.7.4.5-31　　68 週時の体重減少（率）別の有害事象－on-treatment 観察期間－安全性解析対象集団（4374 試験）

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
>= 20% Weight loss	19	26.6			51	72.6			6	7.9		
< 20% Weight loss	360	491.4			337	452.3			369	504.3		
Missing	23	11.8			15	8.2			27	16.1		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
All events												
>= 20% Weight loss	17	(89.5)	154	578.3	45	(88.2)	331	455.9	6	(100)	32	403.3
< 20% Weight loss	296	(82.2)	1643	334.4	296	(87.8)	1811	400.4	288	(78.0)	1285	254.8
Missing	16	(69.6)	62	526.3	12	(80.0)	55	672.5	15	(55.6)	71	442.0
SAEs												
>= 20% Weight loss	3	(15.8)	8	30.0	5	(9.8)	13	17.9	3	(50.0)	8	100.8
< 20% Weight loss	27	(7.5)	44	9.0	32	(9.5)	43	9.5	31	(8.4)	40	7.9
Missing	1	(4.3)	1	8.5	3	(20.0)	15	183.4	3	(11.1)	5	31.1
GIAEs												
>= 20% Weight loss	11	(57.9)	61	229.1	37	(72.5)	142	195.6	3	(50.0)	6	75.6
< 20% Weight loss	208	(57.8)	624	127.0	211	(62.6)	754	166.7	124	(33.6)	239	47.4
Missing	12	(52.2)	39	331.0	8	(53.3)	28	342.4	11	(40.7)	17	105.8

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event,
E: Number of events, R: Event rate per 100 patient-years of exposure, SAEs: Serious adverse events, GIAEs: Gastrointestinal adverse events.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2.7.4.5.4.3結論

セマグルチド投与群の被験者において20%以上の体重減少が認められなかった被験者と比較して、20%以上の体重減少が認められた被験者の安全性プロファイルに安全性の懸念は認められなかった。

2.7.4.5.5　薬物相互作用

肥満を有する被験者は1つ又は複数の合併症（2型糖尿病を含む）を有する可能性が高く[44]、複数の薬剤を使用している可能性が高いことから、薬物相互作用の可能性について評価することは重要である。チトクロムP450酵素及び薬物トランスポーターの阻害及び誘導に関連する、セマグルチドによる臨床的に問題となる薬物相互作用はないと予測されている。しかしながら、GLP-1受容体作動薬で認められた胃内容排出の遅延が、併用する経口薬の吸収に影響を及ぼす可能性がある。

セマグルチド2.4 mgの薬物相互作用の可能性は、2型糖尿病に対するセマグルチド皮下投与（オゼンピック皮下注）における過去の経験に基づき評価した。詳細については、Module 2.7.2.3.1.4に示す。2型糖尿病に対するセマグルチド皮下投与（オゼンピック皮下注）の臨床開発プログラムにおいて、パラセタモール（アセトアミノフェン）吸収法[89, 90]により胃内容排出を評価した。1.0 mgの用量では、標準食摂取後1時間では胃内容排出遅延が認められたものの、標準食摂取後5時間では全体的な胃内容排出に影響は認められなかった（NN9535-3685試験）。薬物相互作用試験では、セマグルチドは経口薬の吸収に対して臨床的に問題となる程度の影響は及ぼさなかった。

セマグルチド1.0 mgの薬物相互作用試験プログラムをセマグルチド2.4 mgにも適用することを可能にするために、臨床薬理試験（4455試験）では、セマグルチド2.4 mgの胃内容排出に対する影響を、同じパラセタモール吸収法を用いて検討した。20週に評価した結果、胃内容排出に対するセマグルチド2.4 mgの臨床的に問題となる影響は認められなかった（Module 2.7.2.3.1.4及び2.7.2.3.2.5に示す）。

全体として、4455試験及びNN9535-3685試験のデータに基づくと、セマグルチド1.0 mgと比較してセマグルチド2.4 mgで胃内容排出のさらなる遅延はみられないと考えられた。したがって、セマグルチド2.4 mgが経口薬の吸収に及ぼす可能性のある影響は、セマグルチド1.0 mgが及ぼす影響を上回るものでないと予想される。以上のことから、セマグルチド1.0 mgの薬物相互作用プログラムが、セマグルチド2.4 mgに適用可能であると考える。

2.7.4.5.6　妊娠及び授乳時の使用

2.7.4.5.6.1　背景及び評価方法

セマグルチドが受胎能、胚・胎児発生、出生前及び出生後の発生に影響を及ぼす可能性について、ラット、ウサギ及びカニクイザルで検討した（Module 2.4）。生殖毒性試験では、セマグルチドの投与に関連する雄の受胎能への影響は認められなかった。雌ラットでは、セマグルチドは性周期を延長し、黄体数減少を伴う着床数及び同腹児数に対して影響を及ぼした。これらの影響は、母動物の体重減少に対する適応反応と考えられた。セマグルチドの胎盤移行性はラット及びウサギで認められ、ラットでは乳汁に低濃度のセマグルチドが検出された。セマグルチドはGLP-1受容体を介したメカニズムでラットの胚・胎児発生に有害作用を及ぼすことが示されているが、このメカニズムには種差があることからヒトに当てはまる可能性は低いと考えられている。しかしながら、その他のメカニズムの関与を完全には否定できない。ウサギ及びサルで認められた妊娠損失及び胎児異常は、偶発的である

か、母動物での顕著な体重減少に関連する可能性が考えられる。しかし、現在利用可能なデータからヒトとの関連性を完全には否定することはできない。2 型糖尿病に対するセマグルチド皮下投与及びセマグルチド経口投与から得られた限られた臨床データからは、妊娠初期や胚・胎児発生に対する有害な影響は示唆されなかった。しかしながら、これらのデータは限られているため、肥満症治療のためのセマグルチドの妊娠又は授乳中には使用すべきではない。

妊娠可能な女性の妊娠を回避し、さらに被験者が妊娠した場合の対応のために、第 3 相試験の治験実施計画書では複数の対策を実施した。妊娠可能な女性は、有効性の高い避妊方法、すなわち一貫して正しく使用した場合の年間失敗率が 1%未満の方法を使用することに同意した場合にのみ、試験への参加が適格であるとした。有効性が高い避妊方法と考えられるものについての詳細な説明は、治験実施計画書において治験責任医師に提供された。さらに、女性被験者は、本試験への参加が適格であると判断される前に妊娠検査が陰性でなければならず、試験期間を通して妊娠検査を定期的（4 週又は 8 週ごと）に実施した。月経がなかった場合や妊娠が疑われる場合には、追加の妊娠検査を実施しなければならなかった。被験者が妊娠した場合には、治験薬の投与を中止しなければならなかった。妊娠は治験責任医師が報告することとし、転帰が異常な妊娠については父親の情報を収集することとした。

確認されたすべての妊娠の概要は、2.7.4.5.6.2 項に示す。叙述は各試験の治験総括報告書（Module 5）に示す。

評価は on-treatment 観察期間に基づき行った。

妊娠の評価に追加して、日本人被験者が参加した 3 つの第 3 相試験おいて、授受胎能に関連する有害事象〔SMQ「生殖能障害」狭域用語のみ、Global summary of safety（Module 5.3.5.3）Appendix 7.8、Section 9 に示す〕及び授乳に関連する有害事象〔SMQ「母乳を介した新生児曝露」〕を on-treatment 観察期間に基づき評価した。

2.7.4.5.6.2　妊娠

4382 試験では妊娠は報告されなかった。

4373 試験では、セマグルチド 2.4 mg 群で 13 件及びプラセボ群で 4 件の妊娠が報告された。さらに、父親を介する曝露が 1 例報告された。セマグルチド 2.4 mg 群では、4 件の妊娠が自然流産、1 件が妊娠中絶となり、1 件の「異所性妊娠」と 1 件の「つわり」の有害事象が認められた。

4374 試験では、プラセボ群で 1 件の妊娠が報告された。セマグルチド群（1.0 mg 及び 2.4 mg）では妊娠の報告はなかった。

その他の完了した試験では、計 18 件の妊娠が報告された。4375 試験ではセマグルチド 2.4 mg に割り付けられた 3 例及びプラセボに割り付けられた 2 例、4376 試験ではセマグルチド投与継続に割り付けられた 7 例及びセマグルチドからプラセボへの切り替えに割り付けられた 1 例、ならびに 4153 試験ではセマグルチドのいずれかの群に割り付けられた 5 例であった。

すべての事例において、女性被験者は妊娠が確認されるまでの短い期間、治験薬に曝露され（又は全く曝露されず）、治験薬の投与が中止された。

妊娠に関する詳細については、各治験総括報告書（Module 5.3.5.1）に示す。

2.7.4.5.6.3　授受胎能

4832 試験では、on-treatment 期間に授受胎能に関連する有害事象は報告されなかった。

4373 試験では授受胎能に関連する有害事象が 7 件報告された。セマグルチド 2.4 mg 群で 4 例 4 件及びプラセボ群で 3 例 3 件であった（付録 2.7.4.7.1、表 9）。4374 試験では授受胎能に関連する有害事象がプラセボ群でのみ 2 例 2 件報告された（付録 2.7.4.7.1、表 10）。セマグルチド 2.4 mg 群の女性被験者で 4 件の事象（3 件の「機能不全性子宮出血」及び 1 件の「多嚢胞性卵巣」）が報告された。これらの事象はいずれも治験責任医師により治験薬との因果関係が「なし」と判定され、治験薬の投与の変更には至らなかった〔4373 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1〕。3 件の「機能不全性子宮出血」（2 件が中等度の事象で 1 件が重度の事象）はいずれも回復したが、軽度の事象であった「多嚢胞性卵巣」は回復しなかった。1 件の「機能不全性子宮出血」は重篤な有害事象であった。本被験者は異常子宮出血の既往歴を有し、当該事象に関連して両側卵管卵巣摘出術を伴う子宮摘出術を受けた。プラセボ群で認められた事象については、4374 試験で報告された 1 件〔「精子吸引」（基本語）〕が重篤な有害事象であった。これら 2 件の重篤な有害事象の詳細については、叙述〔4373 試験（Module 5.3.5.1）Section 14.3.3、4374 試験（Module 5.3.5.1）Section 14.3.3〕に示す。

2.7.4.5.6.4　授乳

日本人被験者が参加した 3 つの第 3 相試験（4382、4373 及び 4374 試験）において、授乳に関連する有害事象は報告されなかった。

2.7.4.5.6.5　結論

現在得られている限られた臨床データからは、妊娠初期のセマグルチドの投与が胚・胎児発生、授受胎能又は授乳に影響を及ぼすことは示唆されていない。しかしながら、情報が限られているため、妊娠中及び授乳中の潜在的リスクを除外することはできない。また、体重減少が妊婦に有益となる可能性がなく、胎児に有害となる可能性があることから、セマグルチド 2.4 mg は妊娠中には使用すべきではない。したがって、セマグルチド 2.4 mg は妊娠中又は授乳中には使用しないこと。

2.7.4.5.7　過量投与、投薬過誤及び薬物乱用又は誤用

2.7.4.5.7.1　背景及び評価方法

非臨床試験及び 2 型糖尿病に対するセマグルチド皮下投与（オゼンピック皮下注）の過去の臨床試験から得られた利用可能な薬理データから、セマグルチドによる薬物乱用の可能性は示唆されていない。

一部の基本語が重複している 3 つの事前に規定した MedDRA 検索は、投与過誤（偶発的過量投与を含む、2.7.4.5.7.2 項）、薬物乱用又は誤用（企図的過量投与を含む、2.7.4.5.7.3 項）ならびに過量投与（偶発的過量投与及び企図的過量投与、2.7.4.5.7.4 項）のすべての有害事象を特定するために定義した。MedDRA 検索に含まれる用語は、4382 試験（Module 5.3.5.1）Appendix 16.1.9、4373 試験（Module 5.3.5.1）Appendix 16.1.9、4374 試験（Module 5.3.5.1）Appendix 16.1.9 に示す。On-treatment 観察期間に基づき評価した。

第 3 相試験では、投与過誤あるいは薬物乱用又は誤用に関連する有害事象の追加データを「Medication error event form」に記録した（表 2.7.4.1-3）。

2.7.4.5.7.2　投与過誤

日本人が参加した 3 つの第 3 相試験において、投与過誤に関連する有害事象を発現した被験者は少なかった。いずれの試験でも、投与過誤の有害事象を発現した被験者の割合及び単位時間あたりの発現件数は投与群間で同様であった。すべての事象が、非重篤で、軽度又は中等度であり、転帰は「回復」又は「軽快」であった。治験薬投与の中止に至った投与過誤の有害事象は認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.49、4373 試験（Module 5.3.5.1） EOT Table 14.3.1.47、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.47〕。

4382 試験で認められた投与過誤の有害事象（基本語）は、セマグルチド 2.4 mg 群で 1 件の「偶発的過量投与」、ならびにセマグルチド 2.4 mg 群とセマグルチド 1.7 mg 群で各 1 件の「製品適用過誤」であった。投与過誤の大部分の有害事象（基本語）が、4373 試験では「偶発的過量投与」及び「過量投与」、4374 試験では「偶発的過量投与」であり、いずれの試験でも投与群間で明らかな違いは認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.50、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.48、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.48〕。

2.7.4.5.7.3　薬物乱用又は誤用

日本人被験者が参加した 3 つの第 3 相試験において、セマグルチド 2.4 mg 群の被験者では薬物乱用又は誤用に関連する有害事象の報告はなかった。4374 試験のセマグルチド 1.0 mg 群で 1 件（「企図的過量投与」）、及び 4373 試験のプラセボ群で 1 件（「自殺企図」）が報告された〔4373 試験（Module 5.3.5.1）EOT Table 14.3.1.51、14.3.1.52、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.51、14.3.1.52〕。「企図的過量投与」は、非重篤で、軽度であり、治験責任医師により治験薬との因果関係は「あり」と判定された。「自殺企図」は、重篤な有害事象で、重症度は重度であり、治験責任医師により治験薬との因果関係は「なし」と判定された。

2.7.4.5.7.4　過量投与

日本人被験者が参加した第 3 相試験のいずれにおいても、過量投与に関連した有害事象を発現した被験者は少なく、過量投与の有害事象を発現した被験者の割合及び単位時間あたりの発現件数に投与群間で明らかな違いは認められなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.51、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.49、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.49〕。過量投与の大部分の有害事象（基本語）が「偶発的過量投与」及び「過量投与」であり、これらの事象は投与過誤の MedDRA 検索でも特定された（2.7.4.5.7.2 項）。4374 試験のセマグルチド 1.0 mg 群で 1 件の「企図的過量投与」、及び 4373 試験のプラセボ群で 1 件の「自殺企図」が報告された。これらの事象は薬物乱用又は誤用の MedDRA 検索でも特定された（2.7.4.5.7.3 項）。この他に、過量投与の MedDRA 検索で特定された過量投与の有害事象はなかった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.52、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.50、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.50〕。

4373 試験のプラセボ群で発現した「自殺企図」の 1 件を除き、すべての事象が非重篤で、軽度又は中等度であった。すべての事象の転帰は「回復」又は「軽快」であった。

2.7.4.5.7.5　結論

日本人被験者が参加したいずれの第 3 相試験（4382、4373 及び 4374 試験）でも、すべての投与群において投与過誤、薬物乱用又は誤用、あるいは過量投与の有害事象は稀であり、これらの事象を発現した被験者の割合及び単位時間あたりの発現件数に投与群間で明らかな違いは認められなかった。セマグルチドの乱用／誤用の可能性は示唆されなかった。

2.7.4.5.8　治験薬による病原体感染の疑い

治験薬による病原体感染が疑われる事象を特定するため、日本人被験者が参加した 3 つの第 3 相試験で報告されたすべての有害事象に対して、事前に規定した MedDRA 検索を実施した〔検索用語の詳細については、4382 試験（Module 5.3.5.1）Appendix 16.1.9、4373 試験（Module 5.3.5.1）Appendix 16.1.9、4374 試験（Module 5.3.5.1）Appendix 16.1.9〕。治験実施計画書に従い、治験薬による病原体感染の疑いは重篤な有害事象とみなされた。評価は on-treatment 観察期間に基づいて行う。

日本人被験者が参加した 3 つの第 3 相試験では、治験薬による病原体感染が疑われる有害事象は特定されなかった。

以上のことから、得られたデータにより、セマグルチドによる治療が治験薬による病原体感染のリスクを増加させることは示唆されなかった。

2.7.4.5.9　離脱症状及び反跳現象

離脱症状とは、投薬の中止又は投与量の減量により起こりうる症状であり、反跳現象は投薬中には認められなかった、あるいは制御されていた症状の出現又は再出現のことである。セマグルチド 2.4 mg の離脱症状及び反跳現象の可能性は、on-treatment 観察期間に基づき評価した。

発現件数が少ないと考えられる当該安全性領域で潜在的な安全性シグナルを検出する目的で、第 3 相試験の併合データを提示し、評価した。

第 3 相試験併合データは、治験薬の投与終了後 7 週間以内に報告されたすべての有害事象の要約表に基づき評価した。早期投与中止後又は予定された投与終了後に報告された有害事象を、2 つの表に別々に提示する〔Global summary of safety（Module 5.3.5.3）Appendix 7.3、Table 7.3.63 及び Table 7.3.64〕。

4376 試験については、無作為割り付け後 7 週間に報告された有害事象に基づき、離脱症状を評価した〔Global summary of safety（Module 5.3.5.3）Appendix 7.3、Table 7.3.65〕。

4376 試験では、試験の最初の 20 週間（16 週間の用量漸増期間を含む）にすべての被験者がセマグルチドの投与を受け、その後、被験者はセマグルチド 2.4 mg の継続投与又はプラセボへの切り替えのいずれかに無作為に割り付けられた。したがって、20 週においてプラセボ群に無作為割り付けされた被験者では離脱症状及び反跳現象が発現する可能性がある。セマグルチド 2.4 mg 群に割り付けられた被験者は投与期間終了時まで体重減少が継続したが、プラセボ群に割り付けられた被験者は徐々に体重

が増加したが、導入期間の開始時の体重に戻ることはなかった〔詳細は 4376 試験（Module 5.3.5.1）に示す〕。

4376 試験では、セマグルチド 2.4 mg 群に無作為割り付けされた被験者と比較してプラセボ群に無作為割り付けされた被験者において、無作為割り付け後の 7 週間以内に「食欲亢進」（セマグルチド 2.4 mg 群：0.2%、プラセボ群：1.9%）及び「空腹」（セマグルチド 2.4 mg 群：0.2%、プラセボ群：0.7%）を発現した被験者の割合が高かった〔Global summary of safety（Module 5.3.5.3）Appendix 7.3、Table 7.3.65〕。第 3 相試験併合データでは、68 週の予定された投与終了後に、「空腹」を発現した被験者の割合は、プラセボ併合群（0%）と比較してセマグルチド 2.4 mg 併合群（0.6%）で高かった〔Global summary of safety（Module 5.3.5.3）Appendix 7.3、Table 7.3.64〕。

4376 試験では、20 週でセマグルチド 2.4 mg 群に無作為割り付けされた被験者において 1 例（0.2%）1 件の「不安」が報告されたのに対し、プラセボ群に無作為割り付けされた被験者では 4 例（1.5%）4 件の「不安」が報告された〔Global summary of safety（Module 5.3.5.3）Appendix 7.3、Table 7.3.65〕。セマグルチドの投与を終了した被験者で報告された 4 件のうち、2 例は食物又は食事に対する不安として報告された〔4376 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1〕。この違いは、第 3 相試験併合データでは認められなかった。第 3 相試験併合データでは、「不安」を発現した被験者の割合は、セマグルチド 2.4 mg の早期投与中止後（0.8%）又は予定された投与終了後（0.2%）ともに低かった〔Global summary of safety（Module 5.3.5.3）Appendix 7.3、Table 7.3.63、Table 7.3.64〕。

第 3 相試験併合データにおいて、治験薬の早期投与中止後に「頭痛」、「浮動性めまい」及び「片頭痛」を発現した被験者の割合は、プラセボの投与を中止した被験者と比較して、セマグルチド 2.4 mg の投与を中止した被験者で高かったが〔Global summary of safety（Module 5.3.5.3）Appendix 7.3、Table 7.3.63〕、第 3 相試験併合データの全体的な期間における単位時間あたりの発現件数と比較して顕著な違いは認められなかった〔Global summary of safety（Module 5.3.5.3）Appendix 7.2、Table 7.2.2〕。この違いは、第 3 相試験併合データの予定された投与終了後、又は 4376 試験の無作為割り付け後の被験者では認められなかった。

以上のことから、少数の被験者から報告された「食欲亢進」及び「空腹」を除き、セマグルチド 2.4 mg の投与中止による離脱症状は認められなかった。4376 試験では、セマグルチドからプラセボに切り替えた被験者において体重が徐々に増加したが、導入期間の開始時の体重に戻ることはなかった。

2.7.4.5.10 自動車運転及び機械操作に対する影響又は精神機能の障害

セマグルチドの自動車運転及び機械操作に対する影響及び精神機能の障害に対する影響は、特定された副作用に基づき評価した。

表 2.7.4.5-32　　副作用

Population	Adverse drug reactions
All subjects	Headache; Dizziness; Increased heart rate; Vomiting; Diarrhoea, Constipation; Nausea; Abdominal pain; Gastritis; Gastroesophageal reflux disease; Dyspepsia; Eructation; Flatulence; Abdominal distension; Acute pancreatitis; Cholelithiasis; Hair loss; Fatigue; Injection site reactions; Increased amylase; Increased lipase; Anaphylactic reaction.
Subjects with T2D	Hypoglycaemia; Diabetic retinopathy.

特定された副作用（表 2.7.4.5-32）のうち、「浮動性めまい」と「低血糖」は被験者の集中力及び又は反応力に影響を与え、自動車運転や機械操作に影響を与える可能性が考えられる。

浮動性めまい

日本人被験者が参加した 3 つの第 3 相試験において、「浮動性めまい」を発現した被験者の割合はプラセボ群と比較してセマグルチド群（1.0、1.7 及び 2.4 mg）に割り付けられた被験者で高かった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.4、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.4、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.4〕。2 件の「浮動性めまい」（4382 試験のセマグルチド 1.7 mg 群及び 4373 試験のセマグルチド 2.4 mg 群で各 1 件）を除き、すべての事象が非重篤であった。また有害事象の大部分が軽度又は中等度であった〔4382 試験（Module 5.3.5.1）EOT Table 14.3.1.11、14.3.1.14、4373 試験（Module 5.3.5.1）EOT Table 14.3.1.11、14.3.1.14、4374 試験（Module 5.3.5.1）EOT Table 14.3.1.11、14.3.1.14〕。

4373 試験のセマグルチド 2.4 mg 群で 1 例 1 件の重篤な「浮動性めまい」が報告された〔叙述は 4373 試験（Module 5.3.5.1）Section 14.3.3 に示す〕。本被験者では「低カリウム血症」も報告されたことから、当該事象は治験責任医師により治験薬との因果関係は「なし」と判定され、他の原因を有していると考えられた。また、本被験者はよくみられる副作用として「浮動性めまい」を伴う利尿剤を併用していた。

もう 1 件の重篤な「浮動性めまい」は 4382 試験のセマグルチド 1.7 mg 群の被験者で報告された〔叙述は 4382 試験（Module 5.3.5.1）Section 14.3.3 に示す〕。被験者の労働環境が変更し、ストレスが偶発的に発現したことにより浮動性めまいが引き起こされた可能性が高いと考えられたことから、当該事象は治験責任医師により治験薬との因果関係は「なし」と判定され、他の原因を有していると考えられた。

低血糖

過体重又は肥満、ならびに 2 型糖尿病を有する被験者は、特にスルホニルウレア薬又はインスリンと併用投与時に、低血糖を発現することがある。

4382 試験では、スクリーニング時に 2 型糖尿病を有する被験者において、重大な低血糖（レベル 3）又は臨床的に問題となる低血糖（レベル 2）を発現した被験者はいなかった。

4374 試験では、セマグルチド 2.4 mg 群で 1 件の重大な低血糖（レベル 3）が認められた。本事象は、「慢性胆嚢炎」の重篤な有害事象のための入院に関連して発現した。臨床的に問題となる低血糖（レベル 2）は、プラセボ群と比較してセマグルチド群でより多く報告された。これらの低血糖を発現した被験者の割合は、セマグルチド 2.4 mg 群とセマグルチド 1.0 mg 群で明らかな違いは認められなか

った。すべての投与群（セマグルチド 2.4 mg 群、セマグルチド 1.0 mg 群及びプラセボ群）において、低血糖の大部分は、低血糖の発現時にスルホニルウレア薬も投与していた被験者で認められた（表 2.7.4.2-58）。

これらの結果は、2 型糖尿病に対するセマグルチド皮下投与で認められた過去の結果と同様である。4382 及び 4374 試験における低血糖の詳細については、2.7.4.2.2.9.3 項に示す。

2 型糖尿病を有さない被験者については、4382 試験では低血糖の有害事象は認められなかった。4373 試験では、低血糖の有害事象を発現した被験者の割合は低く、セマグルチド 2.4 mg 群とプラセボ群で同様であった。すべての事象は非重篤であった（詳細については 2.7.4.2.2.9.2 項に示す）。

結論

セマグルチド群（1.0、1.7 及び 2.4 mg）で報告された「浮動性めまい」又は低血糖の大部分が非重篤で、軽度な事象であったことを考慮すると、セマグルチド 2.4 mg は自動車運転及び機械操作に対する影響や精神機能に障害を与えることはない、もしくはほとんどないと予測される。

2.7.4.5.11 テクニカルな苦情

2.7.4.5.11.1 背景及び評価方法

試験期間中、治験薬に関連するすべてのテクニカルな苦情は収集され、ノボ ノルディスク社に報告されることとした。テクニカルな苦情には、治験薬（薬剤及び医療機器）の不具合に関するすべての連絡が含まれた。テクニカルな苦情には有害事象が伴うことがあるが、苦情自体は有害事象ではない。治験責任医師が、テクニカルな苦情が何らかの有害事象又は重篤な有害事象に関連するかどうかを評価した。

テクニカルな苦情の例：

- 治験薬の物理的及び科学的な外観（変色、粒子又は異物混入等）
- 包装資材（漏出、亀裂、カートリッジのゴム栓の問題、表示文章の誤記等）
- 医療機器に関する問題（投与機構、用量設定、注入ボタン等）

本概要では、日本人被験者が参加した 3 つの第 3 相試験において、テクニカルな苦情に関連する有害事象又は重篤な有害事象を評価した（2.7.4.5.11.2 項）。有害事象及び重篤な有害事象との関連の有無に関わらず、すべてのテクニカルな苦情の一覧は、各治験総括報告書〔4373 試験（Module 5.3.5.1）Section 14.4、4374 試験（Module 5.3.5.1）Section 14.4〕に示す。

2.7.4.5.11.2 テクニカルな苦情に関連する有害事象

4382 試験では、テクニカルな苦情は認められなかったことから、テクニカルな苦情に関連する有害事象は試験期間中に報告されなかった。4374 試験では、22 件のテクニカルな苦情が報告されたが、有害事象が関連するものは認められなかった。

4373 試験では、テクニカルな苦情に関連する 5 件の有害事象が報告された。セマグルチド 2.4 mg 群で 3 件及びプラセボ群で 2 件であった〔4373 試験（Module 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.3〕。テクニカルな苦情に関連するすべての事象は、「注射部位疼痛」、「注射部位腫瘤」又は

「注射部位内出血」であり、治験責任医師により治験薬との因果関係は「あり」又は「可能性あり」と判定された。またすべての事象が非重篤で、軽度であり、転帰は「回復」であった。これらの有害事象が伴った 5 件のテクニカルな苦情のうち、2 件は治験薬の投与に関連する問題（2 つのペンのいずれも検査時に正常であることが判明した）、2 件は刺すような感覚に関する苦情（2 つのペンはいずれも検査時に正常であることが判明した）、1 件は治験薬の溶液中の血液に関する苦情（取り扱い上の不具合と分類された）であった〔4373 試験（Module 5.3.5.1）Section 14.4〕。

2.7.4.6 市販後データ

日本では、セマグルチドを有効成分とする薬剤として、2018 年 3 月に「オゼンピック皮下注 2mg」が 2 型糖尿病を効能又は効果として承認された。その後 2020 年 3 月に「オゼンピック皮下注 0.25mg SD、0.5mg SD、1.0mg SD」が承認され、発売されている。またセマグルチドの経口製剤として、2020 年 6 月に「リベルサス錠」が 2 型糖尿病を効能又は効果として日本において承認され、発売されている。

肥満症のためのセマグルチド 2.4 mg の皮下投与製剤は、2021 年 6 月に米国で上市された。

2.7.4.7　付録

本概要に対する付録は、付録 2.7.4.7.1～付録 2.7.4.7.2 として添付した。

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ウゴービ皮下注 0.25mg SD
ウゴービ皮下注 0.5mg SD
ウゴービ皮下注 1.0mg SD
ウゴービ皮下注 1.7mg SD
ウゴービ皮下注 2.4mg SD

2.7.4.7 付録
1.膵炎及び生殖能に関連する障害
（4373 及び 4374 試験）

ノボ ノルディスク ファーマ株式会社

1 Pancreatitis adverse events - pre-defined MedDRA search - overview - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R
Number of subjects	1306				655			
Patient years of exposure (PYE)	1706.1				829.6			
Patient years of observation (PYO)	1856.4				918.5			
Adverse Events (OT)	2	(0.2)	2	0.1	0			
Adverse Events (IT)	2	(0.2)	4	0.2	0			
Serious								
Yes (OT)	2	(0.2)	2	0.1	0			
Yes (IT)	2	(0.2)	4	0.2	0			
No (OT)	0				0			
No (IT)	0				0			
Severity								
Severe (OT)	0				0			
Severe (IT)	0				0			
Moderate (OT)	1	(0.1)	1	0.1	0			
Moderate (IT)	1	(0.1)	3	0.2	0			
Mild (OT)	1	(0.1)	1	0.1	0			
Mild (IT)	1	(0.1)	1	0.1	0			
Relationship to trial product								
Probable (OT)	0				0			
Probable (IT)	0				0			
Possible (OT)	1	(0.1)	1	0.1	0			
Possible (IT)	1	(0.1)	2	0.1	0			
Unlikely (OT)	1	(0.1)	1	0.1	0			
Unlikely (IT)	2	(0.2)	2	0.1	0			
Missing (OT)	0				0			
Missing (IT)	0				0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years, PYO: The duration of the in-trial period in years, PYE: The duration of the on-treatment period in years, OT: On-treatment, IT: In-trial.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Pancreatitis adverse events - pre-defined MedDRA search - overview - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
	N	(%)	E	R	N	(%)	E	R
Outcome								
Fatal (OT)	0				0			
Fatal (IT)	0				0			
Recovered (OT)	2	(0.2)	2	0.1	0			
Recovered (IT)	2	(0.2)	4	0.2	0			
Recovering (OT)	0				0			
Recovering (IT)	0				0			
Recovered With Sequelae (OT)	0				0			
Recovered With Sequelae (IT)	0				0			
Not Recovered (OT)	0				0			
Not Recovered (IT)	0				0			
Unknown (OT)	0				0			
Unknown (IT)	0				0			
Leading to								
Permanent treatment discontinuation (OT)	1	(0.1)	1	0.1	0			
Permanent treatment discontinuation (IT)	1	(0.1)	1	0.1	0			
Temporary interruption of trial product (OT)	0				0			
Temporary interruption of trial product (IT)	0				0			
Dose reduction of trial product (OT)	0				0			
Dose reduction of trial product (IT)	0				0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years, PYO: The duration of the in-trial period in years, PYE: The duration of the on-treatment period in years, OT: On-treatment, IT: In-trial.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

2 Pancreatitis adverse events by system organ class and preferred term - pre-defined MedDRA search - summary - on-treatment - safety analysis set - STEP 1

System organ class Preferred term	Sema 2.4 mg N	(%)	E	R	Placebo N	(%)	E	R
Number of subjects	1306				655			
Patient years of exposure (PYE)	1706.1				829.6			
Events	2	(0.2)	2	0.1	0			
Gastrointestinal disorders	2	(0.2)	2	0.1	0			
Pancreatitis acute	2	(0.2)	2	0.1	0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years, PYE: The duration of the on-treatment period in years.
Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. Sorted in descending order by system organ class and preferred term based, respectively, on the percentage of subjects in the Sema 2.4 mg arm experiencing at least one event.
MedDRA version 22.1

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3 Pancreatitis adverse events - pre-defined MedDRA search - overview - safety analysis set - STEP 1 Japanese population

There are no data for this table

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4 Pancreatitis adverse events by system organ class and preferred term - pre-defined MedDRA search - summary - on-treatment - safety analysis set - STEP 1 Japanese population

There are no data for this table

5 Pancreatitis adverse events - pre-defined MedDRA search - overview - safety analysis set - STEP 2

	Sema 1.0 mg N	(%)	E	R	Sema 2.4 mg N	(%)	E	R	Placebo N	(%)	E	R
Number of subjects	402				403				402			
Patient years of exposure (PYE)	529.8				533.0				528.3			
Patient years of observation (PYO)	569.1				572.8				566.6			
Adverse Events (OT)	0				1	(0.2)	1	0.2	1	(0.2)	1	0.2
Adverse Events (IT)	0				1	(0.2)	4	0.7	1	(0.2)	1	0.2
Serious												
Yes (OT)	0				0				1	(0.2)	1	0.2
Yes (IT)	0				1	(0.2)	1	0.2	1	(0.2)	1	0.2
No (OT)	0				1	(0.2)	1	0.2	0			
No (IT)	0				1	(0.2)	3	0.5	0			
Severity												
Severe (OT)	0				0				0			
Severe (IT)	0				0				0			
Moderate (OT)	0				1	(0.2)	1	0.2	1	(0.2)	1	0.2
Moderate (IT)	0				1	(0.2)	2	0.3	1	(0.2)	1	0.2
Mild (OT)	0				0				0			
Mild (IT)	0				1	(0.2)	2	0.3	0			
Relationship to trial product												
Probable (OT)	0				1	(0.2)	1	0.2	0			
Probable (IT)	0				1	(0.2)	4	0.7	0			
Possible (OT)	0				0				0			
Possible (IT)	0				0				0			
Unlikely (OT)	0				0				1	(0.2)	1	0.2
Unlikely (IT)	0				0				1	(0.2)	1	0.2
Missing (OT)	0				0				0			
Missing (IT)	0				0				0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years, PYO: The duration of the in-trial period in years, PYE: The duration of the on-treatment period in years, OT: On-treatment, IT: In-trial.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Pancreatitis adverse events - pre-defined MedDRA search - overview - safety analysis set - STEP 2

	Sema 1.0 mg N	(%)	E	R	Sema 2.4 mg N	(%)	E	R	Placebo N	(%)	E	R
Outcome												
Fatal (OT)	0				0				0			
Fatal (IT)	0				0				0			
Recovered (OT)	0				0				1	(0.2)	1	0.2
Recovered (IT)	0				0				1	(0.2)	1	0.2
Recovering (OT)	0				0				0			
Recovering (IT)	0				0				0			
Recovered With Sequelae (OT)	0				1	(0.2)	1	0.2	0			
Recovered With Sequelae (IT)	0				1	(0.2)	1	0.2	0			
Not Recovered (OT)	0				0				0			
Not Recovered (IT)	0				1	(0.2)	3	0.5	0			
Unknown (OT)	0				0				0			
Unknown (IT)	0				0				0			
Leading to												
Permanent treatment discontinuation (OT)	0				1	(0.2)	1	0.2	0			
Permanent treatment discontinuation (IT)	0				1	(0.2)	1	0.2	0			
Temporary interruption of trial product (OT)	0				0				0			
Temporary interruption of trial product (IT)	0				0				0			
Dose reduction of trial product (OT)	0				0				0			
Dose reduction of trial product (IT)	0				0				0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years, PYO: The duration of the in-trial period in years, PYE: The duration of the on-treatment period in years, OT: On-treatment, IT: In-trial.
On-treatment adverse events have onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

6 Pancreatitis adverse events by system organ class and preferred term - pre-defined MedDRA search - summary - on-treatment - safety analysis set - STEP 2

System organ class Preferred term	Sema 1.0 mg N	(%)	E	R	Sema 2.4 mg N	(%)	E	R	Placebo N	(%)	E	R
Number of subjects	402				403				402			
Patient years of exposure (PYE)	529.8				533.0				528.3			
Events	0				1	(0.2)	1	0.2	1	(0.2)	1	0.2
Gastrointestinal disorders	0				1	(0.2)	1	0.2	1	(0.2)	1	0.2
Obstructive pancreatitis	0				0				1	(0.2)	1	0.2
Pancreatitis acute	0				1	(0.2)	1	0.2	0			

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years, PYE: The duration of the on-treatment period in years.
Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. Sorted in descending order by system organ class and preferred term based, respectively, on the percentage of subjects in the Sema 2.4 mg arm experiencing at least one event.
MedDRA version 22.1

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7 Pancreatitis adverse events - pre-defined MedDRA search - overview - safety analysis set - STEP 2 Japanese population

There are no data for this table

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8 Pancreatitis adverse events by system organ class and preferred term - pre-defined MedDRA search - summary - on-treatment - safety analysis set - STEP 2 Japanese population

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There are no data for this table

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9 Fertility disorders adverse events by system organ class and preferred term - pre-defined MedDRA search - summary - on-treatment - safety analysis set - STEP 1

System organ class Preferred term	Sema 2.4 mg N	(%)	E	R	Placebo N	(%)	E	R
Number of subjects	1306				655			
Patient years of exposure (PYE)	1706.1				829.6			
Events	4	(0.3)	4	0.2	3	(0.5)	3	0.4
Reproductive system and breast disorders	4	(0.3)	4	0.2	2	(0.3)	2	0.2
Dysfunctional uterine bleeding	3	(0.2)	3	0.2	0			
Polycystic ovaries	1	(<0.1)	1	<0.1	1	(0.2)	1	0.1
Testicular disorder	0				1	(0.2)	1	0.1
Endocrine disorders	0				1	(0.2)	1	0.1
Hypogonadism	0				1	(0.2)	1	0.1

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years, PYE: The duration of the on-treatment period in years.
Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. Sorted in descending order by system organ class and preferred term based, respectively, on the percentage of subjects in the Sema 2.4 mg arm experiencing at least one event.
MedDRA version 22.1

10 Fertility disorders adverse events by system organ class and preferred term - pre-defined MedDRA search - summary - on-treatment - safety analysis set - STEP 2

System organ class Preferred term	Sema 1.0 mg N	(%)	E	R	Sema 2.4 mg N	(%)	E	R	Placebo N	(%)	E	R
Number of subjects	402				403				402			
Patient years of exposure (PYE)	529.8				533.0				528.3			
Events	0				0				2	(0.5)	2	0.4
Reproductive system and breast disorders	0				0				1	(0.2)	1	0.2
Testicular disorder	0				0				1	(0.2)	1	0.2
Surgical and medical procedures	0				0				1	(0.2)	1	0.2
Sperm aspiration	0				0				1	(0.2)	1	0.2

N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 years, PYE: The duration of the on-treatment period in years.
Adverse events with onset date during on-treatment period. A time-point is considered as on-treatment if any dose of trial product has been administered within the prior 49 days. Sorted in descending order by system organ class and preferred term based, respectively, on the percentage of subjects in the Sema 2.4 mg arm experiencing at least one event.
MedDRA version 22.1

ウゴーヒ皮下注 0.25mg SD
ウゴーヒ皮下注 0.5mg SD
ウゴーヒ皮下注 1.0mg SD
ウゴーヒ皮下注 1.7mg SD
ウゴーヒ皮下注 2.4mg SD

2.7.4.7 付録
2.ベースラインの被験者背景及び疾患特性に基づくサブグループ別の安全性データ
（4373、4374 及び 4382 試験）

ノボ ノルディスク ファーマ株式会社

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1 Adverse events by sex - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
Female	955	1240.8			498	624.7		
Male	351	465.3			157	204.9		
Subjects with events	N	(%)	E	R	N	(%)	E	R
Events								
Female	866	(90.7)	7607	613.1	431	(86.5)	2723	435.9
Male	305	(86.9)	2051	440.8	135	(86.0)	579	282.6
Serious								
Yes								
Female	95	(9.9)	124	10.0	30	(6.0)	41	6.6
Male	33	(9.4)	40	8.6	12	(7.6)	12	5.9
No								
Female	864	(90.5)	7483	603.1	427	(85.7)	2682	429.4
Male	305	(86.9)	2011	432.2	133	(84.7)	567	276.7
Severity								
Severe								
Female	112	(11.7)	189	15.2	36	(7.2)	59	9.4
Male	31	(8.8)	53	11.4	8	(5.1)	9	4.4
Moderate								
Female	557	(58.3)	2072	167.0	255	(51.2)	717	114.8
Male	166	(47.3)	540	116.1	56	(35.7)	146	71.3
Mild								
Female	793	(83.0)	5346	430.9	389	(78.1)	1947	311.7
Male	286	(81.5)	1458	313.3	118	(75.2)	424	206.9

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by sex - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Relationship to trial product								
Missing								
Female	20	(2.1)	26	2.1	4	(0.8)	4	0.6
Male	4	(1.1)	4	0.9	3	(1.9)	4	2.0
Probable								
Female	432	(45.2)	1693	136.4	124	(24.9)	281	45.0
Male	139	(39.6)	455	97.8	23	(14.6)	49	23.9
Possible								
Female	550	(57.6)	2125	171.3	188	(37.8)	487	78.0
Male	176	(50.1)	575	123.6	35	(22.3)	68	33.2
Unlikely								
Female	773	(80.9)	3763	303.3	410	(82.3)	1951	312.3
Male	259	(73.8)	1017	218.6	126	(80.3)	458	223.5
Outcome								
Fatal								
Female	0				1	(0.2)	1	0.2
Male	0				0			
Recovered								
Female	849	(88.9)	6665	537.2	418	(83.9)	2249	360.0
Male	291	(82.9)	1774	381.3	127	(80.9)	461	225.0
Recovering								
Female	48	(5.0)	73	5.9	22	(4.4)	34	5.4
Male	11	(3.1)	18	3.9	3	(1.9)	3	1.5
Recovered With Sequelae								
Female	7	(0.7)	11	0.9	3	(0.6)	3	0.5
Male	4	(1.1)	8	1.7	1	(0.6)	2	1.0
Not Recovered								
Female	377	(39.5)	855	68.9	205	(41.2)	436	69.8

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by sex - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Outcome								
Not Recovered								
Male	136	(38.7)	251	53.9	60	(38.2)	112	54.7
Unknown								
Female	2	(0.2)	3	0.2	0			
Male	0				1	(0.6)	1	0.5
Leading to								
Permanent treatment discontinuation								
Female	73	(7.6)	98	7.9	16	(3.2)	19	3.0
Male	19	(5.4)	25	5.4	4	(2.5)	4	2.0
Temporary interruption of trial product								
Female	99	(10.4)	193	15.6	19	(3.8)	34	5.4
Male	27	(7.7)	72	15.5	7	(4.5)	10	4.9
Dose reduction of trial product								
Female	92	(9.6)	170	13.7	4	(0.8)	9	1.4
Male	32	(9.1)	55	11.8	0			

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

2 Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
Female	955	1240.8			498	624.7		
Male	351	465.3			157	204.9		
Subjects with events	N	(%)	E	R	N	(%)	E	R
Adverse events								
Female	866	(90.7)	7607	613.1	431	(86.5)	2723	435.9
Male	305	(86.9)	2051	440.8	135	(86.0)	579	282.6
Gastrointestinal disorders								
Female	731	(76.5)	3395	273.6	264	(53.0)	646	103.4
Male	238	(67.8)	914	196.4	50	(31.8)	93	45.4
Gastrointestinal signs and symptoms								
Female	638	(66.8)	2210	178.1	176	(35.3)	354	56.7
Male	186	(53.0)	504	108.3	25	(15.9)	41	20.0
Nausea								
Female	473	(49.5)	898	72.4	103	(20.7)	133	21.3
Male	104	(29.6)	170	36.5	11	(7.0)	13	6.3
Vomiting								
Female	266	(27.9)	540	43.5	41	(8.2)	50	8.0
Male	58	(16.5)	96	20.6	2	(1.3)	2	1.0
Dyspepsia								
Female	100	(10.5)	139	11.2	19	(3.8)	26	4.2
Male	35	(10.0)	40	8.6	4	(2.5)	4	2.0
Abdominal pain								
Female	104	(10.9)	132	10.6	33	(6.6)	38	6.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	26 (7.4)	43	9.2	3 (1.9)	3	1.5
Abdominal pain upper						
Female	108 (11.3)	147	11.8	32 (6.4)	34	5.4
Male	17 (4.8)	29	6.2	3 (1.9)	3	1.5
Eructation						
Female	90 (9.4)	110	8.9	3 (0.6)	3	0.5
Male	22 (6.3)	29	6.2	0		
Abdominal distension						
Female	75 (7.9)	104	8.4	28 (5.6)	37	5.9
Male	21 (6.0)	31	6.7	3 (1.9)	5	2.4
Flatulence						
Female	42 (4.4)	50	4.0	14 (2.8)	15	2.4
Male	23 (6.6)	34	7.3	7 (4.5)	7	3.4
Abdominal discomfort						
Female	42 (4.4)	58	4.7	8 (1.6)	8	1.3
Male	14 (4.0)	21	4.5	1 (0.6)	1	0.5
Abdominal pain lower						
Female	10 (1.0)	10	0.8	4 (0.8)	4	0.6
Male	2 (0.6)	2	0.4	0		
Gastrointestinal sounds abnormal						
Female	0			0		
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Epigastric discomfort						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	0		
Faeces soft						
Female	2 (0.2)	3	0.2	4 (0.8)	4	0.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Gastrointestinal pain						
Female	2 (0.2)	3	0.2	0		
Male	1 (0.3)	1	0.2	0		
Regurgitation						
Female	2 (0.2)	3	0.2	0		
Male	1 (0.3)	1	0.2	0		
Breath odour						
Female	1 (0.1)	2	0.2	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Aerophagia						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Faeces hard						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Dysphagia						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Faeces discoloured						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Retching						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Abdominal tenderness						
Female	1 (0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Male	0				0			
Abnormal faeces								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Oesophageal pain								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Gastrointestinal motility and defaecation conditions								
Female	473	(49.5)	952	76.7	144	(28.9)	212	33.9
Male	153	(43.6)	319	68.6	22	(14.0)	27	13.2
Diarrhoea								
Female	306	(32.0)	563	45.4	93	(18.7)	124	19.9
Male	106	(30.2)	203	43.6	11	(7.0)	14	6.8
Constipation								
Female	244	(25.5)	311	25.1	55	(11.0)	66	10.6
Male	62	(17.7)	79	17.0	7	(4.5)	7	3.4
Gastrooesophageal reflux disease								
Female	57	(6.0)	64	5.2	15	(3.0)	16	2.6
Male	25	(7.1)	28	6.0	5	(3.2)	5	2.4
Irritable bowel syndrome								
Female	4	(0.4)	4	0.3	1	(0.2)	2	0.3
Male	2	(0.6)	3	0.6	0			
Frequent bowel movements								
Female	4	(0.4)	4	0.3	3	(0.6)	3	0.5
Male	1	(0.3)	1	0.2	0			
Dyschezia								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Change of bowel habit						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Defaecation urgency						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Infrequent bowel movements						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Oesophageal achalasia						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Impaired gastric emptying						
Female	2 (0.2)	2	0.2	0		
Male	0			1 (0.6)	1	0.5
Bowel movement irregularity						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Gastrointestinal hypermotility						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Gastrointestinal motility disorder						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Gastrointestinal inflammatory conditions						
Female	45 (4.7)	62	5.0	11 (2.2)	12	1.9
Male	26 (7.4)	32	6.9	1 (0.6)	1	0.5
Gastritis						
Female	32 (3.4)	45	3.6	6 (1.2)	7	1.1
Male	18 (5.1)	22	4.7	0		
Colitis						
Female	5 (0.5)	6	0.5	0		
Male	2 (0.6)	3	0.6	1 (0.6)	1	0.5
Reflux gastritis						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	0		
Chronic gastritis						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	0		
Duodenitis						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Gastrointestinal inflammation						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Crohn's disease						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Gastroenteritis eosinophilic						
Female	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	1 (0.3)	1	0.2	0		
Enteritis						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Oesophagitis						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Colitis ischaemic						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Eosinophilic oesophagitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Epiploic appendagitis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Inflammatory bowel disease						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Gastrointestinal conditions NEC						
Female	35 (3.7)	44	3.5	7 (1.4)	10	1.6
Male	13 (3.7)	23	4.9	5 (3.2)	6	2.9
Hyperchlorhydria						
Female	13 (1.4)	20	1.6	2 (0.4)	3	0.5
Male	7 (2.0)	17	3.7	1 (0.6)	2	1.0
Food poisoning						
Female	15 (1.6)	15	1.2	2 (0.4)	4	0.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	3 (0.9)	3	0.6	2 (1.3)	2	1.0
Gastrointestinal disorder						
Female	4 (0.4)	6	0.5	3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Anal fistula						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Barrett's oesophagus						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Functional gastrointestinal disorder						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Gastric mucosal hypertrophy						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Gastrointestinal vascular conditions						
Female	21 (2.2)	22	1.8	5 (1.0)	5	0.8
Male	7 (2.0)	8	1.7	0		
Haemorrhoids						
Female	20 (2.1)	21	1.7	3 (0.6)	3	0.5
Male	6 (1.7)	6	1.3	0		
Haemorrhoidal haemorrhage						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	2	0.4	0		
Haemorrhoids thrombosed						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Salivary gland conditions						
Female	20 (2.1)	20	1.6	7 (1.4)	8	1.3
Male	7 (2.0)	7	1.5	1 (0.6)	1	0.5
Dry mouth						
Female	18 (1.9)	18	1.5	6 (1.2)	7	1.1
Male	7 (2.0)	7	1.5	1 (0.6)	1	0.5
Salivary gland calculus						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Salivary gland cyst						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Salivary gland enlargement						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Dental and gingival conditions						
Female	22 (2.3)	25	2.0	21 (4.2)	24	3.8
Male	5 (1.4)	7	1.5	8 (5.1)	8	3.9
Toothache						
Female	15 (1.6)	16	1.3	13 (2.6)	14	2.2
Male	2 (0.6)	4	0.9	4 (2.5)	4	2.0
Dental caries						
Female	2 (0.2)	3	0.2	7 (1.4)	7	1.1
Male	2 (0.6)	2	0.4	3 (1.9)	3	1.5
Periodontal disease						
Female	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	1 (0.3)	1	0.2	0		
Gingival bleeding						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Gingival disorder						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Gingival pain						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Noninfective gingivitis						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Tooth impacted						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Tooth loss						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Dental necrosis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Dental pulp disorder						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Tooth disorder						
Female	0			1 (0.2)	1	0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Gastrointestinal haemorrhages NEC						
Female	12 (1.3)	12	1.0	2 (0.4)	3	0.5
Male	3 (0.9)	4	0.9	4 (2.5)	4	2.0
Rectal haemorrhage						
Female	5 (0.5)	5	0.4	1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	0		
Haematochezia						
Female	6 (0.6)	6	0.5	1 (0.2)	2	0.3
Male	1 (0.3)	1	0.2	2 (1.3)	2	1.0
Haematemesis						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Lower gastrointestinal haemorrhage						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Melaena						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Upper gastrointestinal haemorrhage						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Benign neoplasms gastrointestinal						
Female	7 (0.7)	7	0.6	4 (0.8)	4	0.6
Male	3 (0.9)	3	0.6	1 (0.6)	1	0.5
Large intestine polyp						
Female	6 (0.6)	6	0.5	3 (0.6)	3	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	3 (0.9)	3	0.6	1 (0.6)	1	0.5
Gastric polyps						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Oral soft tissue conditions						
Female	6 (0.6)	7	0.6	5 (1.0)	5	0.8
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Lip swelling						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Odynophagia						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Aphthous ulcer						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Cheilitis						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			0		
Lip disorder						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Mouth ulceration						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Paraesthesia oral						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Stomatitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Oral mucosal eruption						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Abdominal hernias and other abdominal wall conditions						
Female	8 (0.8)	9	0.7	3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Hiatus hernia						
Female	7 (0.7)	8	0.6	1 (0.2)	1	0.2
Male	0			0		
Abdominal hernia						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Umbilical hernia						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Diverticular disorders						
Female	5 (0.5)	5	0.4	4 (0.8)	4	0.6
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Diverticulum						
Female	5 (0.5)	5	0.4	4 (0.8)	4	0.6
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Anal and rectal conditions NEC						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	7 (0.7)	9	0.7	0		
Male	0			0		
Anal fissure						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Proctalgia						
Female	2 (0.2)	3	0.2	0		
Male	0			0		
Anal pruritus						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Anorectal discomfort						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Rectal fissure						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Gastrointestinal ulceration and perforation						
Female	4 (0.4)	4	0.3	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Peptic ulcer						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Duodenal ulcer						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Gastric ulcer						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Large intestine perforation						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Oesophageal ulcer						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Exocrine pancreas conditions						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Pancreatitis acute						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Gastrointestinal stenosis and obstruction						
Female	3 (0.3)	3	0.2	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Ileus						
Female	1 (0.1)	1	<0.1	0		
Male	0			1 (0.6)	1	0.5
Oesophageal stenosis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Volvulus						
Female	1 (0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Male	0				0			
Intestinal obstruction								
Female	0				1	(0.2)	1	0.2
Male	0				0			
Malabsorption conditions								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Coeliac disease								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Peritoneal and retroperitoneal conditions								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Pneumoperitoneum								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Tongue conditions								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Glossodynia								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Infections and infestations								
Female	548	(57.4)	1291	104.0	293	(58.8)	658	105.3
Male	166	(47.3)	324	69.6	79	(50.3)	144	70.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Infections - pathogen unspecified						
Female	491 (51.4)	1005	81.0	248 (49.8)	512	82.0
Male	135 (38.5)	242	52.0	66 (42.0)	98	47.8
Nasopharyngitis						
Female	213 (22.3)	377	30.4	107 (21.5)	184	29.5
Male	68 (19.4)	103	22.1	26 (16.6)	32	15.6
Upper respiratory tract infection						
Female	93 (9.7)	129	10.4	66 (13.3)	98	15.7
Male	21 (6.0)	29	6.2	14 (8.9)	18	8.8
Gastroenteritis						
Female	63 (6.6)	76	6.1	25 (5.0)	32	5.1
Male	22 (6.3)	28	6.0	5 (3.2)	6	2.9
Sinusitis						
Female	57 (6.0)	67	5.4	34 (6.8)	38	6.1
Male	14 (4.0)	17	3.7	2 (1.3)	2	1.0
Urinary tract infection						
Female	64 (6.7)	79	6.4	26 (5.2)	32	5.1
Male	4 (1.1)	4	0.9	2 (1.3)	2	1.0
Bronchitis						
Female	37 (3.9)	41	3.3	19 (3.8)	21	3.4
Male	10 (2.8)	11	2.4	6 (3.8)	7	3.4
Rhinitis						
Female	15 (1.6)	20	1.6	5 (1.0)	8	1.3
Male	4 (1.1)	5	1.1	4 (2.5)	6	2.9
Pharyngitis						
Female	8 (0.8)	8	0.6	6 (1.2)	6	1.0
Male	5 (1.4)	5	1.1	3 (1.9)	3	1.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Cystitis						
Female	19 (2.0)	21	1.7	3 (0.6)	3	0.5
Male	0			0		
Acute sinusitis						
Female	8 (0.8)	9	0.7	6 (1.2)	6	1.0
Male	3 (0.9)	3	0.6	2 (1.3)	3	1.5
Laryngitis						
Female	13 (1.4)	13	1.0	4 (0.8)	5	0.8
Male	1 (0.3)	1	0.2	0		
Tonsillitis						
Female	10 (1.0)	13	1.0	6 (1.2)	8	1.3
Male	2 (0.6)	2	0.4	4 (2.5)	4	2.0
Tooth infection						
Female	9 (0.9)	10	0.8	4 (0.8)	4	0.6
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Pneumonia						
Female	10 (1.0)	12	1.0	6 (1.2)	6	1.0
Male	1 (0.3)	2	0.4	2 (1.3)	2	1.0
Tooth abscess						
Female	6 (0.6)	6	0.5	7 (1.4)	8	1.3
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Vaginal infection						
Female	11 (1.2)	13	1.0	0		
Male	0			0		
Ear infection						
Female	8 (0.8)	10	0.8	3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Eye infection						
Female	2 (0.2)	2	0.2	0		
Male	3 (0.9)	3	0.6	0		
Lower respiratory tract infection						
Female	9 (0.9)	10	0.8	12 (2.4)	16	2.6
Male	0			0		
Conjunctivitis						
Female	6 (0.6)	6	0.5	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	2 (1.3)	2	1.0
Otitis media						
Female	5 (0.5)	5	0.4	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Folliculitis						
Female	4 (0.4)	4	0.3	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Gastrointestinal infection						
Female	4 (0.4)	6	0.5	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Pulpitis dental						
Female	4 (0.4)	4	0.3	0		
Male	1 (0.3)	1	0.2	0		
Chronic sinusitis						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	0		
Abdominal wall abscess						
Female	0			0		
Male	2 (0.6)	2	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Appendicitis						
Female	5 (0.5)	5	0.4	0		
Male	0			1 (0.6)	1	0.5
Infected bite						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Pharyngotonsillitis						
Female	2 (0.2)	2	0.2	1 (0.2)	2	0.3
Male	1 (0.3)	1	0.2	0		
Subcutaneous abscess						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	0		
Atypical pneumonia						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Infection						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Omphalitis						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Otitis externa						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Breast abscess						
Female	3 (0.3)	3	0.2	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Gingivitis						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Hordeolum						
Female	3 (0.3)	3	0.2	0		
Male	0			1 (0.6)	1	0.5
Kidney infection						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Pyelonephritis						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Device related infection						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Diverticulitis						
Female	0			2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	0		
Epididymitis						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Osteomyelitis						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Perirectal abscess						
Female	0			0		
Male	1 (0.3)	2	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Prostate infection						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Skin infection						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Abscess						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Diarrhoea infectious						
Female	2 (0.2)	2	0.2	1 (0.2)	2	0.3
Male	0			0		
Localised infection						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Periodontitis						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Postoperative wound infection						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Abdominal abscess						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Abscess limb						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Appendicitis perforated						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Bartholinitis						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Carbuncle						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Endometritis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Eyelid infection						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Fracture infection						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Groin abscess						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Haematoma infection						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Large intestine infection						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Mastitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Nail infection						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Oophoritis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Oral infection						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Parasitic gastroenteritis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Paronychia						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Parotitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Peritonitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Purulence						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Respiratory tract infection						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Salpingitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Sepsis syndrome						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Arthritis infective						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Cervicitis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Empyema						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Gastric infection						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Infected dermal cyst						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Lymphangitis						
Female	0			1 (0.2)	1	0.2
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Neutropenic sepsis								
Female	0				1	(0.2)	1	0.2
Male	0				0			
Otitis media acute								
Female	0				1	(0.2)	1	0.2
Male	0				0			
Peritonsillar abscess								
Female	0				1	(0.2)	1	0.2
Male	0				0			
Peritonsillitis								
Female	0				0			
Male	0				1	(0.6)	1	0.5
Root canal infection								
Female	0				2	(0.4)	2	0.3
Male	0				0			
Septic shock								
Female	0				1	(0.2)	1	0.2
Male	0				0			
Tracheitis								
Female	0				1	(0.2)	1	0.2
Male	0				0			
Wound infection								
Female	0				0			
Male	0				1	(0.6)	1	0.5
Viral infectious disorders								
Female	149	(15.6)	192	15.5	82	(16.5)	105	16.8
Male	45	(12.8)	56	12.0	21	(13.4)	31	15.1

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Influenza						
Female	65 (6.8)	80	6.4	47 (9.4)	55	8.8
Male	24 (6.8)	32	6.9	16 (10.2)	24	11.7
Gastroenteritis viral						
Female	31 (3.2)	33	2.7	12 (2.4)	13	2.1
Male	11 (3.1)	11	2.4	2 (1.3)	2	1.0
Viral infection						
Female	12 (1.3)	18	1.5	6 (1.2)	6	1.0
Male	2 (0.6)	2	0.4	2 (1.3)	2	1.0
Herpes zoster						
Female	9 (0.9)	10	0.8	10 (2.0)	10	1.6
Male	3 (0.9)	3	0.6	1 (0.6)	1	0.5
Gastrointestinal viral infection						
Female	6 (0.6)	6	0.5	1 (0.2)	1	0.2
Male	2 (0.6)	3	0.6	0		
Viral upper respiratory tract infection						
Female	6 (0.6)	6	0.5	4 (0.8)	5	0.8
Male	1 (0.3)	1	0.2	0		
Ear infection viral						
Female	4 (0.4)	4	0.3	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Gastroenteritis norovirus						
Female	5 (0.5)	6	0.5	0		
Male	0			0		
Viral pharyngitis						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2

Adverse events with onset prior to randomisation are not included.
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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	1 (0.3)	1	0.2	0		
Herpes simplex						
Female	4 (0.4)	4	0.3	2 (0.4)	2	0.3
Male	0			0		
Oral herpes						
Female	4 (0.4)	5	0.4	1 (0.2)	1	0.2
Male	0			0		
Dengue fever						
Female	3 (0.3)	3	0.2	2 (0.4)	2	0.3
Male	0			0		
Parainfluenzae virus infection						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Varicella						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Herpes virus infection						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Respiratory tract infection viral						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Chronic hepatitis B						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Cytomegalovirus infection						
Female	1 (0.1)	1	<0.1	0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Gastroenteritis astroviral						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Genital herpes zoster						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Hepatitis E						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Infectious mononucleosis						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Oral viral infection						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Papilloma viral infection						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Respiratory syncytial virus infection						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Vestibular neuronitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Viral sinusitis						

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Bronchitis viral						
Female	0			1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Conjunctivitis viral						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Hand-foot-and-mouth disease						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Meningitis viral						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Viral rhinitis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Bacterial infectious disorders						
Female	43 (4.5)	48	3.9	21 (4.2)	22	3.5
Male	14 (4.0)	15	3.2	6 (3.8)	9	4.4
Pharyngitis streptococcal						
Female	8 (0.8)	8	0.6	6 (1.2)	6	1.0
Male	3 (0.9)	3	0.6	0		
Cellulitis						
Female	5 (0.5)	5	0.4	3 (0.6)	4	0.6
Male	4 (1.1)	4	0.9	4 (2.5)	4	2.0
Helicobacter infection						

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	4 (0.4)	4	0.3	2 (0.4)	2	0.3
Male	2 (0.6)	2	0.4	0		
Erysipelas						
Female	1 (0.1)	1	<0.1	0		
Male	2 (0.6)	2	0.4	0		
Staphylococcal infection						
Female	1 (0.1)	1	<0.1	0		
Male	2 (0.6)	2	0.4	2 (1.3)	2	1.0
Ear infection bacterial						
Female	6 (0.6)	6	0.5	2 (0.4)	2	0.3
Male	0			0		
Bacterial vaginosis						
Female	5 (0.5)	8	0.6	2 (0.4)	2	0.3
Male	0			0		
Furuncle						
Female	3 (0.3)	4	0.3	1 (0.2)	1	0.2
Male	0			0		
Bacterial colitis						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Syphilis						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Helicobacter gastritis						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Bacterial vulvovaginitis						

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Genital infection bacterial						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Lyme disease						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Pharyngitis bacterial						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Salmonellosis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Sinusitis bacterial						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Skin bacterial infection						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Tonsillitis bacterial						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Typhoid fever						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Bacteriuria						

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	0			1 (0.2)	1	0.2
Male	0			0		
Gastric ulcer helicobacter						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Listeriosis						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Staphylococcal sepsis						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Streptococcal urinary tract infection						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Upper respiratory tract infection bacterial						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Fungal infectious disorders						
Female	35 (3.7)	43	3.5	17 (3.4)	18	2.9
Male	10 (2.8)	10	2.1	5 (3.2)	6	2.9
Vulvovaginal mycotic infection						
Female	11 (1.2)	13	1.0	2 (0.4)	2	0.3
Male	0			0		
Fungal infection						
Female	10 (1.0)	11	0.9	5 (1.0)	5	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Tinea pedis						
Female	4 (0.4)	4	0.3	1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	0		
Dermatophytosis						
Female	0			0		
Male	2 (0.6)	2	0.4	0		
Vulvovaginal candidiasis						
Female	5 (0.5)	8	0.6	3 (0.6)	3	0.5
Male	0			0		
Body tinea						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Fungal skin infection						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Onychomycosis						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	3 (1.9)	4	2.0
Skin candida						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Candida infection						
Female	0			2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	0		
Tinea cruris						
Female	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	1 (0.3)	1	0.2	0		
Dermatophytosis of nail						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Tinea capitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Tinea infection						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Oral candidiasis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Otitis externa fungal						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Ectoparasitic disorders						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Acarodermatitis						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Protozoal infectious disorders						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Trichomoniasis						
Female	2 (0.2)	2	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Male	0				0			
Toxoplasmosis								
Female	0				1	(0.2)	1	0.2
Male	0				0			
Chlamydial infectious disorders								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Chlamydial infection								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Nervous system disorders								
Female	301	(31.5)	610	49.2	114	(22.9)	183	29.3
Male	90	(25.6)	148	31.8	27	(17.2)	39	19.0
Headaches								
Female	189	(19.8)	382	30.8	75	(15.1)	100	16.0
Male	40	(11.4)	69	14.8	14	(8.9)	18	8.8
Headache								
Female	164	(17.2)	326	26.3	67	(13.5)	88	14.1
Male	34	(9.7)	61	13.1	13	(8.3)	16	7.8
Migraine								
Female	28	(2.9)	47	3.8	8	(1.6)	10	1.6
Male	4	(1.1)	5	1.1	1	(0.6)	1	0.5
Migraine with aura								
Female	0				1	(0.2)	1	0.2
Male	2	(0.6)	2	0.4	0			
Sinus headache								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	5 (0.5)	5	0.4	1 (0.2)	1	0.2
Male	0			0		
Tension headache						
Female	4 (0.4)	4	0.3	0		
Male	0			1 (0.6)	1	0.5
Occipital neuralgia						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Neurological disorders NEC						
Female	132 (13.8)	182	14.7	38 (7.6)	57	9.1
Male	49 (14.0)	66	14.2	9 (5.7)	11	5.4
Dizziness						
Female	73 (7.6)	95	7.7	18 (3.6)	28	4.5
Male	25 (7.1)	35	7.5	5 (3.2)	7	3.4
Dysgeusia						
Female	12 (1.3)	15	1.2	4 (0.8)	11	1.8
Male	6 (1.7)	9	1.9	0		
Paraesthesia						
Female	9 (0.9)	12	1.0	3 (0.6)	3	0.5
Male	4 (1.1)	5	1.1	2 (1.3)	2	1.0
Syncope						
Female	8 (0.8)	8	0.6	1 (0.2)	1	0.2
Male	3 (0.9)	3	0.6	1 (0.6)	1	0.5
Hypoaesthesia						
Female	3 (0.3)	3	0.2	2 (0.4)	2	0.3
Male	4 (1.1)	4	0.9	0		
Lethargy						

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	4 (0.4)	4	0.3	3 (0.6)	3	0.5
Male	3 (0.9)	3	0.6	0		
Somnolence						
Female	4 (0.4)	6	0.5	1 (0.2)	1	0.2
Male	3 (0.9)	3	0.6	0		
Taste disorder						
Female	9 (0.9)	11	0.9	1 (0.2)	1	0.2
Male	0			0		
Neuralgia						
Female	3 (0.3)	3	0.2	1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Hyperaesthesia						
Female	4 (0.4)	6	0.5	0		
Male	0			0		
Burning sensation						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Dizziness postural						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Dysaesthesia						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Allodynia						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Balance disorder						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Presyncope						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Ageusia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Aphasia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Dysarthria						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Hyporeflexia						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			0		
Loss of consciousness						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Restless legs syndrome						
Female	1 (0.1)	2	0.2	2 (0.4)	2	0.3
Male	0			0		
Sensory disturbance						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Vertigo CNS origin						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Sensory loss						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Spinal cord and nerve root disorders						
Female	15 (1.6)	17	1.4	11 (2.2)	11	1.8
Male	5 (1.4)	5	1.1	3 (1.9)	3	1.5
Sciatica						
Female	12 (1.3)	14	1.1	6 (1.2)	6	1.0
Male	2 (0.6)	2	0.4	2 (1.3)	2	1.0
Cervicobrachial syndrome						
Female	0			4 (0.8)	4	0.6
Male	2 (0.6)	2	0.4	0		
Cervical radiculopathy						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Lumbar radiculopathy						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Lumbosacral radiculopathy						
Female	1 (0.1)	1	<0.1	0		
Male	0			1 (0.6)	1	0.5
Spinal cord compression						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Peripheral neuropathies						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	11 (1.2)	11	0.9	5 (1.0)	6	1.0
Male	1 (0.3)	2	0.4	3 (1.9)	3	1.5
Carpal tunnel syndrome						
Female	3 (0.3)	3	0.2	1 (0.2)	1	0.2
Male	1 (0.3)	2	0.4	2 (1.3)	2	1.0
Neuropathy peripheral						
Female	4 (0.4)	4	0.3	2 (0.4)	2	0.3
Male	0			0		
Nerve compression						
Female	3 (0.3)	3	0.2	2 (0.4)	2	0.3
Male	0			0		
Peripheral sensory neuropathy						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Peroneal nerve palsy						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Radial nerve compression						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Movement disorders (incl parkinsonism)						
Female	3 (0.3)	3	0.2	0		
Male	3 (0.9)	3	0.6	2 (1.3)	3	1.5
Tremor						
Female	3 (0.3)	3	0.2	0		
Male	2 (0.6)	2	0.4	2 (1.3)	3	1.5
Essential tremor						

Adverse events with onset prior to randomisation are not included.
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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Cranial nerve disorders (excl neoplasms)						
Female	2 (0.2)	2	0.2	0		
Male	2 (0.6)	2	0.4	0		
Anosmia						
Female	0			0		
Male	2 (0.6)	2	0.4	0		
Cranial nerve disorder						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Parosmia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Mental impairment disorders						
Female	5 (0.5)	5	0.4	2 (0.4)	3	0.5
Male	0			1 (0.6)	1	0.5
Memory impairment						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Amnesia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Dementia Alzheimer's type						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Disturbance in attention						
Female	1 (0.1)	1	<0.1	2 (0.4)	3	0.5
Male	0			1 (0.6)	1	0.5
Sleep disturbances (incl subtypes)						
Female	4 (0.4)	4	0.3	1 (0.2)	1	0.2
Male	0			0		
Poor quality sleep						
Female	4 (0.4)	4	0.3	1 (0.2)	1	0.2
Male	0			0		
Central nervous system vascular disorders						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Cerebral infarction						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Ischaemic stroke						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Increased intracranial pressure and hydrocephalus						
Female	1 (0.1)	2	0.2	0		
Male	0			0		
Idiopathic intracranial hypertension						
Female	1 (0.1)	2	0.2	0		
Male	0			0		
Neurological disorders of the eye						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Visual field defect						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Neuromuscular disorders						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Autonomic nervous system imbalance						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Demyelinating disorders						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Multiple sclerosis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Seizures (incl subtypes)						
Female	0			2 (0.4)	2	0.3
Male	0			0		
Partial seizures						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Psychogenic seizure						
Female	0			1 (0.2)	1	0.2
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Musculoskeletal and connective tissue disorders						
Female	253 (26.5)	416	33.5	157 (31.5)	255	40.8
Male	85 (24.2)	142	30.5	29 (18.5)	49	23.9
Musculoskeletal and connective tissue disorders NEC						
Female	139 (14.6)	179	14.4	83 (16.7)	111	17.8
Male	48 (13.7)	65	14.0	16 (10.2)	21	10.2
Back pain						
Female	78 (8.2)	88	7.1	44 (8.8)	45	7.2
Male	29 (8.3)	33	7.1	10 (6.4)	11	5.4
Pain in extremity						
Female	30 (3.1)	33	2.7	23 (4.6)	26	4.2
Male	14 (4.0)	15	3.2	1 (0.6)	2	1.0
Musculoskeletal pain						
Female	22 (2.3)	22	1.8	13 (2.6)	15	2.4
Male	9 (2.6)	9	1.9	3 (1.9)	3	1.5
Neck pain						
Female	17 (1.8)	19	1.5	8 (1.6)	8	1.3
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Musculoskeletal chest pain						
Female	5 (0.5)	5	0.4	3 (0.6)	3	0.5
Male	3 (0.9)	3	0.6	2 (1.3)	2	1.0
Musculoskeletal stiffness						
Female	2 (0.2)	2	0.2	0		
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Plantar fasciitis						

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	2 (0.2)	2	0.2	6 (1.2)	7	1.1
Male	1 (0.3)	1	0.2	0		
Flank pain						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Axillary mass						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Dupuytren's contracture						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Musculoskeletal discomfort						
Female	1 (0.1)	2	0.2	0		
Male	0			0		
Groin pain						
Female	0			2 (0.4)	2	0.3
Male	0			0		
Limb mass						
Female	0			1 (0.2)	2	0.3
Male	0			0		
Muscle contracture						
Female	0			2 (0.4)	2	0.3
Male	0			1 (0.6)	1	0.5
Neck mass						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Joint disorders						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	97 (10.2)	125	10.1	62 (12.4)	78	12.5
Male	36 (10.3)	44	9.5	13 (8.3)	16	7.8
Arthralgia						
Female	55 (5.8)	62	5.0	35 (7.0)	39	6.2
Male	26 (7.4)	30	6.4	8 (5.1)	8	3.9
Osteoarthritis						
Female	18 (1.9)	22	1.8	14 (2.8)	16	2.6
Male	5 (1.4)	6	1.3	4 (2.5)	4	2.0
Spinal osteoarthritis						
Female	9 (0.9)	10	0.8	0		
Male	3 (0.9)	3	0.6	0		
Rotator cuff syndrome						
Female	3 (0.3)	3	0.2	4 (0.8)	4	0.6
Male	3 (0.9)	3	0.6	1 (0.6)	1	0.5
Joint swelling						
Female	6 (0.6)	6	0.5	4 (0.8)	4	0.6
Male	1 (0.3)	1	0.2	0		
Arthritis						
Female	8 (0.8)	8	0.6	4 (0.8)	4	0.6
Male	0			2 (1.3)	2	1.0
Vertebral foraminal stenosis						
Female	2 (0.2)	3	0.2	0		
Male	1 (0.3)	1	0.2	0		
Joint stiffness						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Facet joint syndrome						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	2 (0.2)	3	0.2	0		
Male	0			0		
Arthropathy						
Female	1 (0.1)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Periarthritis						
Female	1 (0.1)	1	<0.1	1 (0.2)	2	0.3
Male	0			0		
Spondylitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Vertebral osteophyte						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Chondromalacia						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Haemarthrosis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Joint noise						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Joint range of motion decreased						
Female	0			2 (0.4)	2	0.3
Male	0			0		
Joint space narrowing						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	0			1 (0.2)	1	0.2
Male	0			0		
Polyarthritis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Rheumatoid arthritis						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Spondyloarthropathy						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Muscle disorders						
Female	47 (4.9)	52	4.2	20 (4.0)	26	4.2
Male	11 (3.1)	12	2.6	3 (1.9)	3	1.5
Myalgia						
Female	17 (1.8)	19	1.5	7 (1.4)	12	1.9
Male	6 (1.7)	7	1.5	1 (0.6)	1	0.5
Muscle spasms						
Female	17 (1.8)	17	1.4	9 (1.8)	10	1.6
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Fibromyalgia						
Female	3 (0.3)	3	0.2	3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	0		
Muscular weakness						
Female	5 (0.5)	6	0.5	1 (0.2)	1	0.2
Male	0			0		
Myofascial pain syndrome						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Female	1	(0.1)	1	<0.1	0			
Male	1	(0.3)	1	0.2	0			
Myalgia intercostal								
Female	0				0			
Male	1	(0.3)	1	0.2	0			
Muscle disorder								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Muscle fatigue								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Muscle tightness								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Muscle twitching								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Myosclerosis								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Torticollis								
Female	1	(0.1)	1	<0.1	0			
Male	0				1	(0.6)	1	0.5
Tendon, ligament and cartilage disorders								
Female	18	(1.9)	19	1.5	10	(2.0)	12	1.9
Male	7	(2.0)	8	1.7	3	(1.9)	3	1.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Tendonitis						
Female	7 (0.7)	7	0.6	8 (1.6)	10	1.6
Male	6 (1.7)	7	1.5	1 (0.6)	1	0.5
Costochondritis						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	0		
Tenosynovitis						
Female	3 (0.3)	3	0.2	0		
Male	0			1 (0.6)	1	0.5
Tendon disorder						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Osteochondrosis						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Posterior tibial tendon dysfunction						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Tendon discomfort						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Tendon pain						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Trigger finger						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)						
Female	14 (1.5)	19	1.5	7 (1.4)	9	1.4
Male	5 (1.4)	5	1.1	4 (2.5)	4	2.0
Intervertebral disc protrusion						
Female	6 (0.6)	6	0.5	3 (0.6)	4	0.6
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Intervertebral disc degeneration						
Female	4 (0.4)	6	0.5	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Scoliosis						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Finger deformity						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Spinal stenosis						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Cervical spinal stenosis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Intervertebral disc displacement						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Kyphoscoliosis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Spondylolisthesis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Foot deformity						
Female	0			1 (0.2)	1	0.2
Male	0			2 (1.3)	2	1.0
Intervertebral disc annular tear						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Kyphosis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Synovial and bursal disorders						
Female	10 (1.0)	10	0.8	4 (0.8)	4	0.6
Male	6 (1.7)	6	1.3	1 (0.6)	1	0.5
Bursitis						
Female	6 (0.6)	6	0.5	3 (0.6)	3	0.5
Male	4 (1.1)	4	0.9	0		
Synovial cyst						
Female	3 (0.3)	3	0.2	1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	0		
Synovitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Bursal fluid accumulation						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	0			0		
Male	0			1 (0.6)	1	0.5
Bone disorders (excl congenital and fractures)						
Female	9 (0.9)	10	0.8	13 (2.6)	13	2.1
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Osteopenia						
Female	3 (0.3)	3	0.2	2 (0.4)	2	0.3
Male	0			0		
Coccydynia						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Osteonecrosis						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Pain in jaw						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	0			0		
Bone cyst						
Female	1 (0.1)	2	0.2	0		
Male	0			0		
Exostosis						
Female	1 (0.1)	1	<0.1	3 (0.6)	3	0.5
Male	0			0		
Metatarsalgia						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Osteoporosis								
Female	1	(0.1)	1	<0.1	3	(0.6)	3	0.5
Male	0				0			
Pubic pain								
Female	0				1	(0.2)	1	0.2
Male	0				0			
Connective tissue disorders (excl congenital)								
Female	2	(0.2)	2	0.2	2	(0.4)	2	0.3
Male	0				0			
Myofascitis								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Sjogren's syndrome								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Systemic lupus erythematosus								
Female	0				1	(0.2)	1	0.2
Male	0				0			
Systemic scleroderma								
Female	0				1	(0.2)	1	0.2
Male	0				0			
General disorders and administration site conditions								
Female	220	(23.0)	356	28.7	110	(22.1)	189	30.3
Male	71	(20.2)	109	23.4	21	(13.4)	33	16.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
General system disorders NEC						
Female	177 (18.5)	252	20.3	72 (14.5)	94	15.0
Male	48 (13.7)	72	15.5	14 (8.9)	19	9.3
Fatigue						
Female	83 (8.7)	96	7.7	22 (4.4)	22	3.5
Male	21 (6.0)	24	5.2	6 (3.8)	7	3.4
Asthenia						
Female	25 (2.6)	34	2.7	9 (1.8)	10	1.6
Male	10 (2.8)	19	4.1	2 (1.3)	2	1.0
Early satiety						
Female	25 (2.6)	25	2.0	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	0		
Influenza like illness						
Female	12 (1.3)	13	1.0	11 (2.2)	11	1.8
Male	5 (1.4)	5	1.1	2 (1.3)	2	1.0
Pain						
Female	19 (2.0)	21	1.7	7 (1.4)	7	1.1
Male	2 (0.6)	2	0.4	0		
Malaise						
Female	13 (1.4)	14	1.1	4 (0.8)	5	0.8
Male	3 (0.9)	5	1.1	0		
Chest discomfort						
Female	6 (0.6)	6	0.5	2 (0.4)	3	0.5
Male	3 (0.9)	3	0.6	0		
Non-cardiac chest pain						
Female	6 (0.6)	6	0.5	3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hunger						
Female	5 (0.5)	5	0.4	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Oedema peripheral						
Female	2 (0.2)	2	0.2	7 (1.4)	7	1.1
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Chills						
Female	7 (0.7)	7	0.6	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Thirst						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	0		
Feeling cold						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Hernia						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Peripheral swelling						
Female	1 (0.1)	1	<0.1	5 (1.0)	5	0.8
Male	1 (0.3)	1	0.2	0		
Chest pain						
Female	3 (0.3)	3	0.2	5 (1.0)	5	0.8
Male	0			2 (1.3)	2	1.0
Hangover						
Female	0			0		
Male	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Sense of oppression						
Female	0			0		
Male	1 (0.3)	2	0.4	0		
Sluggishness						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Feeling hot						
Female	2 (0.2)	2	0.2	0		
Male	0			1 (0.6)	1	0.5
Ill-defined disorder						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Sensation of foreign body						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Swelling						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Swelling face						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Axillary pain						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Crying						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Fat tissue increased						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Inflammation						
Female	1 (0.1)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Pseudocyst						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Discomfort						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Facial pain						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Granuloma						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Gravitational oedema						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Temperature intolerance						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Administration site reactions						
Female	54 (5.7)	79	6.4	40 (8.0)	77	12.3
Male	11 (3.1)	20	4.3	4 (2.5)	5	2.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Injection site bruising						
Female	27 (2.8)	29	2.3	26 (5.2)	34	5.4
Male	1 (0.3)	2	0.4	0		
Injection site pain						
Female	15 (1.6)	17	1.4	13 (2.6)	18	2.9
Male	4 (1.1)	7	1.5	3 (1.9)	3	1.5
Injection site pruritus						
Female	6 (0.6)	6	0.5	0		
Male	3 (0.9)	3	0.6	1 (0.6)	1	0.5
Injection site erythema						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	0		
Injection site haematoma						
Female	2 (0.2)	7	0.6	4 (0.8)	12	1.9
Male	1 (0.3)	1	0.2	0		
Injection site reaction						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Injection site mass						
Female	4 (0.4)	4	0.3	2 (0.4)	2	0.3
Male	0			1 (0.6)	1	0.5
Application site haematoma						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Injection site inflammation						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	3	0.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Injection site swelling						
Female	0			1 (0.2)	2	0.3
Male	1 (0.3)	1	0.2	0		
Injection site haemorrhage						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Injection site paraesthesia						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	0			0		
Infusion site extravasation						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Injection site induration						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Injection site urticaria						
Female	1 (0.1)	2	0.2	0		
Male	0			0		
Vessel puncture site bruise						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Vessel puncture site rash						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Application site bruise						
Female	0			1 (0.2)	1	0.2
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Puncture site pain						
Female	0			1 (0.2)	2	0.3
Male	0			0		
Body temperature conditions						
Female	15 (1.6)	20	1.6	12 (2.4)	13	2.1
Male	12 (3.4)	13	2.8	5 (3.2)	8	3.9
Pyrexia						
Female	15 (1.6)	20	1.6	12 (2.4)	13	2.1
Male	12 (3.4)	13	2.8	5 (3.2)	8	3.9
Tissue disorders NEC						
Female	2 (0.2)	2	0.2	5 (1.0)	5	0.8
Male	3 (0.9)	3	0.6	0		
Cyst						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	0		
Nodule						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Dysplasia						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Fat necrosis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Hyperplasia						
Female	0			1 (0.2)	1	0.2
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Complications associated with device						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Vascular stent occlusion						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Injury associated with device						
Female	1 (0.1)	1	<0.1	0		
Male	0			1 (0.6)	1	0.5
Therapeutic and nontherapeutic effects (excl toxicity)						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Withdrawal syndrome						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Metabolism and nutrition disorders						
Female	154 (16.1)	209	16.8	55 (11.0)	72	11.5
Male	45 (12.8)	58	12.5	28 (17.8)	36	17.6
Appetite and general nutritional disorders						
Female	114 (11.9)	141	11.4	20 (4.0)	27	4.3
Male	27 (7.7)	31	6.7	8 (5.1)	9	4.4
Decreased appetite						
Female	101 (10.6)	113	9.1	16 (3.2)	19	3.0
Male	23 (6.6)	26	5.6	6 (3.8)	7	3.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hyperphagia						
Female	4 (0.4)	4	0.3	2 (0.4)	4	0.6
Male	3 (0.9)	4	0.9	0		
Food craving						
Female	8 (0.8)	8	0.6	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Increased appetite						
Female	5 (0.5)	6	0.5	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Food aversion						
Female	4 (0.4)	6	0.5	0		
Male	0			0		
Lack of satiety						
Female	3 (0.3)	3	0.2	2 (0.4)	2	0.3
Male	0			0		
Malnutrition						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Lipid metabolism disorders						
Female	13 (1.4)	14	1.1	14 (2.8)	14	2.2
Male	7 (2.0)	7	1.5	6 (3.8)	7	3.4
Dyslipidaemia						
Female	9 (0.9)	9	0.7	6 (1.2)	6	1.0
Male	1 (0.3)	1	0.2	3 (1.9)	4	2.0
Hypercholesterolaemia						
Female	3 (0.3)	3	0.2	4 (0.8)	4	0.6
Male	2 (0.6)	2	0.4	2 (1.3)	2	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hypertriglyceridaemia						
Female	0			1 (0.2)	1	0.2
Male	3 (0.9)	3	0.6	0		
Hyperlipidaemia						
Female	0			3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Cholesterosis						
Female	1 (0.1)	2	0.2	0		
Male	0			0		
Vitamin related disorders						
Female	21 (2.2)	27	2.2	8 (1.6)	10	1.6
Male	1 (0.3)	1	0.2	2 (1.3)	2	1.0
Vitamin D deficiency						
Female	16 (1.7)	16	1.3	7 (1.4)	7	1.1
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Vitamin B12 deficiency						
Female	6 (0.6)	6	0.5	0		
Male	0			0		
Folate deficiency						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Vitamin A deficiency						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Vitamin B complex deficiency						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Vitamin B2 deficiency						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Glucose metabolism disorders (incl diabetes mellitus)						
Female	6 (0.6)	8	0.6	12 (2.4)	13	2.1
Male	4 (1.1)	9	1.9	9 (5.7)	12	5.9
Hypoglycaemia						
Female	4 (0.4)	5	0.4	3 (0.6)	4	0.6
Male	3 (0.9)	8	1.7	2 (1.3)	3	1.5
Type 2 diabetes mellitus						
Female	0			3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	3 (1.9)	4	2.0
Glucose tolerance impaired						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			2 (1.3)	2	1.0
Postprandial hypoglycaemia						
Female	1 (0.1)	2	0.2	0		
Male	0			0		
Diabetes mellitus						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Hyperglycaemia						
Female	0			1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Impaired fasting glucose						
Female	0			1 (0.2)	1	0.2

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			2 (1.3)	2	1.0
Insulin resistance						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Electrolyte and fluid balance conditions						
Female	5 (0.5)	8	0.6	4 (0.8)	4	0.6
Male	4 (1.1)	4	0.9	2 (1.3)	2	1.0
Hyperkalaemia						
Female	0			0		
Male	2 (0.6)	2	0.4	0		
Hypokalaemia						
Female	2 (0.2)	4	0.3	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Hyponatraemia						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Dehydration						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			0		
Electrolyte imbalance						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Polydipsia						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Fluid retention						

Adverse events with onset prior to randomisation are not included.
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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	0			0		
Male	0			1 (0.6)	1	0.5
Purine and pyrimidine metabolism disorders						
Female	0			0		
Male	4 (1.1)	5	1.1	4 (2.5)	4	2.0
Gout						
Female	0			0		
Male	4 (1.1)	5	1.1	3 (1.9)	3	1.5
Hyperuricaemia						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Iron and trace metal metabolism disorders						
Female	5 (0.5)	5	0.4	4 (0.8)	4	0.6
Male	0			0		
Iron deficiency						
Female	5 (0.5)	5	0.4	4 (0.8)	4	0.6
Male	0			0		
Metabolism disorders NEC						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Hyperlipasaemia						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Food intolerance syndromes						
Female	3 (0.3)	3	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
Male	0			0		
Dairy intolerance						
Female	1	(0.1)	1 <0.1	0		
Male	0			0		
Food intolerance						
Female	1	(0.1)	1 <0.1	0		
Male	0			0		
Lactose intolerance						
Female	1	(0.1)	1 <0.1	0		
Male	0			0		
Bone, calcium, magnesium and phosphorus metabolism disorders						
Female	1	(0.1)	1 <0.1	0		
Male	0			0		
Hypomagnesaemia						
Female	1	(0.1)	1 <0.1	0		
Male	0			0		
Protein and amino acid metabolism disorders NEC						
Female	1	(0.1)	1 <0.1	0		
Male	0			0		
Hypoalbuminaemia						
Female	1	(0.1)	1 <0.1	0		
Male	0			0		
Injury, poisoning and procedural complications						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	140 (14.7)	189	15.2	102 (20.5)	147	23.5
Male	48 (13.7)	75	16.1	19 (12.1)	29	14.2
Injuries NEC						
Female	96 (10.1)	122	9.8	80 (16.1)	108	17.3
Male	30 (8.5)	46	9.9	16 (10.2)	22	10.7
Ligament sprain						
Female	17 (1.8)	20	1.6	17 (3.4)	18	2.9
Male	4 (1.1)	4	0.9	2 (1.3)	2	1.0
Fall						
Female	14 (1.5)	14	1.1	12 (2.4)	19	3.0
Male	5 (1.4)	5	1.1	0		
Muscle strain						
Female	12 (1.3)	13	1.0	11 (2.2)	11	1.8
Male	5 (1.4)	5	1.1	4 (2.5)	4	2.0
Contusion						
Female	11 (1.2)	15	1.2	13 (2.6)	17	2.7
Male	4 (1.1)	4	0.9	2 (1.3)	2	1.0
Arthropod bite						
Female	7 (0.7)	7	0.6	5 (1.0)	5	0.8
Male	2 (0.6)	2	0.4	2 (1.3)	2	1.0
Skin laceration						
Female	7 (0.7)	7	0.6	7 (1.4)	7	1.1
Male	2 (0.6)	2	0.4	1 (0.6)	2	1.0
Skin abrasion						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	3 (0.9)	6	1.3	2 (1.3)	2	1.0
Limb injury						

Adverse events with onset prior to randomisation are not included.
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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	4 (0.4)	4	0.3	4 (0.8)	4	0.6
Male	2 (0.6)	2	0.4	0		
Concussion						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	3 (0.9)	3	0.6	0		
Arthropod sting						
Female	5 (0.5)	5	0.4	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Ligament rupture						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	0		
Tooth fracture						
Female	4 (0.4)	4	0.3	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Epicondylitis						
Female	3 (0.3)	3	0.2	4 (0.8)	4	0.6
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Animal bite						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Road traffic accident						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	0		
Injury						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Back injury						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	3 (0.3)	3	0.2	1 (0.2)	1	0.2
Male	0			0		
Muscle rupture						
Female	3 (0.3)	3	0.2	2 (0.4)	2	0.3
Male	0			0		
Eye burns						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Eyelid injury						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Foreign body in eye						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Ligament injury						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Muscle injury						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Wound						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	0			0		
Bone contusion						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Eyelid contusion						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Face injury						
Female	1 (0.1)	1	<0.1	0		
Male	0			1 (0.6)	1	0.5
Head injury						
Female	1 (0.1)	1	<0.1	0		
Male	0			1 (0.6)	1	0.5
Musculoskeletal injury						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Nerve injury						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Post-traumatic neck syndrome						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Post-traumatic pain						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Skeletal injury						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Soft tissue foreign body						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Subdural haematoma						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Tendon injury						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Chest injury						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Corneal abrasion						
Female	0			2 (0.4)	2	0.3
Male	0			0		
Eye injury						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Gun shot wound						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Post concussion syndrome						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Scar						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Tendon rupture						
Female	0			1 (0.2)	1	0.2
Male	0			1 (0.6)	2	1.0
Bone and joint injuries						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	26 (2.7)	29	2.3	19 (3.8)	20	3.2
Male	9 (2.6)	10	2.1	3 (1.9)	3	1.5
Joint injury						
Female	3 (0.3)	3	0.2	0		
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Foot fracture						
Female	4 (0.4)	6	0.5	3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	2 (1.3)	2	1.0
Rib fracture						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	0		
Meniscus injury						
Female	3 (0.3)	3	0.2	4 (0.8)	5	0.8
Male	1 (0.3)	1	0.2	0		
Radius fracture						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Hand fracture						
Female	3 (0.3)	3	0.2	1 (0.2)	1	0.2
Male	0			0		
Joint dislocation						
Female	3 (0.3)	3	0.2	1 (0.2)	1	0.2
Male	0			0		
Femur fracture						
Female	0			0		
Male	1 (0.3)	2	0.4	0		
Spinal compression fracture						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Ankle fracture						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			0		
Facial bones fracture						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Fractured coccyx						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Stress fracture						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Thoracic vertebral fracture						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Tibia fracture						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Upper limb fracture						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Wrist fracture						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Fibula fracture						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	0			1 (0.2)	1	0.2
Male	0			0		
Torus fracture						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Procedural related injuries and complications NEC						
Female	21 (2.2)	22	1.8	11 (2.2)	13	2.1
Male	6 (1.7)	13	2.8	0		
Procedural pain						
Female	8 (0.8)	8	0.6	7 (1.4)	9	1.4
Male	4 (1.1)	5	1.1	0		
Post procedural complication						
Female	3 (0.3)	3	0.2	0		
Male	1 (0.3)	2	0.4	0		
Procedural nausea						
Female	0			1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	0		
Injection related reaction						
Female	4 (0.4)	4	0.3	0		
Male	0			0		
Administration related reaction						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Anaemia postoperative						
Female	0			0		
Male	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Post procedural constipation						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Procedural haemorrhage						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Urinary retention postoperative						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Anaphylactic transfusion reaction						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Post procedural haemorrhage						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Suture related complication						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Vaccination complication						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Procedural vomiting						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Seroma						
Female	0			1 (0.2)	1	0.2
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Medication errors and other product use errors and issues						
Female	8 (0.8)	8	0.6	1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	1 (0.6)	2	1.0
Accidental overdose						
Female	6 (0.6)	6	0.5	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	1 (0.6)	2	1.0
Medication error						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Incorrect dose administered						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Injuries by physical agents						
Female	5 (0.5)	5	0.4	3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	2 (1.3)	2	1.0
Heat exhaustion						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Sunburn						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Heat illness						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Hypobarism						
Female	1 (0.1)	1	<0.1	0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Thermal burn						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			0		
Burns second degree						
Female	0			1 (0.2)	1	0.2
Male	0			2 (1.3)	2	1.0
Overdoses and underdoses NEC						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	2 (0.6)	2	0.4	0		
Overdose						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	2 (0.6)	2	0.4	0		
Exposures, chemical injuries and poisoning						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Reactive gastropathy						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Exposure to toxic agent						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Skin and subcutaneous tissue disorders						
Female	148 (15.5)	201	16.2	60 (12.0)	78	12.5
Male	40 (11.4)	48	10.3	15 (9.6)	18	8.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Epidermal and dermal conditions						
Female	76 (8.0)	95	7.7	41 (8.2)	53	8.5
Male	29 (8.3)	34	7.3	11 (7.0)	12	5.9
Rash						
Female	22 (2.3)	22	1.8	16 (3.2)	22	3.5
Male	4 (1.1)	8	1.7	1 (0.6)	1	0.5
Pruritus						
Female	14 (1.5)	15	1.2	4 (0.8)	4	0.6
Male	3 (0.9)	3	0.6	2 (1.3)	2	1.0
Eczema						
Female	10 (1.0)	10	0.8	4 (0.8)	4	0.6
Male	3 (0.9)	3	0.6	0		
Dry skin						
Female	6 (0.6)	6	0.5	3 (0.6)	3	0.5
Male	2 (0.6)	2	0.4	0		
Skin burning sensation						
Female	5 (0.5)	11	0.9	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	0		
Skin lesion						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	0		
Erythema						
Female	1 (0.1)	1	<0.1	4 (0.8)	4	0.6
Male	2 (0.6)	2	0.4	0		
Blister						
Female	0			2 (0.4)	2	0.3
Male	2 (0.6)	2	0.4	3 (1.9)	3	1.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Decubitus ulcer						
Female	0			0		
Male	2 (0.6)	2	0.4	0		
Dermatitis contact						
Female	5 (0.5)	7	0.6	3 (0.6)	3	0.5
Male	0			1 (0.6)	1	0.5
Pain of skin						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Psoriasis						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	0		
Rash pruritic						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	0		
Skin irritation						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Dermatitis						
Female	3 (0.3)	3	0.2	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Dermatitis atopic						
Female	0			0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Rash maculo-papular						
Female	0			0		
Male	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Skin discolouration						
Female	0			2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	0		
Skin odour abnormal						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Xanthelasma						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Dermatitis allergic						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Skin disorder						
Female	2 (0.2)	3	0.2	1 (0.2)	1	0.2
Male	0			0		
Macule						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Papule						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Perioral dermatitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Pityriasis rosea						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Prurigo						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Drug eruption						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Photosensitivity reaction						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Rash erythematous						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Rash macular						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Skin reaction						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Skin appendage conditions						
Female	72 (7.5)	82	6.6	15 (3.0)	16	2.6
Male	10 (2.8)	10	2.1	4 (2.5)	5	2.4
Alopecia						
Female	47 (4.9)	49	3.9	5 (1.0)	5	0.8
Male	6 (1.7)	6	1.3	0		
Hyperhidrosis						
Female	7 (0.7)	7	0.6	7 (1.4)	7	1.1
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Ingrowing nail						
Female	1 (0.1)	1	<0.1	0		
Male	2 (0.6)	2	0.4	1 (0.6)	2	1.0
Acne						
Female	4 (0.4)	4	0.3	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Miliaria						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Cold sweat						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Hirsutism						
Female	3 (0.3)	4	0.3	1 (0.2)	1	0.2
Male	0			0		
Hair growth abnormal						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Hidradenitis						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Rosacea						
Female	2 (0.2)	3	0.2	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Diffuse alopecia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hypertrichosis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Nail bed inflammation						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Nail discolouration						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Night sweats						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Onychoclasis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Angioedema and urticaria						
Female	10 (1.0)	10	0.8	5 (1.0)	5	0.8
Male	3 (0.9)	3	0.6	1 (0.6)	1	0.5
Urticaria						
Female	10 (1.0)	10	0.8	4 (0.8)	4	0.6
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Cold urticaria						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Angioedema						
Female	0			1 (0.2)	1	0.2
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Cornification and dystrophic skin disorders						
Female	7 (0.7)	9	0.7	0		
Male	0			0		
Actinic keratosis						
Female	3 (0.3)	4	0.3	0		
Male	0			0		
Hyperkeratosis						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Lichenoid keratosis						
Female	1 (0.1)	2	0.2	0		
Male	0			0		
Skin striae						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Cutaneous neoplasms benign						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Dermal cyst						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Pigmentation disorders						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Ephelides						
Female	2 (0.2)	2	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Skin hyperpigmentation						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Skin vascular abnormalities						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Ecchymosis						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Skin and subcutaneous tissue disorders NEC						
Female	0			2 (0.4)	2	0.3
Male	0			0		
Erythema nodosum						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Skin ulcer						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Respiratory, thoracic and mediastinal disorders						
Female	132 (13.8)	178	14.3	81 (16.3)	105	16.8
Male	41 (11.7)	47	10.1	23 (14.6)	29	14.2
Respiratory tract signs and symptoms						
Female	60 (6.3)	66	5.3	30 (6.0)	34	5.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	15 (4.3)	15	3.2	3 (1.9)	3	1.5
Oropharyngeal pain						
Female	42 (4.4)	47	3.8	23 (4.6)	26	4.2
Male	6 (1.7)	6	1.3	0		
Rhinorrhoea						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	4 (1.1)	4	0.9	0		
Upper respiratory tract inflammation						
Female	3 (0.3)	4	0.3	2 (0.4)	2	0.3
Male	2 (0.6)	2	0.4	2 (1.3)	2	1.0
Hiccups						
Female	1 (0.1)	1	<0.1	0		
Male	2 (0.6)	2	0.4	0		
Dysphonia						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Upper-airway cough syndrome						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Catarrh						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Diaphragmalgia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Oropharyngeal discomfort						
Female	1 (0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Paranasal sinus discomfort						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			0		
Pleuritic pain						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Sinus pain						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Yawning						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Upper respiratory tract congestion						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Respiratory disorders NEC						
Female	48 (5.0)	57	4.6	42 (8.4)	46	7.4
Male	13 (3.7)	13	2.8	9 (5.7)	10	4.9
Cough						
Female	29 (3.0)	34	2.7	26 (5.2)	27	4.3
Male	11 (3.1)	11	2.4	7 (4.5)	8	3.9
Dyspnoea						
Female	8 (0.8)	8	0.6	8 (1.6)	8	1.3
Male	0			0		
Sleep apnoea syndrome						
Female	5 (0.5)	5	0.4	3 (0.6)	3	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Haemoptysis						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Productive cough						
Female	3 (0.3)	3	0.2	2 (0.4)	2	0.3
Male	0			0		
Dyspnoea exertional						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Respiratory disorder						
Female	2 (0.2)	2	0.2	3 (0.6)	3	0.5
Male	0			1 (0.6)	1	0.5
Hyperventilation						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Respiratory tract congestion						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Acute respiratory failure						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Pulmonary mass						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Upper respiratory tract disorders (excl infections)						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	35 (3.7)	37	3.0	9 (1.8)	11	1.8
Male	16 (4.6)	16	3.4	9 (5.7)	10	4.9
Sinus congestion						
Female	10 (1.0)	10	0.8	3 (0.6)	5	0.8
Male	3 (0.9)	3	0.6	2 (1.3)	2	1.0
Rhinitis allergic						
Female	7 (0.7)	7	0.6	2 (0.4)	2	0.3
Male	4 (1.1)	4	0.9	4 (2.5)	5	2.4
Nasal congestion						
Female	8 (0.8)	8	0.6	4 (0.8)	4	0.6
Male	3 (0.9)	3	0.6	2 (1.3)	2	1.0
Epistaxis						
Female	5 (0.5)	5	0.4	0		
Male	2 (0.6)	2	0.4	0		
Nasal polyps						
Female	0			0		
Male	2 (0.6)	2	0.4	0		
Nasal septum deviation						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Tonsillar hypertrophy						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Paranasal sinus hypersecretion						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Nasal dryness						

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Paranasal cyst								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Vocal cord polyp								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Nasal adhesions								
Female	0				0			
Male	0				1	(0.6)	1	0.5
Bronchial disorders (excl neoplasms)								
Female	12	(1.3)	12	1.0	9	(1.8)	12	1.9
Male	2	(0.6)	2	0.4	4	(2.5)	4	2.0
Asthma								
Female	10	(1.0)	10	0.8	6	(1.2)	8	1.3
Male	1	(0.3)	1	0.2	3	(1.9)	3	1.5
Chronic obstructive pulmonary disease								
Female	1	(0.1)	1	<0.1	1	(0.2)	1	0.2
Male	1	(0.3)	1	0.2	1	(0.6)	1	0.5
Wheezing								
Female	1	(0.1)	1	<0.1	1	(0.2)	1	0.2
Male	0				0			
Allergic bronchitis								
Female	0				1	(0.2)	2	0.3
Male	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Lower respiratory tract disorders (excl obstruction and infection)						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Atelectasis						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Pulmonary fibrosis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Pleural disorders						
Female	2 (0.2)	2	0.2	0		
Male	0			1 (0.6)	1	0.5
Pleural effusion						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Pleurisy						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Pulmonary vascular disorders						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	0			0		
Pulmonary embolism						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	0			0		
Psychiatric disorders						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	93 (9.7)	125	10.1	69 (13.9)	92	14.7
Male	31 (8.8)	35	7.5	14 (8.9)	21	10.2
Anxiety disorders and symptoms						
Female	36 (3.8)	37	3.0	25 (5.0)	26	4.2
Male	10 (2.8)	11	2.4	6 (3.8)	6	2.9
Anxiety						
Female	25 (2.6)	25	2.0	16 (3.2)	16	2.6
Male	7 (2.0)	8	1.7	4 (2.5)	4	2.0
Stress						
Female	7 (0.7)	7	0.6	5 (1.0)	5	0.8
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Panic attack						
Female	3 (0.3)	3	0.2	2 (0.4)	2	0.3
Male	0			0		
Nervousness						
Female	0			0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Post-traumatic stress disorder						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Acute stress disorder						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Burnout syndrome						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Agitation						

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	0			2 (0.4)	2	0.3
Male	0			0		
Generalised anxiety disorder						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Sleep disorders and disturbances						
Female	33 (3.5)	35	2.8	23 (4.6)	25	4.0
Male	7 (2.0)	7	1.5	6 (3.8)	8	3.9
Insomnia						
Female	23 (2.4)	24	1.9	15 (3.0)	16	2.6
Male	5 (1.4)	5	1.1	3 (1.9)	3	1.5
Sleep disorder						
Female	6 (0.6)	6	0.5	4 (0.8)	4	0.6
Male	0			3 (1.9)	4	2.0
Initial insomnia						
Female	2 (0.2)	3	0.2	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Nightmare						
Female	0			2 (0.4)	3	0.5
Male	1 (0.3)	1	0.2	0		
Abnormal dreams						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Middle insomnia						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Sleep terror						

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	0			0		
Male	0			1 (0.6)	1	0.5
Depressed mood disorders and disturbances						
Female	24 (2.5)	30	2.4	25 (5.0)	27	4.3
Male	9 (2.6)	9	1.9	2 (1.3)	2	1.0
Depression						
Female	10 (1.0)	12	1.0	13 (2.6)	14	2.2
Male	5 (1.4)	5	1.1	1 (0.6)	1	0.5
Depressed mood						
Female	12 (1.3)	13	1.0	9 (1.8)	9	1.4
Male	2 (0.6)	2	0.4	0		
Major depression						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	0		
Negative thoughts						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Anhedonia						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Tearfulness						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Depressive symptom						
Female	0			0		
Male	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Persistent depressive disorder						
Female	0			3 (0.6)	3	0.5
Male	0			0		
Mood disorders and disturbances NEC						
Female	7 (0.7)	7	0.6	2 (0.4)	2	0.3
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Irritability						
Female	4 (0.4)	4	0.3	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Apathy						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Mood swings						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Affective disorder						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Sexual dysfunctions, disturbances and gender identity disorders						
Female	2 (0.2)	2	0.2	0		
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Libido decreased						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Libido increased						
Female	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	1 (0.3)	1	0.2	0		
Suicidal and self-injurious behaviours NEC						
Female	2 (0.2)	2	0.2	3 (0.6)	5	0.8
Male	2 (0.6)	2	0.4	0		
Suicidal ideation						
Female	2 (0.2)	2	0.2	2 (0.4)	4	0.6
Male	2 (0.6)	2	0.4	0		
Suicide attempt						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Changes in physical activity						
Female	3 (0.3)	3	0.2	0		
Male	1 (0.3)	1	0.2	0		
Restlessness						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	0		
Tic						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Cognitive and attention disorders and disturbances						
Female	1 (0.1)	2	0.2	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Attention deficit/hyperactivity disorder						
Female	0			1 (0.2)	1	0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	1 (0.3)	1	0.2	0		
Mental fatigue						
Female	1 (0.1)	2	0.2	0		
Male	0			0		
Adjustment disorders (incl subtypes)						
Female	3 (0.3)	3	0.2	4 (0.8)	4	0.6
Male	0			0		
Adjustment disorder						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Adjustment disorder with depressed mood						
Female	1 (0.1)	1	<0.1	3 (0.6)	3	0.5
Male	0			0		
Grief reaction						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Deliria (incl confusion)						
Female	1 (0.1)	2	0.2	0		
Male	0			1 (0.6)	1	0.5
Disorientation						
Female	1 (0.1)	2	0.2	0		
Male	0			1 (0.6)	1	0.5
Manic and bipolar mood disorders and disturbances						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Bipolar disorder						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Psychiatric and behavioural symptoms NEC						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			0		
Abulia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Psychiatric symptom						
Female	0			2 (0.4)	2	0.3
Male	0			0		
Psychiatric disorders NEC						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Alcoholic hangover						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Somatic symptom and related disorders						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Conversion disorder						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Investigations						

Adverse events with onset prior to randomisation are not included.
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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	71 (7.4)	93	7.5	34 (6.8)	45	7.2
Male	22 (6.3)	25	5.4	15 (9.6)	22	10.7
Gastrointestinal investigations						
Female	8 (0.8)	9	0.7	1 (0.2)	1	0.2
Male	5 (1.4)	6	1.3	1 (0.6)	1	0.5
Lipase increased						
Female	6 (0.6)	6	0.5	1 (0.2)	1	0.2
Male	5 (1.4)	5	1.1	1 (0.6)	1	0.5
Amylase increased						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Gastric pH						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Pancreatic enzymes increased						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Hepatobiliary investigations						
Female	13 (1.4)	14	1.1	8 (1.6)	11	1.8
Male	3 (0.9)	3	0.6	3 (1.9)	4	2.0
Hepatic enzyme increased						
Female	4 (0.4)	4	0.3	2 (0.4)	2	0.3
Male	2 (0.6)	2	0.4	0		
Gamma-glutamyltransferase increased						
Female	6 (0.6)	6	0.5	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Alanine aminotransferase increased						

Adverse events with onset prior to randomisation are not included.
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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			1 (0.6)	1	0.5
Aspartate aminotransferase increased						
Female	1 (0.1)	1	<0.1	3 (0.6)	3	0.5
Male	0			1 (0.6)	1	0.5
Blood bilirubin increased						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Transaminases increased						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Endocrine investigations (incl sex hormones)						
Female	4 (0.4)	6	0.5	3 (0.6)	3	0.5
Male	4 (1.1)	4	0.9	0		
Blood calcitonin increased						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	3 (0.9)	3	0.6	0		
Blood thyroid stimulating hormone decreased						
Female	3 (0.3)	3	0.2	1 (0.2)	1	0.2
Male	0			0		
Blood thyroid stimulating hormone abnormal						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Thyroxine free increased						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Thyroxine increased						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Blood thyroid stimulating hormone increased						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Protein and chemistry analyses NEC						
Female	12 (1.3)	12	1.0	4 (0.8)	4	0.6
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
C-reactive protein increased						
Female	12 (1.3)	12	1.0	4 (0.8)	4	0.6
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Cardiac and vascular investigations (excl enzyme tests)						
Female	8 (0.8)	9	0.7	6 (1.2)	6	1.0
Male	2 (0.6)	3	0.6	1 (0.6)	1	0.5
Heart rate increased						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Electrocardiogram ST segment depression						
Female	0			0		
Male	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Electrocardiogram T wave amplitude decreased						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
QRS axis abnormal						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Blood pressure abnormal						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Blood pressure decreased						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Blood pressure increased						
Female	1 (0.1)	1	<0.1	5 (1.0)	5	0.8
Male	0			1 (0.6)	1	0.5
Cardiac murmur						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Electrocardiogram T wave inversion						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Pulse abnormal						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Electrocardiogram T wave abnormal						
Female	0			1 (0.2)	1	0.2

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Lipid analyses						
Female	9 (0.9)	16	1.3	4 (0.8)	5	0.8
Male	0			0		
High density lipoprotein decreased						
Female	5 (0.5)	5	0.4	0		
Male	0			0		
Blood cholesterol increased						
Female	4 (0.4)	4	0.3	1 (0.2)	1	0.2
Male	0			0		
Low density lipoprotein increased						
Female	3 (0.3)	3	0.2	2 (0.4)	2	0.3
Male	0			0		
Lipids increased						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Blood triglycerides increased						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Very low density lipoprotein increased						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Physical examination and organ system status topics						
Female	6 (0.6)	6	0.5	0		
Male	1 (0.3)	1	0.2	3 (1.9)	4	2.0

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Weight increased						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	2 (1.3)	2	1.0
Weight decreased						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Body mass index decreased						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Respiratory rate increased						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Body temperature increased						
Female	0			0		
Male	0			1 (0.6)	2	1.0
Enzyme investigations NEC						
Female	5 (0.5)	5	0.4	4 (0.8)	4	0.6
Male	1 (0.3)	1	0.2	4 (2.5)	4	2.0
Blood creatine phosphokinase increased						
Female	4 (0.4)	4	0.3	3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	4 (2.5)	4	2.0
Enzyme level increased						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Blood alkaline phosphatase increased						
Female	0			1 (0.2)	1	0.2

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Cytogenetic investigations						
Female	0			0		
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Prostatic specific antigen increased						
Female	0			0		
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Investigations, imaging and histopathology procedures NEC						
Female	0			1 (0.2)	1	0.2
Male	2 (0.6)	2	0.4	0		
Precancerous cells present						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Smear test						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Endoscopy						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Haematology investigations (incl blood groups)						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	1 (0.6)	4	2.0
Haematology test abnormal						
Female	0			0		
Male	1 (0.3)	1	0.2	0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Haemoglobin decreased						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Haematocrit increased						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Haemoglobin increased						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Red blood cell count increased						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Red cell distribution width increased						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Microbiology and serology investigations						
Female	4 (0.4)	4	0.3	0		
Male	0			0		
HIV test positive						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Helicobacter test positive						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Human papilloma virus test positive						

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Renal and urinary tract investigations and urinalyses						
Female	4 (0.4)	4	0.3	3 (0.6)	3	0.5
Male	0			0		
Blood creatinine increased						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Glomerular filtration rate decreased						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			0		
White blood cells urine						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Blood urine present						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Metabolic, nutritional and blood gas investigations						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	2 (1.3)	2	1.0
Blood glucose increased						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Blood uric acid increased						
Female	1 (0.1)	1	<0.1	0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Glycosylated haemoglobin increased						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Vitamin D decreased						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Reproductive organ and breast investigations (excl hormone analyses)						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Biopsy breast						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Water, electrolyte and mineral investigations						
Female	2 (0.2)	2	0.2	3 (0.6)	3	0.5
Male	0			0		
Blood calcium decreased						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Blood potassium increased						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Blood iron decreased						
Female	0			1 (0.2)	1	0.2
Male	0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Blood sodium increased						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Serum ferritin decreased						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Musculoskeletal and soft tissue investigations (excl enzyme tests)						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Arthroscopy						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Immunology and allergy investigations						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Antinuclear antibody positive						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Vascular disorders						
Female	74 (7.7)	79	6.4	35 (7.0)	39	6.2
Male	16 (4.6)	18	3.9	10 (6.4)	11	5.4
Vascular hypertensive disorders						
Female	33 (3.5)	33	2.7	20 (4.0)	23	3.7
Male	9 (2.6)	9	1.9	8 (5.1)	9	4.4
Hypertension						

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	31 (3.2)	31	2.5	19 (3.8)	22	3.5
Male	9 (2.6)	9	1.9	8 (5.1)	9	4.4
Essential hypertension						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Hypertensive emergency						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Hypertensive crisis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Decreased and nonspecific blood pressure disorders and shock						
Female	16 (1.7)	18	1.5	2 (0.4)	2	0.3
Male	3 (0.9)	3	0.6	0		
Hypotension						
Female	8 (0.8)	9	0.7	2 (0.4)	2	0.3
Male	2 (0.6)	2	0.4	0		
Orthostatic hypotension						
Female	7 (0.7)	8	0.6	0		
Male	1 (0.3)	1	0.2	0		
Circulatory collapse						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Arteriosclerosis, stenosis, vascular insufficiency and necrosis						
Female	3 (0.3)	3	0.2	4 (0.8)	4	0.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	4 (1.1)	4	0.9	0		
Peripheral coldness						
Female	0			0		
Male	2 (0.6)	2	0.4	0		
Peripheral venous disease						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Aortic arteriosclerosis						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Arteriosclerosis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Raynaud's phenomenon						
Female	0			3 (0.6)	3	0.5
Male	0			0		
Venous varices						
Female	4 (0.4)	4	0.3	0		
Male	2 (0.6)	2	0.4	0		
Varicose vein						
Female	4 (0.4)	4	0.3	0		
Male	2 (0.6)	2	0.4	0		
Vascular disorders NEC						
Female	9 (0.9)	10	0.8	4 (0.8)	4	0.6
Male	0			0		
Hot flush						
Female	8 (0.8)	8	0.6	3 (0.6)	3	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Flushing						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Vascular haemorrhagic disorders						
Female	6 (0.6)	6	0.5	2 (0.4)	2	0.3
Male	0			2 (1.3)	2	1.0
Haematoma						
Female	6 (0.6)	6	0.5	2 (0.4)	2	0.3
Male	0			2 (1.3)	2	1.0
Embolism and thrombosis						
Female	3 (0.3)	3	0.2	3 (0.6)	3	0.5
Male	0			0		
Thrombosis						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Thrombophlebitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Deep vein thrombosis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Thrombophlebitis superficial						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Vascular infections and inflammations						
Female	2 (0.2)	2	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Arteritis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Phlebitis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Lymphatic vessel disorders						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Lymphoedema						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Reproductive system and breast disorders						
Female	92 (9.6)	118	9.5	27 (5.4)	34	5.4
Male	4 (1.1)	4	0.9	5 (3.2)	5	2.4
Menstrual cycle and uterine bleeding disorders						
Female	45 (4.7)	53	4.3	7 (1.4)	10	1.6
Male	0			0		
Menstruation irregular						
Female	14 (1.5)	14	1.1	0		
Male	0			0		
Menorrhagia						
Female	10 (1.0)	12	1.0	3 (0.6)	3	0.5
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Dysmenorrhoea						
Female	7 (0.7)	8	0.6	1 (0.2)	3	0.5
Male	0			0		
Metrorrhagia						
Female	7 (0.7)	7	0.6	1 (0.2)	1	0.2
Male	0			0		
Menstrual disorder						
Female	5 (0.5)	5	0.4	0		
Male	0			0		
Dysfunctional uterine bleeding						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Amenorrhoea						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Menstruation delayed						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Oligomenorrhoea						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Premenstrual syndrome						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Premenstrual pain						
Female	0			1 (0.2)	1	0.2
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Breast disorders								
Female	17	(1.8)	20	1.6	7	(1.4)	8	1.3
Male	0				0			
Breast mass								
Female	8	(0.8)	8	0.6	1	(0.2)	2	0.3
Male	0				0			
Breast cyst								
Female	4	(0.4)	4	0.3	1	(0.2)	1	0.2
Male	0				0			
Breast disorder								
Female	2	(0.2)	2	0.2	0			
Male	0				0			
Breast pain								
Female	2	(0.2)	2	0.2	1	(0.2)	1	0.2
Male	0				0			
Fibrocystic breast disease								
Female	2	(0.2)	2	0.2	2	(0.4)	2	0.3
Male	0				0			
Breast inflammation								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Nipple pain								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Breast fibrosis								
Female	0				1	(0.2)	1	0.2
Male	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Breast haematoma						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Uterine, pelvic and broad ligament disorders						
Female	11 (1.2)	11	0.9	2 (0.4)	2	0.3
Male	0			0		
Uterine haemorrhage						
Female	3 (0.3)	3	0.2	1 (0.2)	1	0.2
Male	0			0		
Adenomyosis						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Endometriosis						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Uterine polyp						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Uterine enlargement						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Vaginal prolapse						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Menopause related conditions						
Female	9 (0.9)	9	0.7	4 (0.8)	5	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Atrophic vulvovaginitis						
Female	4 (0.4)	4	0.3	2 (0.4)	2	0.3
Male	0			0		
Menopausal symptoms						
Female	4 (0.4)	4	0.3	1 (0.2)	1	0.2
Male	0			0		
Postmenopausal haemorrhage						
Female	1 (0.1)	1	<0.1	1 (0.2)	2	0.3
Male	0			0		
Ovarian and fallopian tube disorders						
Female	9 (0.9)	9	0.7	3 (0.6)	3	0.5
Male	0			0		
Ovarian cyst						
Female	7 (0.7)	7	0.6	2 (0.4)	2	0.3
Male	0			0		
Hydrosalpinx						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Polycystic ovaries						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Vulvovaginal disorders (excl infections and inflammations)						
Female	9 (0.9)	9	0.7	5 (1.0)	5	0.8
Male	0			0		
Vaginal haemorrhage						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	6 (0.6)	6	0.5	2 (0.4)	2	0.3
Male	0			0		
Vulvovaginal discomfort						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Vulvovaginal dryness						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Vulvovaginal pain						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Vaginal polyp						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Vulvovaginal pruritus						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Testicular and epididymal disorders						
Female	0			0		
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Testicular mass						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Testicular pain						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Testicular disorder						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Female	0				0			
Male	0				1	(0.6)	1	0.5
Sexual function and fertility disorders								
Female	1	(0.1)	1	<0.1	0			
Male	1	(0.3)	1	0.2	1	(0.6)	1	0.5
Erectile dysfunction								
Female	0				0			
Male	1	(0.3)	1	0.2	1	(0.6)	1	0.5
Dyspareunia								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Reproductive tract disorders NEC								
Female	3	(0.3)	3	0.2	0			
Male	0				1	(0.6)	1	0.5
Pelvic pain								
Female	2	(0.2)	2	0.2	0			
Male	0				0			
Genital rash								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Genital pain								
Female	0				0			
Male	0				1	(0.6)	1	0.5
Prostatic disorders (excl infections and inflammations)								
Female	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Benign prostatic hyperplasia						
Female	0			0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Cervix disorders (excl infections and inflammations)						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Cervical dysplasia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Cervical leukoplakia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Uterine cervical erosion						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Female reproductive tract infections and inflammations						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Uterine inflammation						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Penile and scrotal disorders (excl infections and inflammations)						
Female	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			1 (0.6)	1	0.5
Scrotal pain						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Cardiac disorders						
Female	36 (3.8)	39	3.1	25 (5.0)	30	4.8
Male	18 (5.1)	23	4.9	8 (5.1)	14	6.8
Cardiac arrhythmias						
Female	20 (2.1)	21	1.7	11 (2.2)	11	1.8
Male	12 (3.4)	17	3.7	6 (3.8)	10	4.9
Atrial fibrillation						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	5 (1.4)	8	1.7	2 (1.3)	3	1.5
Atrioventricular block first degree						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	3 (0.9)	3	0.6	3 (1.9)	3	1.5
Tachycardia						
Female	5 (0.5)	5	0.4	5 (1.0)	5	0.8
Male	0			0		
Bundle branch block left						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Sinus tachycardia						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Atrioventricular block						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Defect conduction intraventricular						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Nodal rhythm						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Supraventricular extrasystoles						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Arrhythmia						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	0			0		
Ventricular extrasystoles						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Atrial flutter						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Atrial tachycardia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Atrioventricular block second degree						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Bradycardia						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			2 (1.3)	2	1.0
Bundle branch block right						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Cardiac flutter						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Sinus bradycardia						
Female	1 (0.1)	1	<0.1	0		
Male	0			1 (0.6)	1	0.5
Cardiac disorders, signs and symptoms NEC						
Female	10 (1.0)	10	0.8	8 (1.6)	10	1.6
Male	2 (0.6)	2	0.4	0		
Palpitations						
Female	9 (0.9)	9	0.7	6 (1.2)	8	1.3
Male	1 (0.3)	1	0.2	0		
Cardiovascular disorder						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Hypertensive heart disease						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Coronary artery disorders						
Female	5 (0.5)	5	0.4	5 (1.0)	5	0.8
Male	2 (0.6)	2	0.4	2 (1.3)	3	1.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Angina pectoris						
Female	1 (0.1)	1	<0.1	3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Coronary artery stenosis						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Acute myocardial infarction						
Female	2 (0.2)	2	0.2	0		
Male	0			1 (0.6)	1	0.5
Angina unstable						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Arteriosclerosis coronary artery						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Coronary artery disease						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Myocardial infarction						
Female	0			2 (0.4)	2	0.3
Male	0			0		
Cardiac valve disorders						
Female	0			1 (0.2)	2	0.3
Male	2 (0.6)	2	0.4	0		
Aortic valve incompetence						
Female	0			0		
Male	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Aortic valve sclerosis						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Mitral valve incompetence						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Tricuspid valve incompetence						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Cardiac neoplasms						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Pericardial cyst						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Myocardial disorders						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			1 (0.6)	1	0.5
Left ventricular hypertrophy						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Cardiomegaly						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Cardiomyopathy						
Female	0			0		
Male	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Myocarditis								
Female	0				1	(0.2)	1	0.2
Male	0				0			
Pericardial disorders								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Pericardial disease								
Female	1	(0.1)	1	<0.1	0			
Male	0				0			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)								
Female	34	(3.6)	38	3.1	21	(4.2)	21	3.4
Male	12	(3.4)	14	3.0	4	(2.5)	6	2.9
Cutaneous neoplasms benign								
Female	7	(0.7)	9	0.7	4	(0.8)	4	0.6
Male	3	(0.9)	5	1.1	2	(1.3)	2	1.0
Melanocytic naevus								
Female	4	(0.4)	4	0.3	2	(0.4)	2	0.3
Male	3	(0.9)	4	0.9	0			
Acrochordon								
Female	1	(0.1)	1	<0.1	1	(0.2)	1	0.2
Male	1	(0.3)	1	0.2	0			
Seborrhoeic keratosis								
Female	2	(0.2)	2	0.2	0			
Male	0				1	(0.6)	1	0.5
Dysplastic naevus								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Skin papilloma						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Pyogenic granuloma						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Soft tissue neoplasms benign						
Female	3 (0.3)	3	0.2	2 (0.4)	2	0.3
Male	2 (0.6)	2	0.4	0		
Lipoma						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	2 (0.6)	2	0.4	0		
Leiomyoma						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Reproductive neoplasms female benign						
Female	6 (0.6)	6	0.5	4 (0.8)	4	0.6
Male	0			0		
Uterine leiomyoma						
Female	5 (0.5)	5	0.4	4 (0.8)	4	0.6
Male	0			0		
Ovarian adenoma						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Skin neoplasms malignant and unspecified						
Female	3 (0.3)	3	0.2	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Basal cell carcinoma						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Malignant melanoma						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Malignant melanoma in situ						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Neoplasm skin						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Breast neoplasms malignant and unspecified (incl nipple)						
Female	4 (0.4)	4	0.3	3 (0.6)	3	0.5
Male	0			0		
Intraductal proliferative breast lesion						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Breast cancer						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Invasive ductal breast carcinoma						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Lobular breast carcinoma in situ						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Phyllodes tumour						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Miscellaneous and site unspecified neoplasms malignant and unspecified						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Neoplasm						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Squamous cell carcinoma						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Gastrointestinal neoplasms benign						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Colon adenoma						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Gastrointestinal neoplasms malignant and unspecified						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Gastrointestinal stromal tumour						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Hepatobiliary neoplasms malignant and unspecified						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Hepatic neoplasm						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Miscellaneous and site unspecified neoplasms benign						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Fibroma						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Adenoma benign						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Reproductive neoplasms male malignant and unspecified						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Prostate cancer						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Soft tissue neoplasms malignant and unspecified						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Dermatofibrosarcoma protuberans						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Breast neoplasms benign (incl nipple)						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	0			0		
Benign breast neoplasm						
Female	2 (0.2)	2	0.2	2 (0.4)	2	0.3
Male	0			0		
Endocrine neoplasms benign						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Benign neoplasm of thyroid gland						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Parathyroid tumour benign						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Hepatic and biliary neoplasms benign						
Female	2 (0.2)	2	0.2	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Haemangioma of liver						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Endocrine neoplasms malignant and unspecified						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Papillary thyroid cancer						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Reproductive neoplasms female malignant and unspecified						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Cervix carcinoma stage 0						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Skeletal neoplasms benign						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Haemangioma of bone						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Leukaemias						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Hairy cell leukaemia						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
Female	0			1	(0.2)	1 0.2
Male	0			0		
Nervous system neoplasms malignant and unspecified NEC						
Female	0			1	(0.2)	1 0.2
Male	0			0		
Glioblastoma						
Female	0			1	(0.2)	1 0.2
Male	0			0		
Ocular neoplasms						
Female	0			0		
Male	0			1	(0.6)	1 0.5
Eyelid haemangioma						
Female	0			0		
Male	0			1	(0.6)	1 0.5
Plasma cell neoplasms						
Female	0			0		
Male	0			1	(0.6)	1 0.5
Paraproteinaemia						
Female	0			0		
Male	0			1	(0.6)	1 0.5
Renal and urinary tract neoplasms benign						
Female	0			0		
Male	0			1	(0.6)	1 0.5
Kidney angiomyolipoma						
Female	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			1 (0.6)	1	0.5
Renal and urinary tract neoplasms malignant and unspecified						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Urinary tract neoplasm						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Renal and urinary disorders						
Female	29 (3.0)	37	3.0	17 (3.4)	19	3.0
Male	12 (3.4)	14	3.0	5 (3.2)	5	2.4
Urinary tract signs and symptoms						
Female	20 (2.1)	23	1.9	6 (1.2)	7	1.1
Male	6 (1.7)	6	1.3	2 (1.3)	2	1.0
Dysuria						
Female	8 (0.8)	10	0.8	0		
Male	1 (0.3)	1	0.2	0		
Haematuria						
Female	1 (0.1)	1	<0.1	0		
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Renal pain						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Urine flow decreased						
Female	0			0		
Male	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Urine odour abnormal						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Chromaturia						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Pollakiuria						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Stress urinary incontinence						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Bladder pain						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Micturition urgency						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Nocturia						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Renal colic						
Female	1 (0.1)	2	0.2	0		
Male	0			0		
Polyuria						
Female	0			1 (0.2)	1	0.2
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Urinary incontinence						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Urinary retention						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Urolithiases						
Female	6 (0.6)	6	0.5	5 (1.0)	5	0.8
Male	5 (1.4)	6	1.3	1 (0.6)	1	0.5
Nephrolithiasis						
Female	4 (0.4)	4	0.3	5 (1.0)	5	0.8
Male	4 (1.1)	4	0.9	1 (0.6)	1	0.5
Calculus urinary						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	0		
Ureterolithiasis						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Renal disorders (excl nephropathies)						
Female	5 (0.5)	7	0.6	5 (1.0)	6	1.0
Male	2 (0.6)	2	0.4	2 (1.3)	2	1.0
Renal cyst						
Female	1 (0.1)	1	<0.1	3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Acute kidney injury						
Female	3 (0.3)	3	0.2	0		
Male	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hydronephrosis						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Chronic kidney disease						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Nephrectasia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Renal impairment						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Hypertensive nephropathy						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Bladder and bladder neck disorders (excl calculi)						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Cystitis noninfective						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Urethral disorders (excl calculi)						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Urethritis noninfective						
Female	0			1 (0.2)	1	0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Eye disorders						
Female	34 (3.6)	48	3.9	21 (4.2)	25	4.0
Male	10 (2.8)	10	2.1	3 (1.9)	6	2.9
Vision disorders						
Female	12 (1.3)	15	1.2	3 (0.6)	3	0.5
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Vision blurred						
Female	6 (0.6)	6	0.5	1 (0.2)	1	0.2
Male	0			0		
Diplopia						
Female	2 (0.2)	3	0.2	0		
Male	1 (0.3)	1	0.2	0		
Myopia						
Female	3 (0.3)	3	0.2	0		
Male	0			1 (0.6)	1	0.5
Visual impairment						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Anisometropia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Astigmatism						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Photopsia						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Scintillating scotoma						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Eye disorders NEC						
Female	5 (0.5)	5	0.4	5 (1.0)	5	0.8
Male	3 (0.9)	3	0.6	1 (0.6)	1	0.5
Dry eye						
Female	1 (0.1)	1	<0.1	3 (0.6)	3	0.5
Male	3 (0.9)	3	0.6	1 (0.6)	1	0.5
Eyelid disorder						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Eye pain						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Lacrimation increased						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Ocular discomfort						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Ocular infections, irritations and inflammations						
Female	6 (0.6)	8	0.6	5 (1.0)	7	1.1
Male	2 (0.6)	2	0.4	2 (1.3)	3	1.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Eye allergy						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Eye discharge						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Eye pruritus						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Conjunctival irritation						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Conjunctivitis allergic						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Eczema eyelids						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Meibomian gland dysfunction						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Ocular hyperaemia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Swelling of eyelid						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Blepharitis						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Conjunctival hyperaemia						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Erythema of eyelid						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Eye inflammation						
Female	0			1 (0.2)	2	0.3
Male	0			0		
Eye irritation						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Keratitis						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Ulcerative keratitis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Anterior eye structural change, deposit and degeneration						
Female	7 (0.7)	8	0.6	2 (0.4)	3	0.5
Male	0			1 (0.6)	1	0.5
Cataract						
Female	6 (0.6)	7	0.6	1 (0.2)	2	0.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
Male	0			0		
Xerophthalmia						
Female	1	(0.1)	1 <0.1	0		
Male	0			0		
Ectropion						
Female	0			1	(0.2)	1 0.2
Male	0			0		
Pterygium						
Female	0			0		
Male	0			1	(0.6)	1 0.5
Ocular haemorrhages and vascular disorders NEC						
Female	1	(0.1)	1 <0.1	1	(0.2)	1 0.2
Male	2	(0.6)	2 0.4	0		
Optic ischaemic neuropathy						
Female	1	(0.1)	1 <0.1	0		
Male	1	(0.3)	1 0.2	0		
Eyelid haematoma						
Female	0			0		
Male	1	(0.3)	1 0.2	0		
Conjunctival haemorrhage						
Female	0			1	(0.2)	1 0.2
Male	0			0		
Glaucoma and ocular hypertension						
Female	4	(0.4)	4 0.3	1	(0.2)	2 0.3
Male	0			0		
Glaucoma						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	4 (0.4)	4	0.3	1 (0.2)	2	0.3
Male	0			0		
Ocular structural change, deposit and degeneration NEC						
Female	3 (0.3)	4	0.3	2 (0.4)	2	0.3
Male	0			0		
Macular degeneration						
Female	3 (0.3)	4	0.3	0		
Male	0			0		
Vitreous detachment						
Female	0			2 (0.4)	2	0.3
Male	0			0		
Ocular neuromuscular disorders						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Blepharospasm						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Retina, choroid and vitreous haemorrhages and vascular disorders						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Retinopathy						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Retinal aneurysm						
Female	0			1 (0.2)	1	0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Ocular sensory symptoms NEC						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Asthenopia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Blood and lymphatic system disorders						
Female	22 (2.3)	22	1.8	12 (2.4)	17	2.7
Male	13 (3.7)	15	3.2	4 (2.5)	4	2.0
Anaemias nonhaemolytic and marrow depression						
Female	16 (1.7)	16	1.3	9 (1.8)	10	1.6
Male	8 (2.3)	9	1.9	1 (0.6)	1	0.5
Anaemia						
Female	13 (1.4)	13	1.0	8 (1.6)	9	1.4
Male	6 (1.7)	7	1.5	1 (0.6)	1	0.5
Iron deficiency anaemia						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Pernicious anaemia						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Blood loss anaemia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hypochromic anaemia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Pancytopenia						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Spleen, lymphatic and reticuloendothelial system disorders						
Female	5 (0.5)	5	0.4	3 (0.6)	4	0.6
Male	2 (0.6)	2	0.4	0		
Lymphadenopathy						
Female	3 (0.3)	3	0.2	1 (0.2)	2	0.3
Male	1 (0.3)	1	0.2	0		
Splenomegaly						
Female	0			2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	0		
Hypersplenism						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Splenic haemorrhage						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
White blood cell disorders						
Female	1 (0.1)	1	<0.1	0		
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Leukocytosis						
Female	1 (0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Eosinophilia						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Platelet disorders						
Female	0			2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	2 (1.3)	2	1.0
Thrombocytopenia						
Female	0			2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	2 (1.3)	2	1.0
Red blood cell disorders						
Female	0			1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Polycythaemia						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Microcytosis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Ear and labyrinth disorders						
Female	38 (4.0)	45	3.6	21 (4.2)	25	4.0
Male	7 (2.0)	11	2.4	3 (1.9)	4	2.0
Inner ear and VIIIth cranial nerve disorders						
Female	18 (1.9)	18	1.5	15 (3.0)	18	2.9
Male	4 (1.1)	8	1.7	3 (1.9)	4	2.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Vertigo						
Female	14 (1.5)	14	1.1	10 (2.0)	10	1.6
Male	3 (0.9)	3	0.6	2 (1.3)	3	1.5
Vertigo positional						
Female	1 (0.1)	1	<0.1	2 (0.4)	3	0.5
Male	2 (0.6)	3	0.6	1 (0.6)	1	0.5
Tinnitus						
Female	2 (0.2)	2	0.2	2 (0.4)	3	0.5
Male	1 (0.3)	2	0.4	0		
Meniere's disease						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Motion sickness						
Female	0			1 (0.2)	2	0.3
Male	0			0		
Aural disorders NEC						
Female	14 (1.5)	15	1.2	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	0		
Ear pain						
Female	12 (1.3)	13	1.0	2 (0.4)	2	0.3
Male	0			0		
Ear discomfort						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Ear congestion						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Middle ear disorders (excl congenital)						
Female	5 (0.5)	6	0.5	2 (0.4)	2	0.3
Male	1 (0.3)	1	0.2	0		
Eustachian tube dysfunction						
Female	3 (0.3)	4	0.3	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Eustachian tube disorder						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Tympanic membrane disorder						
Female	0			1 (0.2)	1	0.2
Male	0			0		
External ear disorders (excl congenital)						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	1 (0.3)	1	0.2	0		
Cerumen impaction						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	0		
Excessive cerumen production						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Hearing disorders						
Female	4 (0.4)	4	0.3	2 (0.4)	2	0.3
Male	0			0		
Deafness neurosensory						
Female	2 (0.2)	2	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Hypoacusis						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Sudden hearing loss						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Deafness						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Hyperacusis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Hepatobiliary disorders						
Female	39 (4.1)	49	3.9	11 (2.2)	12	1.9
Male	5 (1.4)	7	1.5	2 (1.3)	2	1.0
Gallbladder disorders						
Female	27 (2.8)	32	2.6	5 (1.0)	5	0.8
Male	4 (1.1)	6	1.3	0		
Cholelithiasis						
Female	19 (2.0)	20	1.6	4 (0.8)	4	0.6
Male	4 (1.1)	4	0.9	0		
Cholecystitis acute						
Female	2 (0.2)	2	0.2	0		
Male	2 (0.6)	2	0.4	0		
Cholecystitis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	4 (0.4)	4	0.3	1 (0.2)	1	0.2
Male	0			0		
Gallbladder disorder						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Cholecystitis chronic						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Biliary dyskinesia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Hepatic and hepatobiliary disorders						
Female	12 (1.3)	15	1.2	7 (1.4)	7	1.1
Male	1 (0.3)	1	0.2	2 (1.3)	2	1.0
Hepatic steatosis						
Female	5 (0.5)	5	0.4	5 (1.0)	5	0.8
Male	1 (0.3)	1	0.2	2 (1.3)	2	1.0
Hepatic cyst						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Hepatic function abnormal						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Granulomatous liver disease						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Hepatic pain						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Hypertransaminasaemia						
Female	1 (0.1)	3	0.2	0		
Male	0			0		
Nonalcoholic fatty liver disease						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Portal vein thrombosis						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Bile duct disorders						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Bile duct stone						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Biliary colic						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Immune system disorders						
Female	22 (2.3)	22	1.8	18 (3.6)	20	3.2
Male	6 (1.7)	6	1.3	3 (1.9)	3	1.5
Allergic conditions						
Female	21 (2.2)	21	1.7	18 (3.6)	20	3.2
Male	6 (1.7)	6	1.3	3 (1.9)	3	1.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Seasonal allergy						
Female	11 (1.2)	11	0.9	12 (2.4)	12	1.9
Male	4 (1.1)	4	0.9	2 (1.3)	2	1.0
Allergy to arthropod bite						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	0		
Food allergy						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Hypersensitivity						
Female	3 (0.3)	3	0.2	6 (1.2)	6	1.0
Male	0			0		
Drug hypersensitivity						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Allergy to arthropod sting						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Rubber sensitivity						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Mite allergy						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Multiple allergies						
Female	0			1 (0.2)	1	0.2
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Immune disorders NEC						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Immunisation reaction						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Surgical and medical procedures						
Female	17 (1.8)	18	1.5	6 (1.2)	6	1.0
Male	1 (0.3)	1	0.2	2 (1.3)	2	1.0
Head and neck therapeutic procedures						
Female	5 (0.5)	5	0.4	0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Tooth extraction						
Female	1 (0.1)	1	<0.1	0		
Male	1 (0.3)	1	0.2	0		
Dental operation						
Female	2 (0.2)	2	0.2	0		
Male	0			1 (0.6)	1	0.5
Dental implantation						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Sinus operation						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Therapeutic procedures and supportive care NEC						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	4 (0.4)	4	0.3	1 (0.2)	1	0.2
Male	0			0		
Polypectomy						
Female	2 (0.2)	2	0.2	1 (0.2)	1	0.2
Male	0			0		
Cyst removal						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Spinal anaesthesia						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Skin and subcutaneous tissue therapeutic procedures						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Acrochordon excision						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Skin neoplasm excision						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Bone and joint therapeutic procedures						
Female	1 (0.1)	1	<0.1	2 (0.4)	2	0.3
Male	0			0		
Synovial cyst removal						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Bone prosthesis insertion						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Hip surgery						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Eye therapeutic procedures						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Glaucoma surgery						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Gastrointestinal therapeutic procedures						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			1 (0.6)	1	0.5
Gastric bypass						
Female	1 (0.1)	1	<0.1	0		
Male	0			1 (0.6)	1	0.5
Abdominoplasty						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Hepatobiliary therapeutic procedures						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Cholecystectomy						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Nervous system, skull and spine therapeutic procedures						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Intervertebral disc operation						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Obstetric and gynaecological therapeutic procedures						
Female	1 (0.1)	1	<0.1	1 (0.2)	1	0.2
Male	0			0		
Abortion induced						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Ovarian operation						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Soft tissue therapeutic procedures						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Lipoma excision						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Endocrine disorders						
Female	12 (1.3)	14	1.1	5 (1.0)	5	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	2 (0.6)	2	0.4	1 (0.6)	2	1.0
Thyroid gland disorders						
Female	11 (1.2)	13	1.0	5 (1.0)	5	0.8
Male	2 (0.6)	2	0.4	1 (0.6)	1	0.5
Hypothyroidism						
Female	3 (0.3)	3	0.2	3 (0.6)	3	0.5
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Goitre						
Female	2 (0.2)	2	0.2	0		
Male	1 (0.3)	1	0.2	0		
Hyperthyroidism						
Female	3 (0.3)	4	0.3	0		
Male	0			0		
Thyroid mass						
Female	3 (0.3)	3	0.2	1 (0.2)	1	0.2
Male	0			0		
Thyroid cyst						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Primary hyperthyroidism						
Female	0			1 (0.2)	1	0.2
Male	0			0		
Adrenal gland disorders						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Hyperadrenocorticism						
Female	1 (0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Male	0			0		
Endocrine disorders of gonadal function						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Hypogonadism						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Social circumstances						
Female	5 (0.5)	5	0.4	0		
Male	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Lifestyle issues						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Bedridden						
Female	0			0		
Male	1 (0.3)	1	0.2	0		
Age related factors						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Menopause						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Economic and housing issues						
Female	2 (0.2)	2	0.2	0		
Male	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Stress at work						
Female	2 (0.2)	2	0.2	0		
Male	0			1 (0.6)	1	0.5
Family issues						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Family stress						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Pregnancy, puerperium and perinatal conditions						
Female	5 (0.5)	5	0.4	0		
Male	0			0		
Abortions and stillbirth						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Abortion spontaneous						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Abortion						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Maternal complications of pregnancy						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Ectopic pregnancy						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Morning sickness						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Congenital, familial and genetic disorders						
Female	4 (0.4)	4	0.3	0		
Male	0			1 (0.6)	1	0.5
Metabolic and nutritional disorders congenital						
Female	3 (0.3)	3	0.2	0		
Male	0			0		
Type V hyperlipidaemia						
Female	2 (0.2)	2	0.2	0		
Male	0			0		
Gilbert's syndrome						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Musculoskeletal and connective tissue disorders congenital						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Carpus curvus						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Skin and subcutaneous tissue disorders congenital						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Dermoid cyst						
Female	0			0		
Male	0			1 (0.6)	1	0.5
Product issues						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Device issues						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		
Device expulsion						
Female	1 (0.1)	1	<0.1	0		
Male	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

3 Adverse events by sex - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
Female	202	268.3			222	297.0			190	253.9		
Male	200	261.5			181	236.1			212	274.4		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Events												
Female	167	(82.7)	1047	390.3	204	(91.9)	1313	442.1	150	(78.9)	775	305.2
Male	162	(81.0)	812	310.5	149	(82.3)	884	374.5	159	(75.0)	613	223.4
Serious												
Yes												
Female	12	(5.9)	17	6.3	22	(9.9)	45	15.2	13	(6.8)	18	7.1
Male	19	(9.5)	36	13.8	18	(9.9)	26	11.0	24	(11.3)	35	12.8
No												
Female	167	(82.7)	1030	383.9	204	(91.9)	1268	427.0	149	(78.4)	757	298.1
Male	159	(79.5)	776	296.7	148	(81.8)	858	363.5	158	(74.5)	578	210.6
Severity												
Severe												
Female	9	(4.5)	15	5.6	13	(5.9)	33	11.1	13	(6.8)	19	7.5
Male	13	(6.5)	28	10.7	14	(7.7)	18	7.6	15	(7.1)	20	7.3
Moderate												
Female	75	(37.1)	180	67.1	109	(49.1)	321	108.1	66	(34.7)	157	61.8
Male	60	(30.0)	135	51.6	64	(35.4)	187	79.2	52	(24.5)	107	39.0
Mild												
Female	159	(78.7)	852	317.6	186	(83.8)	959	322.9	137	(72.1)	599	235.9
Male	147	(73.5)	649	248.2	142	(78.5)	679	287.6	142	(67.0)	486	177.1

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by sex - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Relationship to trial product												
Missing												
Female	4	(2.0)	5	1.9	7	(3.2)	7	2.4	1	(0.5)	1	0.4
Male	6	(3.0)	6	2.3	3	(1.7)	3	1.3	5	(2.4)	6	2.2
Probable												
Female	73	(36.1)	211	78.7	95	(42.8)	257	86.5	33	(17.4)	56	22.1
Male	60	(30.0)	133	50.9	74	(40.9)	199	84.3	29	(13.7)	44	16.0
Possible												
Female	83	(41.1)	248	92.4	117	(52.7)	338	113.8	44	(23.2)	104	41.0
Male	70	(35.0)	159	60.8	65	(35.9)	196	83.0	49	(23.1)	66	24.1
Unlikely												
Female	148	(73.3)	583	217.3	169	(76.1)	711	239.4	143	(75.3)	614	241.8
Male	148	(74.0)	514	196.6	132	(72.9)	486	205.9	146	(68.9)	497	181.1
Outcome												
Fatal												
Female	0				0				0			
Male	0				1	(0.6)	1	0.4	1	(0.5)	1	0.4
Recovered												
Female	161	(79.7)	867	323.2	194	(87.4)	1079	363.3	140	(73.7)	606	238.7
Male	154	(77.0)	636	243.2	139	(76.8)	733	310.5	145	(68.4)	448	163.3
Recovering												
Female	11	(5.4)	17	6.3	10	(4.5)	18	6.1	9	(4.7)	11	4.3
Male	8	(4.0)	15	5.7	7	(3.9)	8	3.4	8	(3.8)	8	2.9
Recovered With Sequelae												
Female	1	(0.5)	1	0.4	3	(1.4)	3	1.0	1	(0.5)	1	0.4
Male	4	(2.0)	4	1.5	2	(1.1)	2	0.8	0			
Not Recovered												
Female	70	(34.7)	162	60.4	97	(43.7)	209	70.4	76	(40.0)	156	61.4

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by sex - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Outcome												
Not Recovered												
Male	77	(38.5)	157	60.0	66	(36.5)	136	57.6	80	(37.7)	154	56.1
Unknown												
Female	0				1	(0.5)	4	1.3	1	(0.5)	1	0.4
Male	0				3	(1.7)	4	1.7	2	(0.9)	2	0.7
Leading to												
Permanent treatment discontinuation												
Female	8	(4.0)	9	3.4	16	(7.2)	23	7.7	6	(3.2)	6	2.4
Male	12	(6.0)	14	5.4	9	(5.0)	11	4.7	8	(3.8)	12	4.4
Temporary interruption of trial product												
Female	14	(6.9)	28	10.4	19	(8.6)	52	17.5	7	(3.7)	10	3.9
Male	12	(6.0)	19	7.3	18	(9.9)	38	16.1	8	(3.8)	10	3.6
Dose reduction of trial product												
Female	9	(4.5)	11	4.1	19	(8.6)	38	12.8	3	(1.6)	3	1.2
Male	9	(4.5)	17	6.5	16	(8.8)	28	11.9	0			

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

4 Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N		PYE		N		PYE		N		PYE	
Female	202		268.3		222		297.0		190		253.9	
Male	200		261.5		181		236.1		212		274.4	
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Adverse events												
Female	167	(82.7)	1047	390.3	204	(91.9)	1313	442.1	150	(78.9)	775	305.2
Male	162	(81.0)	812	310.5	149	(82.3)	884	374.5	159	(75.0)	613	223.4
Gastrointestinal disorders												
Female	132	(65.3)	446	166.2	155	(69.8)	554	186.5	72	(37.9)	154	60.7
Male	99	(49.5)	278	106.3	101	(55.8)	370	156.7	66	(31.1)	108	39.4
Gastrointestinal signs and symptoms												
Female	114	(56.4)	291	108.5	122	(55.0)	368	123.9	43	(22.6)	75	29.5
Male	73	(36.5)	141	53.9	78	(43.1)	233	98.7	33	(15.6)	40	14.6
Nausea												
Female	86	(42.6)	137	51.1	83	(37.4)	149	50.2	23	(12.1)	30	11.8
Male	43	(21.5)	61	23.3	53	(29.3)	100	42.4	14	(6.6)	15	5.5
Vomiting												
Female	42	(20.8)	76	28.3	58	(26.1)	130	43.8	7	(3.7)	8	3.2
Male	12	(6.0)	17	6.5	30	(16.6)	58	24.6	4	(1.9)	4	1.5
Dyspepsia												
Female	13	(6.4)	13	4.8	14	(6.3)	16	5.4	1	(0.5)	1	0.4
Male	14	(7.0)	14	5.4	11	(6.1)	14	5.9	4	(1.9)	4	1.5
Abdominal distension												
Female	5	(2.5)	8	3.0	12	(5.4)	16	5.4	8	(4.2)	10	3.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	4 (2.0)	4	1.5	12 (6.6)	14	5.9	3 (1.4)	3	1.1
Flatulence									
Female	10 (5.0)	12	4.5	5 (2.3)	7	2.4	5 (2.6)	6	2.4
Male	11 (5.5)	13	5.0	11 (6.1)	14	5.9	2 (0.9)	3	1.1
Eructation									
Female	7 (3.5)	9	3.4	9 (4.1)	11	3.7	0		
Male	4 (2.0)	7	2.7	7 (3.9)	10	4.2	1 (0.5)	1	0.4
Abdominal pain upper									
Female	8 (4.0)	8	3.0	10 (4.5)	14	4.7	8 (4.2)	10	3.9
Male	3 (1.5)	3	1.1	6 (3.3)	7	3.0	3 (1.4)	3	1.1
Abdominal discomfort									
Female	7 (3.5)	9	3.4	7 (3.2)	9	3.0	4 (2.1)	4	1.6
Male	8 (4.0)	8	3.1	6 (3.3)	6	2.5	3 (1.4)	3	1.1
Abdominal pain									
Female	11 (5.4)	13	4.8	8 (3.6)	10	3.4	4 (2.1)	4	1.6
Male	6 (3.0)	7	2.7	5 (2.8)	5	2.1	1 (0.5)	1	0.4
Abdominal pain lower									
Female	2 (1.0)	2	0.7	2 (0.9)	2	0.7	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	2 (0.9)	2	0.7
Regurgitation									
Female	0			2 (0.9)	2	0.7	0		
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Abnormal faeces									
Female	0			0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Gastrointestinal pain									
Female	1 (0.5)	1	0.4	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			1 (0.6)	1	0.4	0		
Gastrointestinal sounds abnormal									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Aerophagia									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Epigastric discomfort									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Abdominal rigidity									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Anal incontinence									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Breath odour									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Dysphagia									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	0			0		
Faeces discoloured									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Faeces soft									
Female	1 (0.5)	1	0.4	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	0			0		
Retching									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Gastrointestinal motility and defaecation conditions									
Female	68 (33.7)	135	50.3	81 (36.5)	135	45.5	38 (20.0)	56	22.1
Male	57 (28.5)	108	41.3	62 (34.3)	104	44.1	32 (15.1)	45	16.4
Diarrhoea									
Female	46 (22.8)	90	33.5	51 (23.0)	81	27.3	23 (12.1)	32	12.6
Male	43 (21.5)	68	26.0	35 (19.3)	60	25.4	25 (11.8)	34	12.4
Constipation									
Female	30 (14.9)	39	14.5	39 (17.6)	47	15.8	14 (7.4)	18	7.1
Male	21 (10.5)	31	11.9	31 (17.1)	35	14.8	8 (3.8)	8	2.9
Gastrooesophageal reflux disease									
Female	6 (3.0)	6	2.2	5 (2.3)	6	2.0	4 (2.1)	4	1.6
Male	7 (3.5)	8	3.1	7 (3.9)	7	3.0	3 (1.4)	3	1.1
Change of bowel habit									
Female	0			0			1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	0		
Gastrointestinal motility disorder									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Irritable bowel syndrome									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Gastrointestinal hypermotility									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Gastrooesophageal sphincter insufficiency									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Gastrointestinal conditions NEC									
Female	4 (2.0)	5	1.9	12 (5.4)	15	5.1	5 (2.6)	5	2.0
Male	3 (1.5)	3	1.1	6 (3.3)	6	2.5	1 (0.5)	1	0.4
Hyperchlorhydria									
Female	3 (1.5)	4	1.5	8 (3.6)	11	3.7	2 (1.1)	2	0.8
Male	2 (1.0)	2	0.8	3 (1.7)	3	1.3	0		
Food poisoning									
Female	1 (0.5)	1	0.4	2 (0.9)	2	0.7	0		
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	0		
Gastrointestinal disorder									
Female	0			2 (0.9)	2	0.7	0		
Male	0			1 (0.6)	1	0.4	0		
Barrett's oesophagus									
Female	0			0			2 (1.1)	2	0.8
Male	0			0			0		
Gastric disorder									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Gastrointestinal melanosis									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gastrointestinal inflammatory conditions									
Female	6 (3.0)	6	2.2	13 (5.9)	16	5.4	3 (1.6)	5	2.0
Male	3 (1.5)	3	1.1	4 (2.2)	4	1.7	3 (1.4)	3	1.1
Gastritis									
Female	4 (2.0)	4	1.5	8 (3.6)	10	3.4	3 (1.6)	5	2.0
Male	2 (1.0)	2	0.8	3 (1.7)	3	1.3	1 (0.5)	1	0.4
Enteritis									
Female	0			3 (1.4)	3	1.0	0		
Male	0			0			1 (0.5)	1	0.4
Enterocolitis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			1 (0.6)	1	0.4	0		
Chronic gastritis									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Duodenitis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Colitis									
Female	2 (1.0)	2	0.7	0			0		
Male	0			0			0		
Dental and gingival conditions									
Female	4 (2.0)	5	1.9	5 (2.3)	6	2.0	3 (1.6)	3	1.2
Male	4 (2.0)	4	1.5	5 (2.8)	5	2.1	4 (1.9)	4	1.5
Toothache									
Female	3 (1.5)	4	1.5	3 (1.4)	3	1.0	2 (1.1)	2	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	0		
Dental caries									
Female	0			2 (0.9)	2	0.7	1 (0.5)	1	0.4
Male	2 (1.0)	2	0.8	2 (1.1)	2	0.8	4 (1.9)	4	1.5
Gingival swelling									
Female	1 (0.5)	1	0.4	0			0		
Male	0			1 (0.6)	1	0.4	0		
Tooth deposit									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Periodontal disease									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Gastrointestinal vascular conditions									
Female	0			3 (1.4)	3	1.0	0		
Male	3 (1.5)	5	1.9	6 (3.3)	6	2.5	2 (0.9)	2	0.7
Haemorrhoids									
Female	0			3 (1.4)	3	1.0	0		
Male	2 (1.0)	3	1.1	6 (3.3)	6	2.5	1 (0.5)	1	0.4
Haemorrhoids thrombosed									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Varices oesophageal									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Salivary gland conditions									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	3 (1.7)	4	1.7	1 (0.5)	1	0.4
Dry mouth									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	0		
Salivary hypersecretion									
Female	0			0			0		
Male	0			1 (0.6)	2	0.8	0		
Parotid gland enlargement									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Noninfective sialoadenitis									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Abdominal hernias and other abdominal wall conditions									
Female	0			2 (0.9)	2	0.7	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	3 (1.4)	3	1.1
Abdominal hernia									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Umbilical hernia									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Abdominal wall haematoma									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			0		
Hiatus hernia									

Adverse events with onset prior to randomisation are not included.
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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Inguinal hernia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Gastrointestinal haemorrhages NEC									
Female	1 (0.5)	1	0.4	4 (1.8)	4	1.3	2 (1.1)	2	0.8
Male	2 (1.0)	2	0.8	0			0		
Haematochezia									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	2 (1.0)	2	0.8	0			0		
Intra-abdominal haemorrhage									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Mallory-Weiss syndrome									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Upper gastrointestinal haemorrhage									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Intra-abdominal haematoma									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Rectal haemorrhage									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Benign neoplasms gastrointestinal									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	3 (1.5)	4	1.5	2 (1.1)	2	0.8	2 (0.9)	2	0.7
Gastric polyps									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Large intestine polyp									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	3 (1.5)	3	1.1	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Oral soft tissue conditions									
Female	0			2 (0.9)	2	0.7	2 (1.1)	2	0.8
Male	0			0			2 (0.9)	2	0.7
Mouth ulceration									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Stomatitis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Aphthous ulcer									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Lip swelling									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Odynophagia									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Anal and rectal conditions NEC									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Anal fissure									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Exocrine pancreas conditions									
Female	0			0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Pancreatitis acute									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Obstructive pancreatitis									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Pancreatic cyst									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Gastrointestinal stenosis and obstruction									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Small intestinal obstruction									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Gastrointestinal ulceration and perforation									
Female	0			0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Gastritis erosive									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Diverticular perforation									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Gastric ulcer									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Diverticular disorders									
Female	0			1 (0.5)	1	0.3	0		
Male	2 (1.0)	2	0.8	0			3 (1.4)	3	1.1
Diverticulum intestinal									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			0		
Diverticulum									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			3 (1.4)	3	1.1
Malabsorption conditions									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Malabsorption									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Peritoneal and retroperitoneal conditions									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Retroperitoneal mass									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Tongue conditions									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Glossodynia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Infections and infestations									
Female	81 (40.1)	170	63.4	108 (48.6)	202	68.0	96 (50.5)	222	87.4
Male	85 (42.5)	148	56.6	71 (39.2)	143	60.6	79 (37.3)	137	49.9
Infections - pathogen unspecified									
Female	75 (37.1)	137	51.1	94 (42.3)	166	55.9	85 (44.7)	176	69.3
Male	71 (35.5)	113	43.2	68 (37.6)	123	52.1	62 (29.2)	105	38.3
Nasopharyngitis									
Female	17 (8.4)	24	8.9	30 (13.5)	47	15.8	29 (15.3)	49	19.3
Male	30 (15.0)	45	17.2	38 (21.0)	68	28.8	30 (14.2)	43	15.7
Upper respiratory tract infection									
Female	17 (8.4)	28	10.4	25 (11.3)	28	9.4	23 (12.1)	33	13.0
Male	20 (10.0)	26	9.9	17 (9.4)	20	8.5	15 (7.1)	17	6.2
Bronchitis									
Female	7 (3.5)	8	3.0	8 (3.6)	8	2.7	9 (4.7)	10	3.9
Male	3 (1.5)	3	1.1	6 (3.3)	8	3.4	4 (1.9)	5	1.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gastroenteritis									
Female	10 (5.0)	14	5.2	10 (4.5)	10	3.4	8 (4.2)	10	3.9
Male	14 (7.0)	14	5.4	4 (2.2)	5	2.1	5 (2.4)	5	1.8
Sinusitis									
Female	6 (3.0)	6	2.2	10 (4.5)	14	4.7	7 (3.7)	9	3.5
Male	0			4 (2.2)	5	2.1	4 (1.9)	4	1.5
Urinary tract infection									
Female	17 (8.4)	21	7.8	11 (5.0)	14	4.7	9 (4.7)	12	4.7
Male	0			2 (1.1)	2	0.8	3 (1.4)	4	1.5
Conjunctivitis									
Female	1 (0.5)	1	0.4	5 (2.3)	5	1.7	3 (1.6)	4	1.6
Male	2 (1.0)	4	1.5	0			1 (0.5)	1	0.4
Cystitis									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	1 (0.5)	2	0.8
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	2 (0.9)	3	1.1
Paronychia									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Tonsillitis									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	4 (2.1)	4	1.6
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Pneumonia									
Female	1 (0.5)	1	0.4	4 (1.8)	5	1.7	5 (2.6)	5	2.0
Male	1 (0.5)	1	0.4	0			0		
Lower respiratory tract infection									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	5 (2.4)	5	1.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Pharyngitis									
Female	0			2 (0.9)	2	0.7	4 (2.1)	4	1.6
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	3 (1.4)	3	1.1
Gastrointestinal infection									
Female	1 (0.5)	1	0.4	3 (1.4)	4	1.3	1 (0.5)	1	0.4
Male	0			0			0		
Tooth infection									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	2 (1.0)	3	1.1	2 (1.1)	2	0.8	0		
Otitis externa									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	3 (1.5)	3	1.1	1 (0.6)	1	0.4	0		
Acute sinusitis									
Female	4 (2.0)	4	1.5	2 (0.9)	2	0.7	3 (1.6)	5	2.0
Male	0			0			0		
Localised infection									
Female	1 (0.5)	1	0.4	2 (0.9)	2	0.7	0		
Male	0			0			0		
Chronic sinusitis									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Infected dermal cyst									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Post procedural infection									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Respiratory tract infection									
Female	0			0			4 (2.1)	4	1.6
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Skin infection									
Female	0			0			1 (0.5)	1	0.4
Male	0			1 (0.6)	2	0.8	0		
Abscess									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Appendicitis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			1 (0.5)	1	0.4
Breast abscess									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Diverticulitis									
Female	0			1 (0.5)	1	0.3	3 (1.6)	3	1.2
Male	1 (0.5)	1	0.4	0			0		
Implant site infection									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Kidney infection									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Mastitis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Otitis media acute									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			0		
Periodontitis									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	2	0.8
Male	0			0			0		
Rhinitis									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			3 (1.4)	3	1.1
Tooth abscess									
Female	4 (2.0)	4	1.5	1 (0.5)	1	0.3	1 (0.5)	2	0.8
Male	0			0			0		
Urosepsis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Vulvovaginitis									
Female	1 (0.5)	1	0.4	1 (0.5)	2	0.7	0		
Male	0			0			0		
Colonic abscess									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Ear infection									
Female	0			0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	0			0		
Empyema									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Eye infection									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	0			0		
Gingival abscess									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Gingivitis									
Female	0			0			2 (1.1)	2	0.8
Male	0			0			1 (0.5)	1	0.4
Hordeolum									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	0			0			0		
Joint abscess									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Labyrinthitis									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Laryngitis									
Female	2 (1.0)	3	1.1	0			0		
Male	1 (0.5)	1	0.4	0			0		
Mastoiditis									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Osteomyelitis									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Otitis media									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Otitis media chronic									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Pericoronitis									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Postoperative wound infection									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Pulpitis dental									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Pyelonephritis acute									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Sepsis									
Female	1 (0.5)	1	0.4	0			0		
Male	2 (1.0)	2	0.8	0			0		
Sialoadenitis									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Sinobronchitis									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subcutaneous abscess									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Tracheitis									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Tracheobronchitis									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Vaginal infection									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Wound infection									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Viral infectious disorders									
Female	18 (8.9)	20	7.5	21 (9.5)	24	8.1	25 (13.2)	30	11.8
Male	17 (8.5)	21	8.0	15 (8.3)	17	7.2	11 (5.2)	12	4.4
Influenza									
Female	6 (3.0)	8	3.0	12 (5.4)	13	4.4	11 (5.8)	14	5.5
Male	11 (5.5)	11	4.2	3 (1.7)	3	1.3	7 (3.3)	8	2.9
Gastroenteritis viral									
Female	5 (2.5)	5	1.9	2 (0.9)	3	1.0	6 (3.2)	6	2.4
Male	0			4 (2.2)	4	1.7	1 (0.5)	1	0.4
Viral infection									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	2 (1.1)	3	1.2
Male	1 (0.5)	1	0.4	3 (1.7)	4	1.7	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Herpes zoster									
Female	1 (0.5)	1	0.4	2 (0.9)	2	0.7	2 (1.1)	2	0.8
Male	2 (1.0)	2	0.8	2 (1.1)	2	0.8	0		
Herpes simplex									
Female	1 (0.5)	1	0.4	0			0		
Male	0			1 (0.6)	1	0.4	0		
Herpes virus infection									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Oral herpes									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	1 (0.5)	2	0.8	1 (0.6)	1	0.4	0		
Viral pharyngitis									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Gastroenteritis norovirus									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			0		
Ophthalmic herpes zoster									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Pneumonia influenzal									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Respiratory tract infection viral									
Female	0			1 (0.5)	1	0.3	0		
Male	2 (1.0)	2	0.8	0			2 (0.9)	2	0.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Viral diarrhoea									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Chikungunya virus infection									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Ear infection viral									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Rhinovirus infection									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Viral upper respiratory tract infection									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	2 (1.0)	3	1.1	0			0		
Bacterial infectious disorders									
Female	3 (1.5)	5	1.9	7 (3.2)	7	2.4	3 (1.6)	4	1.6
Male	7 (3.5)	8	3.1	1 (0.6)	1	0.4	9 (4.2)	14	5.1
Cellulitis									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	4 (2.0)	5	1.9	1 (0.6)	1	0.4	4 (1.9)	5	1.8
Bacterial vaginosis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Breast cellulitis									
Female	0			1 (0.5)	1	0.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			0		
Ear infection bacterial									
Female	1 (0.5)	3	1.1	1 (0.5)	1	0.3	0		
Male	0			0			0		
Furuncle									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			2 (0.9)	2	0.7
Pharyngitis streptococcal									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	2 (1.1)	3	1.2
Male	0			0			1 (0.5)	1	0.4
Staphylococcal infection									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			1 (0.5)	2	0.7
Clostridium difficile colitis									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Helicobacter gastritis									
Female	0			0			0		
Male	0			0			2 (0.9)	2	0.7
Helicobacter infection									
Female	0			0			0		
Male	2 (1.0)	2	0.8	0			1 (0.5)	1	0.4
Wound infection staphylococcal									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Fungal infectious disorders									
Female	8 (4.0)	8	3.0	5 (2.3)	5	1.7	9 (4.7)	11	4.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	6 (3.0)	6	2.3	2 (1.1)	2	0.8	6 (2.8)	6	2.2
Onychomycosis									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Tinea pedis									
Female	0			0			2 (1.1)	2	0.8
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Fungal infection									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			0		
Fungal skin infection									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			1 (0.5)	1	0.4
Vulvovaginal candidiasis									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	3 (1.6)	4	1.6
Male	0			0			0		
Vulvovaginal mycotic infection									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	3 (1.6)	3	1.2
Male	0			0			0		
Balanitis candida									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Candida infection									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Dermatophytosis of nail									
Female	0			0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			0		
Genital candidiasis									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	0			0		
Genital infection fungal									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Skin candida									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Tinea infection									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			2 (0.9)	2	0.7
Tinea versicolour									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	0			0		
Ectoparasitic disorders									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Acarodermatitis									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Musculoskeletal and connective tissue disorders									
Female	59 (29.2)	96	35.8	61 (27.5)	96	32.3	40 (21.1)	63	24.8
Male	40 (20.0)	51	19.5	37 (20.4)	55	23.3	44 (20.8)	63	23.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Musculoskeletal and connective tissue disorders NEC									
Female	33 (16.3)	40	14.9	31 (14.0)	38	12.8	14 (7.4)	15	5.9
Male	24 (12.0)	26	9.9	25 (13.8)	28	11.9	19 (9.0)	23	8.4
Back pain									
Female	15 (7.4)	17	6.3	11 (5.0)	13	4.4	5 (2.6)	6	2.4
Male	13 (6.5)	13	5.0	16 (8.8)	17	7.2	9 (4.2)	9	3.3
Pain in extremity									
Female	8 (4.0)	8	3.0	11 (5.0)	11	3.7	3 (1.6)	3	1.2
Male	4 (2.0)	4	1.5	5 (2.8)	5	2.1	7 (3.3)	7	2.6
Neck pain									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	5 (2.8)	5	2.1	2 (0.9)	2	0.7
Musculoskeletal pain									
Female	4 (2.0)	4	1.5	6 (2.7)	6	2.0	4 (2.1)	4	1.6
Male	4 (2.0)	4	1.5	1 (0.6)	1	0.4	2 (0.9)	2	0.7
Flank pain									
Female	3 (1.5)	3	1.1	1 (0.5)	1	0.3	0		
Male	0			0			0		
Muscle contracture									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Musculoskeletal chest pain									
Female	2 (1.0)	3	1.1	1 (0.5)	1	0.3	0		
Male	3 (1.5)	3	1.1	0			1 (0.5)	1	0.4
Neck mass									
Female	0			1 (0.5)	1	0.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			1 (0.5)	1	0.4
Rheumatic disorder									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Axillary mass									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Limb mass									
Female	1 (0.5)	2	0.7	0			0		
Male	0			0			0		
Musculoskeletal discomfort									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Musculoskeletal stiffness									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Plantar fasciitis									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	0			0		
Joint disorders									
Female	29 (14.4)	35	13.0	29 (13.1)	38	12.8	22 (11.6)	29	11.4
Male	9 (4.5)	11	4.2	15 (8.3)	19	8.0	19 (9.0)	20	7.3
Arthralgia									
Female	20 (9.9)	22	8.2	15 (6.8)	18	6.1	10 (5.3)	10	3.9
Male	4 (2.0)	5	1.9	8 (4.4)	11	4.7	10 (4.7)	10	3.6
Osteoarthritis									
Female	1 (0.5)	1	0.4	9 (4.1)	12	4.0	7 (3.7)	8	3.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	5 (2.4)	5	1.8
Rotator cuff syndrome									
Female	4 (2.0)	5	1.9	0			0		
Male	1 (0.5)	2	0.8	3 (1.7)	4	1.7	0		
Periarthritis									
Female	2 (1.0)	2	0.7	2 (0.9)	4	1.3	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Arthritis									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	0		
Spinal osteoarthritis									
Female	1 (0.5)	1	0.4	2 (0.9)	2	0.7	3 (1.6)	3	1.2
Male	1 (0.5)	1	0.4	0			3 (1.4)	3	1.1
Joint swelling									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			0		
Arthritis climacteric									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Arthropathy									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Femoroacetabular impingement									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Gouty arthritis									
Female	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			1 (0.5)	1	0.4
Joint effusion									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Neuropathic arthropathy									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Psoriatic arthropathy									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Rheumatoid arthritis									
Female	0			0			1 (0.5)	2	0.8
Male	0			0			0		
Sacroiliitis									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Muscle disorders									
Female	6 (3.0)	8	3.0	6 (2.7)	6	2.0	3 (1.6)	3	1.2
Male	6 (3.0)	8	3.1	4 (2.2)	6	2.5	5 (2.4)	6	2.2
Myalgia									
Female	4 (2.0)	5	1.9	2 (0.9)	2	0.7	1 (0.5)	1	0.4
Male	2 (1.0)	3	1.1	3 (1.7)	5	2.1	3 (1.4)	4	1.5
Muscle spasms									
Female	3 (1.5)	3	1.1	4 (1.8)	4	1.3	2 (1.1)	2	0.8
Male	4 (2.0)	5	1.9	1 (0.6)	1	0.4	0		
Diastasis recti abdominis									
Female	0			0			0		

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			1 (0.5)	1	0.4
Muscular weakness									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Tendon, ligament and cartilage disorders									
Female	3 (1.5)	3	1.1	3 (1.4)	3	1.0	4 (2.1)	4	1.6
Male	3 (1.5)	3	1.1	2 (1.1)	2	0.8	5 (2.4)	6	2.2
Trigger finger									
Female	0			1 (0.5)	1	0.3	0		
Male	0			1 (0.6)	1	0.4	2 (0.9)	2	0.7
Tendonitis									
Female	1 (0.5)	1	0.4	0			3 (1.6)	3	1.2
Male	0			1 (0.6)	1	0.4	3 (1.4)	3	1.1
Osteochondrosis									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			0		
Tendon disorder									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			1 (0.5)	1	0.4
Costochondritis									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	0			0			0		
Ligament calcification									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Meniscal degeneration									

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Tendon pain									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Synovial and bursal disorders									
Female	1 (0.5)	1	0.4	4 (1.8)	4	1.3	4 (2.1)	5	2.0
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Bursitis									
Female	1 (0.5)	1	0.4	4 (1.8)	4	1.3	4 (2.1)	5	2.0
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Bone disorders (excl congenital and fractures)									
Female	6 (3.0)	6	2.2	3 (1.4)	4	1.3	2 (1.1)	2	0.8
Male	0			0			2 (0.9)	2	0.7
Bone lesion									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Exostosis									
Female	3 (1.5)	3	1.1	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Osteopenia									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			0		
Osteoporosis									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			0		

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Bone pain									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Metatarsalgia									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Osteitis									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)									
Female	3 (1.5)	3	1.1	3 (1.4)	3	1.0	4 (2.1)	5	2.0
Male	2 (1.0)	2	0.8	0			4 (1.9)	4	1.5
Intervertebral disc protrusion									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	1 (0.5)	1	0.4
Male	0			0			2 (0.9)	2	0.7
Foot deformity									
Female	0			0			1 (0.5)	2	0.8
Male	1 (0.5)	1	0.4	0			0		
Intervertebral disc degeneration									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Scoliosis									
Female	1 (0.5)	1	0.4	0			2 (1.1)	2	0.8
Male	0			0			0		
Spinal flattening									

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Spondylolisthesis									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Connective tissue disorders (excl congenital)									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Polymyalgia rheumatica									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Nervous system disorders									
Female	37 (18.3)	70	26.1	51 (23.0)	71	23.9	36 (18.9)	57	22.4
Male	26 (13.0)	35	13.4	31 (17.1)	47	19.9	27 (12.7)	35	12.8
Headaches									
Female	25 (12.4)	42	15.7	24 (10.8)	30	10.1	18 (9.5)	25	9.8
Male	11 (5.5)	14	5.4	13 (7.2)	16	6.8	6 (2.8)	7	2.6
Headache									
Female	24 (11.9)	37	13.8	19 (8.6)	25	8.4	15 (7.9)	22	8.7
Male	9 (4.5)	11	4.2	12 (6.6)	15	6.4	5 (2.4)	5	1.8
Migraine									
Female	2 (1.0)	2	0.7	3 (1.4)	3	1.0	0		
Male	0			0			0		
Migraine with aura									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			1 (0.6)	1	0.4	0		
Tension headache									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	3 (1.5)	3	1.1	0			1 (0.5)	1	0.4
Occipital neuralgia									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Sinus headache									
Female	1 (0.5)	2	0.7	0			1 (0.5)	1	0.4
Male	0			0			0		
Neurological disorders NEC									
Female	18 (8.9)	22	8.2	22 (9.9)	24	8.1	16 (8.4)	23	9.1
Male	10 (5.0)	11	4.2	14 (7.7)	22	9.3	15 (7.1)	15	5.5
Dizziness									
Female	15 (7.4)	18	6.7	13 (5.9)	14	4.7	6 (3.2)	8	3.2
Male	3 (1.5)	3	1.1	6 (3.3)	6	2.5	7 (3.3)	7	2.6
Paraesthesia									
Female	1 (0.5)	1	0.4	4 (1.8)	4	1.3	5 (2.6)	6	2.4
Male	1 (0.5)	1	0.4	1 (0.6)	3	1.3	1 (0.5)	1	0.4
Dysgeusia									
Female	0			1 (0.5)	1	0.3	0		
Male	0			3 (1.7)	7	3.0	1 (0.5)	1	0.4
Hypoaesthesia									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			2 (1.1)	2	0.8	1 (0.5)	1	0.4
Syncope									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	0		
Dizziness postural									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	2	0.8	1 (0.6)	1	0.4	0		
Hyperaesthesia									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Somnolence									
Female	0			2 (0.9)	2	0.7	2 (1.1)	2	0.8
Male	0			0			0		
Ageusia									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Aphasia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Coordination abnormal									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Dysaesthesia									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Head discomfort									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Hypogeusia									
Female	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	0			0		
Lethargy									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Loss of consciousness									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Neuralgia									
Female	0			0			2 (1.1)	2	0.8
Male	0			0			0		
Phantom limb syndrome									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Presyncope									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Restless legs syndrome									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Central nervous system vascular disorders									
Female	0			6 (2.7)	9	3.0	1 (0.5)	1	0.4
Male	2 (1.0)	2	0.8	2 (1.1)	2	0.8	1 (0.5)	2	0.7
Carotid artery stenosis									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Carotid arteriosclerosis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			2 (0.9)	2	0.7	0		
Male	0			0			0		
Cerebrovascular accident									
Female	0			2 (0.9)	2	0.7	1 (0.5)	1	0.4
Male	0			0			0		
Cerebral infarction									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Cerebral artery stenosis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Cerebral artery thrombosis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Spinal epidural haematoma									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Subarachnoid haemorrhage									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Ischaemic stroke									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	2	0.7
Peripheral neuropathies									
Female	4 (2.0)	4	1.5	3 (1.4)	3	1.0	4 (2.1)	4	1.6
Male	2 (1.0)	3	1.1	1 (0.6)	1	0.4	3 (1.4)	4	1.5
Diabetic neuropathy									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Carpal tunnel syndrome									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	1 (0.5)	2	0.8	0			0		
Meralgia paraesthetica									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Neuropathy peripheral									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			2 (0.9)	3	1.1
Nerve compression									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Polyneuropathy									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Spinal cord and nerve root disorders									
Female	1 (0.5)	1	0.4	2 (0.9)	3	1.0	1 (0.5)	1	0.4
Male	4 (2.0)	4	1.5	1 (0.6)	1	0.4	3 (1.4)	3	1.1
Sciatica									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Radiculopathy									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Sacral radiculopathy									

Adverse events with onset prior to randomisation are not included.
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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Cervical radiculopathy									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Cervicobrachial syndrome									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Lumbar radiculopathy									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			2 (0.9)	2	0.7
Cranial nerve disorders (excl neoplasms)									
Female	0			1 (0.5)	1	0.3	0		
Male	0			1 (0.6)	1	0.4	0		
Facial paralysis									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Anosmia									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Encephalopathies									
Female	0			1 (0.5)	1	0.3	0		
Male	0			1 (0.6)	1	0.4	0		
Hyponatraemic encephalopathy									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Hepatic encephalopathy									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Mental impairment disorders									
Female	0			0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	3 (1.4)	3	1.1
Memory impairment									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Amnesia									
Female	0			0			0		
Male	0			0			3 (1.4)	3	1.1
Dementia Alzheimer's type									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Vascular dementia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Sleep disturbances (incl subtypes)									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Hypersomnia									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Structural brain disorders									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		

Adverse events with onset prior to randomisation are not included.
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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Cerebral ventricle dilatation									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Movement disorders (incl parkinsonism)									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Tremor									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Neurological disorders of the eye									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Visual field defect									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Seizures (incl subtypes)									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Partial seizures									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
General disorders and administration site conditions									
Female	30 (14.9)	40	14.9	42 (18.9)	56	18.9	22 (11.6)	29	11.4
Male	21 (10.5)	29	11.1	27 (14.9)	37	15.7	24 (11.3)	32	11.7
General system disorders NEC									

Adverse events with onset prior to randomisation are not included.
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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	26 (12.9)	34	12.7	34 (15.3)	42	14.1	13 (6.8)	14	5.5
Male	14 (7.0)	18	6.9	23 (12.7)	26	11.0	15 (7.1)	16	5.8
Fatigue									
Female	10 (5.0)	15	5.6	18 (8.1)	18	6.1	2 (1.1)	2	0.8
Male	9 (4.5)	11	4.2	10 (5.5)	11	4.7	2 (0.9)	2	0.7
Asthenia									
Female	2 (1.0)	2	0.7	5 (2.3)	6	2.0	0		
Male	2 (1.0)	2	0.8	2 (1.1)	2	0.8	1 (0.5)	1	0.4
Influenza like illness									
Female	1 (0.5)	1	0.4	3 (1.4)	4	1.3	1 (0.5)	1	0.4
Male	0			2 (1.1)	2	0.8	2 (0.9)	2	0.7
Malaise									
Female	1 (0.5)	2	0.7	2 (0.9)	2	0.7	0		
Male	0			2 (1.1)	2	0.8	1 (0.5)	1	0.4
Early satiety									
Female	3 (1.5)	3	1.1	4 (1.8)	4	1.3	0		
Male	1 (0.5)	1	0.4	0			2 (0.9)	2	0.7
Non-cardiac chest pain									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			2 (1.1)	2	0.8	0		
Pain									
Female	4 (2.0)	4	1.5	1 (0.5)	1	0.3	3 (1.6)	3	1.2
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	0		
Oedema peripheral									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	0			1 (0.6)	1	0.4	2 (0.9)	2	0.7
Peripheral swelling									

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	0			1 (0.6)	1	0.4	2 (0.9)	2	0.7
Hunger									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Swelling									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Thirst decreased									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Chest discomfort									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	0			0			0		
Chest pain									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			2 (0.9)	3	1.1
Face oedema									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Feeling cold									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Chills									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Discomfort									

Adverse events with onset prior to randomisation are not included.
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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Inflammation									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Polyp									
Female	0			0			0		
Male	1 (0.5)	2	0.8	0			0		
Sensation of foreign body									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Thirst									
Female	2 (1.0)	2	0.7	0			0		
Male	0			0			0		
Administration site reactions									
Female	3 (1.5)	3	1.1	6 (2.7)	8	2.7	4 (2.1)	8	3.2
Male	3 (1.5)	4	1.5	7 (3.9)	11	4.7	6 (2.8)	10	3.6
Injection site pain									
Female	1 (0.5)	1	0.4	4 (1.8)	5	1.7	1 (0.5)	3	1.2
Male	3 (1.5)	3	1.1	3 (1.7)	4	1.7	2 (0.9)	4	1.5
Injection site erythema									
Female	0			1 (0.5)	1	0.3	0		
Male	0			2 (1.1)	2	0.8	0		
Injection site bruising									
Female	2 (1.0)	2	0.7	0			3 (1.6)	3	1.2
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	2 (0.9)	3	1.1
Injection site reaction									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (0.5)	1	0.3	0		
Male	0			1 (0.6)	1	0.4	0		
Injection site mass									
Female	0			0			0		
Male	0			1 (0.6)	2	0.8	1 (0.5)	1	0.4
Implant site pain									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Injection site discomfort									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Injection site haemorrhage									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Injection site urticaria									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Body temperature conditions									
Female	3 (1.5)	3	1.1	4 (1.8)	4	1.3	5 (2.6)	7	2.8
Male	6 (3.0)	6	2.3	0			4 (1.9)	5	1.8
Pyrexia									
Female	3 (1.5)	3	1.1	4 (1.8)	4	1.3	5 (2.6)	7	2.8
Male	6 (3.0)	6	2.3	0			4 (1.9)	5	1.8
Therapeutic and nontherapeutic effects (excl toxicity)									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Drug intolerance									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Tissue disorders NEC									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			0		
Mass									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Nodule									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Complications associated with device									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Complication associated with device									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Metabolism and nutrition disorders									
Female	17 (8.4)	28	10.4	38 (17.1)	42	14.1	29 (15.3)	34	13.4
Male	31 (15.5)	40	15.3	18 (9.9)	24	10.2	24 (11.3)	27	9.8
Appetite and general nutritional disorders									
Female	12 (5.9)	18	6.7	28 (12.6)	31	10.4	9 (4.7)	11	4.3
Male	20 (10.0)	22	8.4	13 (7.2)	15	6.4	7 (3.3)	7	2.6
Decreased appetite									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	11 (5.4)	14	5.2	26 (11.7)	28	9.4	9 (4.7)	11	4.3
Male	18 (9.0)	20	7.6	12 (6.6)	13	5.5	6 (2.8)	6	2.2
Hyperphagia									
Female	0			2 (0.9)	2	0.7	0		
Male	0			0			0		
Overweight									
Female	0			0			0		
Male	0			1 (0.6)	2	0.8	0		
Increased appetite									
Female	3 (1.5)	4	1.5	1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			0		
Cachexia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Obesity									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Electrolyte and fluid balance conditions									
Female	3 (1.5)	4	1.5	2 (0.9)	2	0.7	2 (1.1)	2	0.8
Male	3 (1.5)	3	1.1	5 (2.8)	5	2.1	1 (0.5)	1	0.4
Dehydration									
Female	1 (0.5)	1	0.4	0			2 (1.1)	2	0.8
Male	2 (1.0)	2	0.8	3 (1.7)	3	1.3	0		
Hypokalaemia									
Female	1 (0.5)	2	0.7	2 (0.9)	2	0.7	0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Hyponatraemia									
Female	1 (0.5)	1	0.4	0			0		
Male	0			1 (0.6)	1	0.4	0		
Hyperkalaemia									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Lipid metabolism disorders									
Female	2 (1.0)	2	0.7	4 (1.8)	4	1.3	6 (3.2)	6	2.4
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	3 (1.4)	3	1.1
Dyslipidaemia									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	4 (2.1)	4	1.6
Male	1 (0.5)	1	0.4	0			2 (0.9)	2	0.7
Hyperlipidaemia									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	0		
Hypertriglyceridaemia									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			0		
Hypercholesterolaemia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Purine and pyrimidine metabolism disorders									
Female	0			1 (0.5)	1	0.3	1 (0.5)	2	0.8
Male	3 (1.5)	4	1.5	1 (0.6)	1	0.4	2 (0.9)	3	1.1
Gout									
Female	0			1 (0.5)	1	0.3	1 (0.5)	2	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	3 (1.5)	4	1.5	1 (0.6)	1	0.4	1 (0.5)	2	0.7
Hyperuricaemia									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Vitamin related disorders									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Vitamin B complex deficiency									
Female	0			0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Folate deficiency									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Vitamin D deficiency									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Bone, calcium, magnesium and phosphorus metabolism disorders									
Female	1 (0.5)	1	0.4	0			2 (1.1)	2	0.8
Male	3 (1.5)	3	1.1	1 (0.6)	1	0.4	2 (0.9)	2	0.7
Hypomagnesaemia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Hypercalcaemia									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Hypercalcitoninaemia									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Hypocalcaemia									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Acid-base disorders									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			0		
Ketoacidosis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Lactic acidosis									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Diabetic complications									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			1 (0.5)	1	0.4
Diabetic ketoacidosis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Diabetic metabolic decompensation									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Glucose metabolism disorders (incl diabetes mellitus)									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	10 (5.3)	10	3.9
Male	1 (0.5)	2	0.8	0			10 (4.7)	10	3.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Diabetes mellitus									
Female	0			1 (0.5)	1	0.3	4 (2.1)	4	1.6
Male	0			0			2 (0.9)	2	0.7
Diabetes mellitus inadequate control									
Female	0			0			2 (1.1)	2	0.8
Male	1 (0.5)	2	0.8	0			3 (1.4)	3	1.1
Hyperglycaemia									
Female	1 (0.5)	1	0.4	0			3 (1.6)	3	1.2
Male	0			0			2 (0.9)	2	0.7
Hyperinsulinaemia									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Hypoglycaemia									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Type 2 diabetes mellitus									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			2 (0.9)	2	0.7
Iron and trace metal metabolism disorders									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Iron deficiency									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Metabolism disorders NEC									
Female	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	2	0.8	0			0		
Hyperamylasaemia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Hyperlipasaemia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Eye disorders									
Female	20 (9.9)	28	10.4	30 (13.5)	42	14.1	21 (11.1)	31	12.2
Male	26 (13.0)	37	14.1	20 (11.0)	27	11.4	21 (9.9)	25	9.1
Retina, choroid and vitreous haemorrhages and vascular disorders									
Female	5 (2.5)	5	1.9	13 (5.9)	15	5.1	4 (2.1)	4	1.6
Male	7 (3.5)	8	3.1	8 (4.4)	8	3.4	7 (3.3)	8	2.9
Diabetic retinopathy									
Female	4 (2.0)	4	1.5	9 (4.1)	10	3.4	4 (2.1)	4	1.6
Male	7 (3.5)	8	3.1	6 (3.3)	6	2.5	7 (3.3)	8	2.9
Non-proliferative retinopathy									
Female	0			1 (0.5)	1	0.3	0		
Male	0			1 (0.6)	1	0.4	0		
Retinal haemorrhage									
Female	0			2 (0.9)	2	0.7	0		
Male	0			0			0		
Retinopathy hypertensive									
Female	0			2 (0.9)	2	0.7	0		
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Retinal artery occlusion									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Retinopathy									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Anterior eye structural change, deposit and degeneration									
Female	3 (1.5)	3	1.1	6 (2.7)	7	2.4	6 (3.2)	8	3.2
Male	5 (2.5)	5	1.9	3 (1.7)	4	1.7	6 (2.8)	7	2.6
Cataract									
Female	2 (1.0)	2	0.7	4 (1.8)	5	1.7	4 (2.1)	5	2.0
Male	3 (1.5)	3	1.1	1 (0.6)	1	0.4	4 (1.9)	4	1.5
Cataract subcapsular									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Narrow anterior chamber angle									
Female	0			0			0		
Male	0			1 (0.6)	2	0.8	0		
Cataract cortical									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Dermatochalasis									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Cataract nuclear									
Female	1 (0.5)	1	0.4	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	0			1 (0.5)	2	0.7
Pinguecula									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Posterior capsule opacification									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Ocular infections, irritations and inflammations									
Female	5 (2.5)	5	1.9	5 (2.3)	6	2.0	3 (1.6)	3	1.2
Male	8 (4.0)	8	3.1	3 (1.7)	4	1.7	3 (1.4)	3	1.1
Blepharitis									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	2 (1.0)	2	0.8	2 (1.1)	3	1.3	1 (0.5)	1	0.4
Macular oedema									
Female	0			2 (0.9)	3	1.0	0		
Male	1 (0.5)	1	0.4	0			0		
Ocular hyperaemia									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	2 (0.9)	2	0.7
Eyelid rash									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Keratitis									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			0		
Meibomian gland dysfunction									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Conjunctivitis allergic									
Female	1 (0.5)	1	0.4	0			0		
Male	2 (1.0)	2	0.8	0			0		
Episcleritis									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Eye pruritus									
Female	0			0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	0			0		
Punctate keratitis									
Female	2 (1.0)	2	0.7	0			0		
Male	0			0			0		
Swelling of eyelid									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Uveitis									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Eye disorders NEC									
Female	2 (1.0)	2	0.7	7 (3.2)	7	2.4	5 (2.6)	5	2.0
Male	6 (3.0)	6	2.3	1 (0.6)	1	0.4	2 (0.9)	2	0.7
Dry eye									
Female	1 (0.5)	1	0.4	5 (2.3)	5	1.7	4 (2.1)	4	1.6
Male	3 (1.5)	3	1.1	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Lacrimation increased									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			0		
Vitreous disorder									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Eyelid disorder									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Retinal disorder									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Ocular structural change, deposit and degeneration NEC									
Female	6 (3.0)	7	2.6	2 (0.9)	2	0.7	3 (1.6)	4	1.6
Male	4 (2.0)	5	1.9	4 (2.2)	4	1.7	0		
Macular fibrosis									
Female	1 (0.5)	2	0.7	0			0		
Male	0			1 (0.6)	1	0.4	0		
Optic disc disorder									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Retinal degeneration									
Female	0			0			1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	0		
Vitreous detachment									
Female	0			0			1 (0.5)	1	0.4
Male	1 (0.5)	2	0.8	1 (0.6)	1	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Detachment of retinal pigment epithelium									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Retinal depigmentation									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Age-related macular degeneration									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	0			0		
Choroidal dystrophy									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Macular degeneration									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Optic atrophy									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Retinal drusen									
Female	2 (1.0)	2	0.7	0			0		
Male	0			0			0		
Vitreous floaters									
Female	0			0			1 (0.5)	1	0.4
Male	2 (1.0)	2	0.8	0			0		
Vision disorders									
Female	4 (2.0)	4	1.5	3 (1.4)	3	1.0	6 (3.2)	6	2.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	4 (2.0)	4	1.5	2 (1.1)	2	0.8	2 (0.9)	2	0.7
Vision blurred									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	2 (1.0)	2	0.8	2 (1.1)	2	0.8	0		
Myopia									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Visual impairment									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Astigmatism									
Female	0			0			2 (1.1)	2	0.8
Male	0			0			1 (0.5)	1	0.4
Hypermetropia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Pathologic myopia									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Presbyopia									
Female	2 (1.0)	2	0.7	0			0		
Male	0			0			0		
Glaucoma and ocular hypertension									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			1 (0.6)	2	0.8	1 (0.5)	1	0.4
Glaucoma									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			1 (0.6)	2	0.8	1 (0.5)	1	0.4
Ocular neuromuscular disorders									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Eyelid ptosis									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Ocular sensory symptoms NEC									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Asthenopia									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Ocular haemorrhages and vascular disorders NEC									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			2 (0.9)	2	0.7
Eye haemorrhage									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			1 (0.5)	1	0.4
Conjunctival haemorrhage									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Optic disc haemorrhage									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Injury, poisoning and procedural complications									
Female	23 (11.4)	28	10.4	28 (12.6)	44	14.8	24 (12.6)	29	11.4
Male	28 (14.0)	43	16.4	20 (11.0)	24	10.2	25 (11.8)	32	11.7
Injuries NEC									
Female	15 (7.4)	16	6.0	17 (7.7)	23	7.7	15 (7.9)	18	7.1
Male	22 (11.0)	33	12.6	15 (8.3)	16	6.8	21 (9.9)	22	8.0
Muscle strain									
Female	3 (1.5)	3	1.1	4 (1.8)	4	1.3	0		
Male	2 (1.0)	2	0.8	4 (2.2)	4	1.7	1 (0.5)	1	0.4
Fall									
Female	2 (1.0)	2	0.7	5 (2.3)	6	2.0	1 (0.5)	2	0.8
Male	6 (3.0)	6	2.3	0			1 (0.5)	1	0.4
Ligament sprain									
Female	0			1 (0.5)	1	0.3	4 (2.1)	4	1.6
Male	6 (3.0)	8	3.1	2 (1.1)	2	0.8	2 (0.9)	2	0.7
Limb injury									
Female	3 (1.5)	3	1.1	1 (0.5)	1	0.3	0		
Male	0			2 (1.1)	2	0.8	0		
Skin laceration									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	2 (1.0)	2	0.8	2 (1.1)	2	0.8	2 (0.9)	2	0.7
Contusion									
Female	0			1 (0.5)	1	0.3	3 (1.6)	4	1.6
Male	0			1 (0.6)	2	0.8	5 (2.4)	5	1.8
Bone contusion									
Female	0			2 (0.9)	2	0.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			1 (0.5)	1	0.4
Animal bite									
Female	0			0			1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Epicondylitis									
Female	0			0			0		
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Muscle injury									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Post-traumatic pain									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Arthropod sting									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Face injury									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Head injury									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Road traffic accident									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	0			0		
Skin abrasion									
Female	0			1 (0.5)	1	0.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	0			0		
Tooth fracture									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	2 (1.0)	2	0.8	0			1 (0.5)	1	0.4
Traumatic haemothorax									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Abdominal injury									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Arthropod bite									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Chest injury									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Craniocerebral injury									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Foreign body in eye									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Injury corneal									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Ligament rupture									
Female	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	2 (1.0)	2	0.8	0			0		
Muscle rupture									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Post-traumatic neck syndrome									
Female	0			0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	0			0		
Soft tissue injury									
Female	2 (1.0)	2	0.7	0			0		
Male	3 (1.5)	3	1.1	0			0		
Spinal column injury									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Subdural haematoma									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Tendon injury									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Tendon rupture									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			1 (0.5)	1	0.4
Wound									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			2 (0.9)	2	0.7
Bone and joint injuries									
Female	7 (3.5)	8	3.0	11 (5.0)	15	5.1	8 (4.2)	8	3.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	3 (1.7)	4	1.7	5 (2.4)	5	1.8
Rib fracture									
Female	0			2 (0.9)	2	0.7	0		
Male	0			2 (1.1)	2	0.8	0		
Foot fracture									
Female	0			3 (1.4)	3	1.0	2 (1.1)	2	0.8
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Humerus fracture									
Female	1 (0.5)	1	0.4	2 (0.9)	2	0.7	0		
Male	0			0			0		
Wrist fracture									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Cervical vertebral fracture									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Joint injury									
Female	0			1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	0			3 (1.4)	3	1.1
Meniscus injury									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			0		
Radius fracture									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Spinal compression fracture									
Female	0			1 (0.5)	1	0.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			0		
Stress fracture									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			0		
Thoracic vertebral fracture									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Upper limb fracture									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Ankle fracture									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Bone fissure									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Cartilage injury									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Hand fracture									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Hip fracture									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Joint dislocation									
Female	1 (0.5)	1	0.4	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			1 (0.5)	1	0.4
Lisfranc fracture									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Spinal fracture									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Sternal fracture									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Procedural related injuries and complications NEC									
Female	2 (1.0)	2	0.7	4 (1.8)	4	1.3	2 (1.1)	2	0.8
Male	0			1 (0.6)	1	0.4	3 (1.4)	3	1.1
Post procedural haemorrhage									
Female	0			2 (0.9)	2	0.7	0		
Male	0			0			0		
Anaemia postoperative									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Graft complication									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Procedural pain									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			1 (0.5)	1	0.4
Dental restoration failure									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Incision site pain									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Post procedural complication									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Surgical skin tear									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Injuries by physical agents									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	0		
Hypobarism									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Sunburn									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Thermal burn									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			0		
Heat illness									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Medication errors and other product use errors and issues									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	4 (2.0)	7	2.7	1 (0.6)	1	0.4	1 (0.5)	2	0.7
Accidental overdose									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	2 (1.0)	4	1.5	1 (0.6)	1	0.4	1 (0.5)	2	0.7
Extra dose administered									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Dose calculation error									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Incorrect dose administered									
Female	0			0			0		
Male	1 (0.5)	2	0.8	0			0		
Overdoses and underdoses NEC									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Intentional overdose									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Respiratory, thoracic and mediastinal disorders									
Female	17 (8.4)	19	7.1	29 (13.1)	40	13.5	20 (10.5)	23	9.1
Male	19 (9.5)	25	9.6	18 (9.9)	22	9.3	16 (7.5)	20	7.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Respiratory tract signs and symptoms									
Female	5 (2.5)	5	1.9	11 (5.0)	11	3.7	5 (2.6)	5	2.0
Male	8 (4.0)	8	3.1	8 (4.4)	8	3.4	4 (1.9)	4	1.5
Oropharyngeal pain									
Female	3 (1.5)	3	1.1	5 (2.3)	5	1.7	4 (2.1)	4	1.6
Male	5 (2.5)	5	1.9	2 (1.1)	2	0.8	2 (0.9)	2	0.7
Rhinorrhoea									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	0		
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	0		
Dysphonia									
Female	0			1 (0.5)	1	0.3	0		
Male	0			1 (0.6)	1	0.4	0		
Dry throat									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Hiccups									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Oropharyngeal discomfort									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Painful respiration									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Aphonia									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Upper respiratory tract congestion									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Nasal discomfort									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Upper-airway cough syndrome									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Respiratory disorders NEC									
Female	8 (4.0)	9	3.4	10 (4.5)	10	3.4	11 (5.8)	13	5.1
Male	8 (4.0)	8	3.1	8 (4.4)	9	3.8	4 (1.9)	5	1.8
Cough									
Female	6 (3.0)	7	2.6	5 (2.3)	5	1.7	5 (2.6)	5	2.0
Male	4 (2.0)	4	1.5	4 (2.2)	4	1.7	2 (0.9)	3	1.1
Pulmonary mass									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	0		
Productive cough									
Female	0			2 (0.9)	2	0.7	0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Respiratory disorder									
Female	1 (0.5)	1	0.4	0			2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	1 (0.5)	1	0.4
Acute respiratory failure									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Sleep apnoea syndrome									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	3 (1.6)	3	1.2
Male	0			0			1 (0.5)	1	0.4
Dyspnoea									
Female	0			0			2 (1.1)	2	0.8
Male	0			0			0		
Hypoxia									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Upper respiratory tract disorders (excl infections)									
Female	2 (1.0)	2	0.7	8 (3.6)	9	3.0	2 (1.1)	2	0.8
Male	4 (2.0)	5	1.9	2 (1.1)	3	1.3	6 (2.8)	7	2.6
Epistaxis									
Female	0			2 (0.9)	2	0.7	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	2 (1.1)	3	1.3	4 (1.9)	4	1.5
Rhinitis allergic									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	0		
Male	0			0			0		
Nasal congestion									
Female	0			2 (0.9)	2	0.7	1 (0.5)	1	0.4
Male	2 (1.0)	3	1.1	0			1 (0.5)	2	0.7
Sinus congestion									
Female	1 (0.5)	1	0.4	2 (0.9)	2	0.7	0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Bronchial disorders (excl neoplasms)									
Female	3 (1.5)	3	1.1	6 (2.7)	8	2.7	2 (1.1)	2	0.8

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	4 (1.9)	4	1.5
Asthma									
Female	2 (1.0)	2	0.7	5 (2.3)	6	2.0	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	0			2 (0.9)	2	0.7
Bronchospasm									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	0		
Chronic obstructive pulmonary disease									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Childhood asthma									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Lower respiratory tract disorders (excl obstruction and infection)									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	2	0.8	1 (0.6)	1	0.4	0		
Atelectasis									
Female	0			0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Idiopathic interstitial pneumonia									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Emphysema									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Pleural disorders									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Pneumothorax									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Investigations									
Female	9 (4.5)	12	4.5	21 (9.5)	24	8.1	21 (11.1)	25	9.8
Male	9 (4.5)	11	4.2	19 (10.5)	24	10.2	12 (5.7)	17	6.2
Cardiac and vascular investigations (excl enzyme tests)									
Female	1 (0.5)	1	0.4	6 (2.7)	6	2.0	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	2 (1.1)	3	1.3	2 (0.9)	2	0.7
Heart rate increased									
Female	1 (0.5)	1	0.4	2 (0.9)	2	0.7	0		
Male	1 (0.5)	1	0.4	0			0		
Cardiac murmur									
Female	0			0			1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	0		
Cardiac stress test abnormal									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Carotid pulse decreased									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Blood pressure decreased									

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Blood pressure increased									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Electrocardiogram Q waves									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Electrocardiogram QT prolonged									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			1 (0.5)	1	0.4
Electrocardiogram PR prolongation									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Electrocardiogram ST-T segment abnormal									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Gastrointestinal investigations									
Female	4 (2.0)	4	1.5	2 (0.9)	2	0.7	1 (0.5)	2	0.8
Male	1 (0.5)	1	0.4	4 (2.2)	4	1.7	2 (0.9)	2	0.7
Lipase increased									
Female	3 (1.5)	3	1.1	2 (0.9)	2	0.7	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Colonoscopy normal									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		

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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Occult blood									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Occult blood positive									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Amylase increased									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Faecal volume increased									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Pancreatic enzymes increased									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Renal and urinary tract investigations and urinalyses									
Female	0			4 (1.8)	4	1.3	0		
Male	0			2 (1.1)	2	0.8	0		
Glomerular filtration rate decreased									
Female	0			2 (0.9)	2	0.7	0		
Male	0			1 (0.6)	1	0.4	0		
Urine albumin/creatinine ratio increased									
Female	0			1 (0.5)	1	0.3	0		
Male	0			1 (0.6)	1	0.4	0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Urine albumin/creatinine ratio abnormal									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Haematology investigations (incl blood groups)									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			3 (1.7)	5	2.1	0		
Haemoglobin decreased									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			2 (1.1)	2	0.8	0		
Haematocrit decreased									
Female	0			0			0		
Male	0			2 (1.1)	2	0.8	0		
Platelet count decreased									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Endocrine investigations (incl sex hormones)									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Blood thyroid stimulating hormone increased									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	0			1 (0.6)	1	0.4	0		
Blood thyroid stimulating hormone decreased									

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			2 (0.9)	2	0.7	0		
Male	0			0			0		
Blood parathyroid hormone increased									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Enzyme investigations NEC									
Female	0			0			1 (0.5)	1	0.4
Male	2 (1.0)	2	0.8	3 (1.7)	3	1.3	0		
Blood creatine phosphokinase increased									
Female	0			0			1 (0.5)	1	0.4
Male	2 (1.0)	2	0.8	3 (1.7)	3	1.3	0		
Hepatobiliary investigations									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	3 (1.6)	5	2.0
Male	2 (1.0)	3	1.1	2 (1.1)	2	0.8	4 (1.9)	5	1.8
Liver function test abnormal									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Liver function test increased									
Female	0			0			1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	0		
Hepatic enzyme increased									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Alanine aminotransferase increased									
Female	0			0			2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	0			2 (0.9)	2	0.7

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Aspartate aminotransferase increased									
Female	0			0			2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	0			0		
Blood bilirubin increased									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Transaminases increased									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Lipid analyses									
Female	0			2 (0.9)	2	0.7	2 (1.1)	2	0.8
Male	0			0			0		
Lipids abnormal									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Low density lipoprotein increased									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Blood cholesterol increased									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Blood triglycerides increased									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Investigations, imaging and histopathology procedures NEC									
Female	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			1 (0.6)	1	0.4	0		
Endoscopy abnormal									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Metabolic, nutritional and blood gas investigations									
Female	2 (1.0)	2	0.7	0			6 (3.2)	6	2.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	2 (0.9)	3	1.1
Vitamin B12 decreased									
Female	0			0			1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	0		
Blood glucose decreased									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Blood glucose increased									
Female	0			0			2 (1.1)	2	0.8
Male	0			0			2 (0.9)	2	0.7
Blood uric acid increased									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Brain natriuretic peptide increased									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Glycosylated haemoglobin increased									
Female	1 (0.5)	1	0.4	0			2 (1.1)	2	0.8
Male	0			0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Physical examination and organ system status topics									
Female	0			0			1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	0		
Weight decreased									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Weight increased									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Water, electrolyte and mineral investigations									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Blood potassium increased									
Female	1 (0.5)	1	0.4	0			0		
Male	0			1 (0.6)	1	0.4	0		
Blood potassium decreased									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Blood sodium increased									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Microbiology and serology investigations									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Helicobacter test positive									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			0		
Neurological, special senses and psychiatric investigations									
Female	0			1 (0.5)	2	0.7	0		
Male	0			0			0		
Intraocular pressure increased									
Female	0			1 (0.5)	2	0.7	0		
Male	0			0			0		
Protein and chemistry analyses NEC									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	0			2 (0.9)	2	0.7
C-reactive protein increased									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	0			2 (0.9)	2	0.7
Reproductive organ and breast investigations (excl hormone analyses)									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Mammogram abnormal									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Cytogenetic investigations									
Female	0			0			0		
Male	0			0			2 (0.9)	2	0.7
Prostatic specific antigen increased									

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			0		
Male	0			0			2 (0.9)	2	0.7
Immunology and allergy investigations									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Antinuclear antibody increased									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Skin and subcutaneous tissue disorders									
Female	26 (12.9)	27	10.1	25 (11.3)	32	10.8	17 (8.9)	20	7.9
Male	12 (6.0)	16	6.1	15 (8.3)	22	9.3	20 (9.4)	22	8.0
Epidermal and dermal conditions									
Female	14 (6.9)	14	5.2	14 (6.3)	15	5.1	9 (4.7)	9	3.5
Male	9 (4.5)	11	4.2	13 (7.2)	20	8.5	13 (6.1)	14	5.1
Rash									
Female	4 (2.0)	4	1.5	4 (1.8)	4	1.3	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	3 (1.7)	6	2.5	2 (0.9)	2	0.7
Eczema									
Female	4 (2.0)	4	1.5	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			3 (1.7)	3	1.3	1 (0.5)	1	0.4
Dry skin									
Female	1 (0.5)	1	0.4	2 (0.9)	2	0.7	0		
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Blister									
Female	0			0			0		
Male	0			2 (1.1)	3	1.3	0		

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Rash pruritic									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	2	0.8	1 (0.6)	1	0.4	0		
Drug eruption									
Female	0			0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	2 (0.9)	3	1.1
Intertrigo									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Pain of skin									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Pruritus									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	2 (0.9)	2	0.7
Sensitive skin									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Skin lesion									
Female	0			0			0		
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Decubitus ulcer									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Dermatitis allergic									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Dermatitis contact									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			1 (0.5)	1	0.4
Perioral dermatitis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Psoriasis									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Skin burning sensation									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Skin exfoliation									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Dermatitis									
Female	2 (1.0)	2	0.7	0			1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Erythema									
Female	0			0			0		
Male	1 (0.5)	2	0.8	0			0		
Neurodermatitis									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Parapsoriasis									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Rash erythematous									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	0			0			0		
Stasis dermatitis									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Xanthelasma									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Skin appendage conditions									
Female	9 (4.5)	9	3.4	8 (3.6)	11	3.7	5 (2.6)	5	2.0
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	3 (1.4)	3	1.1
Alopecia									
Female	5 (2.5)	5	1.9	4 (1.8)	5	1.7	2 (1.1)	2	0.8
Male	0			0			0		
Acne									
Female	1 (0.5)	1	0.4	0			0		
Male	0			1 (0.6)	1	0.4	0		
Alopecia areata									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Hyperhidrosis									
Female	2 (1.0)	2	0.7	1 (0.5)	2	0.7	2 (1.1)	2	0.8
Male	0			0			1 (0.5)	1	0.4
Ingrowing nail									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Onychomadesis									
Female	0			1 (0.5)	2	0.7	0		
Male	0			0			0		
Miliaria									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Nail dystrophy									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Cornification and dystrophic skin disorders									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	2 (0.9)	2	0.7
Actinic keratosis									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Dermatitis papillaris capillitii									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Hyperkeratosis									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Punctate keratosis									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Angioedema and urticaria									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	2 (1.1)	2	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			0		
Urticaria									
Female	0			1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	0			0			0		
Chronic spontaneous urticaria									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Cutaneous neoplasms benign									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	3 (1.6)	4	1.6
Male	0			0			0		
Dermal cyst									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	3 (1.6)	4	1.6
Male	0			0			0		
Skin and subcutaneous tissue disorders NEC									
Female	0			1 (0.5)	4	1.3	0		
Male	1 (0.5)	1	0.4	0			2 (0.9)	2	0.7
Diabetic foot									
Female	0			1 (0.5)	3	1.0	0		
Male	0			0			0		
Skin ulcer									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			2 (0.9)	2	0.7
Skin vascular abnormalities									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Ecchymosis									

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Haemorrhage subcutaneous									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Renal and urinary disorders									
Female	9 (4.5)	10	3.7	17 (7.7)	21	7.1	13 (6.8)	16	6.3
Male	10 (5.0)	12	4.6	14 (7.7)	16	6.8	15 (7.1)	18	6.6
Urinary tract signs and symptoms									
Female	3 (1.5)	3	1.1	8 (3.6)	8	2.7	10 (5.3)	11	4.3
Male	4 (2.0)	4	1.5	9 (5.0)	9	3.8	6 (2.8)	8	2.9
Microalbuminuria									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	3 (1.7)	3	1.3	0		
Haematuria									
Female	0			0			0		
Male	0			3 (1.7)	3	1.3	1 (0.5)	1	0.4
Dysuria									
Female	0			2 (0.9)	2	0.7	3 (1.6)	3	1.2
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Nocturia									
Female	0			1 (0.5)	1	0.3	0		
Male	0			1 (0.6)	1	0.4	0		
Proteinuria									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	2 (0.9)	2	0.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Renal colic									
Female	0			2 (0.9)	2	0.7	1 (0.5)	1	0.4
Male	0			0			0		
Pollakiuria									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	2 (1.0)	2	0.8	0			1 (0.5)	1	0.4
Lower urinary tract symptoms									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Micturition disorder									
Female	0			0			0		
Male	0			0			1 (0.5)	2	0.7
Polyuria									
Female	0			0			2 (1.1)	2	0.8
Male	0			0			0		
Urethral pain									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Urinary incontinence									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Renal disorders (excl nephropathies)									
Female	2 (1.0)	2	0.7	3 (1.4)	5	1.7	3 (1.6)	3	1.2
Male	3 (1.5)	3	1.1	3 (1.7)	3	1.3	4 (1.9)	4	1.5
Acute kidney injury									
Female	0			1 (0.5)	2	0.7	2 (1.1)	2	0.8
Male	2 (1.0)	2	0.8	2 (1.1)	2	0.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Renal cyst									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	2 (0.9)	2	0.7
Chronic kidney disease									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			1 (0.5)	1	0.4
Renal impairment									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Hydronephrosis									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Kidney fibrosis									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Nephropathies									
Female	1 (0.5)	1	0.4	4 (1.8)	4	1.3	0		
Male	2 (1.0)	2	0.8	2 (1.1)	2	0.8	1 (0.5)	1	0.4
Diabetic nephropathy									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	0		
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	1 (0.5)	1	0.4
Nephropathy									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			0		
Urolithiases									
Female	4 (2.0)	4	1.5	3 (1.4)	3	1.0	2 (1.1)	2	0.8
Male	2 (1.0)	3	1.1	1 (0.6)	1	0.4	4 (1.9)	4	1.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Nephrolithiasis									
Female	4 (2.0)	4	1.5	2 (0.9)	2	0.7	1 (0.5)	1	0.4
Male	2 (1.0)	3	1.1	0			3 (1.4)	3	1.1
Calculus urinary									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Stag horn calculus									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Ureterolithiasis									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Bladder and bladder neck disorders (excl calculi)									
Female	0			1 (0.5)	1	0.3	0		
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Bladder outlet obstruction									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Hypertonic bladder									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Bladder hypertrophy									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Psychiatric disorders									

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	10 (5.0)	15	5.6	11 (5.0)	12	4.0	9 (4.7)	10	3.9
Male	13 (6.5)	13	5.0	13 (7.2)	17	7.2	6 (2.8)	6	2.2
Sleep disorders and disturbances									
Female	2 (1.0)	2	0.7	5 (2.3)	5	1.7	2 (1.1)	2	0.8
Male	4 (2.0)	4	1.5	5 (2.8)	5	2.1	2 (0.9)	2	0.7
Insomnia									
Female	2 (1.0)	2	0.7	4 (1.8)	4	1.3	2 (1.1)	2	0.8
Male	4 (2.0)	4	1.5	3 (1.7)	3	1.3	2 (0.9)	2	0.7
Abnormal dreams									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Middle insomnia									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Sleep disorder									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Depressed mood disorders and disturbances									
Female	2 (1.0)	2	0.7	3 (1.4)	3	1.0	3 (1.6)	3	1.2
Male	3 (1.5)	3	1.1	4 (2.2)	4	1.7	2 (0.9)	2	0.7
Depressed mood									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	0		
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	0		
Depression									
Female	0			0			3 (1.6)	3	1.2
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	2 (0.9)	2	0.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Anhedonia									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Major depression									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Anxiety disorders and symptoms									
Female	7 (3.5)	8	3.0	2 (0.9)	2	0.7	5 (2.6)	5	2.0
Male	3 (1.5)	3	1.1	3 (1.7)	3	1.3	1 (0.5)	1	0.4
Anxiety									
Female	5 (2.5)	6	2.2	1 (0.5)	1	0.3	4 (2.1)	4	1.6
Male	2 (1.0)	2	0.8	2 (1.1)	2	0.8	0		
Stress									
Female	0			0			1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	0		
Anxiety disorder due to a general medical condition									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Generalised anxiety disorder									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Nervousness									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	0			0		
Post-traumatic stress disorder									
Female	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			1 (0.5)	1	0.4
Mood disorders and disturbances NEC									
Female	0			0			0		
Male	2 (1.0)	2	0.8	2 (1.1)	3	1.3	1 (0.5)	1	0.4
Irritability									
Female	0			0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Mood altered									
Female	0			0			0		
Male	0			1 (0.6)	2	0.8	1 (0.5)	1	0.4
Mood swings									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Adjustment disorders (incl subtypes)									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	0		
Male	0			1 (0.6)	1	0.4	0		
Grief reaction									
Female	1 (0.5)	1	0.4	0			0		
Male	0			1 (0.6)	1	0.4	0		
Adjustment disorder with depressed mood									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			0		
Suicidal and self-injurious behaviours NEC									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Suicidal ideation									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Changes in physical activity									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Restlessness									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Psychiatric disorders NEC									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Mental status changes									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Sexual dysfunctions, disturbances and gender identity disorders									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Libido decreased									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Vascular disorders									
Female	10 (5.0)	10	3.7	14 (6.3)	15	5.1	12 (6.3)	13	5.1
Male	12 (6.0)	13	5.0	10 (5.5)	11	4.7	18 (8.5)	19	6.9
Vascular hypertensive disorders									

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	5 (2.5)	5	1.9	4 (1.8)	4	1.3	4 (2.1)	4	1.6
Male	4 (2.0)	4	1.5	6 (3.3)	7	3.0	11 (5.2)	12	4.4
Hypertension									
Female	5 (2.5)	5	1.9	4 (1.8)	4	1.3	4 (2.1)	4	1.6
Male	4 (2.0)	4	1.5	6 (3.3)	7	3.0	8 (3.8)	8	2.9
Hypertensive crisis									
Female	0			0			0		
Male	0			0			3 (1.4)	3	1.1
Hypertensive urgency									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Decreased and nonspecific blood pressure disorders and shock									
Female	1 (0.5)	1	0.4	3 (1.4)	4	1.3	3 (1.6)	3	1.2
Male	4 (2.0)	5	1.9	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Hypotension									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	3 (1.5)	4	1.5	1 (0.6)	1	0.4	0		
Blood pressure inadequately controlled									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			0		
Orthostatic hypotension									
Female	0			1 (0.5)	2	0.7	1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Shock									
Female	0			0			0		

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	0			0		
Vascular disorders NEC									
Female	0			3 (1.4)	3	1.0	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	0			0		
Aortic dilatation									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Aortic rupture									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Hot flush									
Female	0			1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	0			0		
Vascular haemorrhagic disorders									
Female	0			3 (1.4)	3	1.0	0		
Male	0			0			1 (0.5)	1	0.4
Haematoma									
Female	0			3 (1.4)	3	1.0	0		
Male	0			0			1 (0.5)	1	0.4
Aneurysms and artery dissections									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Aortic aneurysm									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Embolism and thrombosis									
Female	0			0			0		

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Post thrombotic syndrome									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Deep vein thrombosis									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Vascular infections and inflammations									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Temporal arteritis									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Arteriosclerosis, stenosis, vascular insufficiency and necrosis									
Female	3 (1.5)	3	1.1	1 (0.5)	1	0.3	2 (1.1)	3	1.2
Male	3 (1.5)	3	1.1	0			3 (1.4)	3	1.1
Aortic arteriosclerosis									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	2 (1.0)	2	0.8	0			0		
Arteriosclerosis									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Peripheral arterial occlusive disease									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Peripheral artery stenosis									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Peripheral coldness									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	0			0		
Peripheral venous disease									
Female	0			0			1 (0.5)	2	0.8
Male	0			0			1 (0.5)	1	0.4
Lymphatic vessel disorders									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Lymphoedema									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Venous varices									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			1 (0.5)	1	0.4
Varicose vein									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			1 (0.5)	1	0.4
Cardiac disorders									
Female	6 (3.0)	7	2.6	12 (5.4)	16	5.4	6 (3.2)	9	3.5
Male	14 (7.0)	17	6.5	10 (5.5)	12	5.1	7 (3.3)	8	2.9
Cardiac arrhythmias									
Female	3 (1.5)	4	1.5	8 (3.6)	10	3.4	3 (1.6)	4	1.6

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	7 (3.5)	8	3.1	5 (2.8)	6	2.5	1 (0.5)	1	0.4
Atrial fibrillation									
Female	0			3 (1.4)	3	1.0	1 (0.5)	1	0.4
Male	2 (1.0)	2	0.8	2 (1.1)	2	0.8	1 (0.5)	1	0.4
Supraventricular extrasystoles									
Female	0			3 (1.4)	3	1.0	0		
Male	0			1 (0.6)	1	0.4	0		
Tachycardia									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Atrioventricular block first degree									
Female	0			0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Supraventricular tachycardia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Bundle branch block right									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			0		
Sinus tachycardia									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	0			0		
Ventricular extrasystoles									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Atrial flutter									
Female	0			0			1 (0.5)	2	0.8

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			0		
Bradycardia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Bundle branch block left									
Female	3 (1.5)	3	1.1	0			0		
Male	0			0			0		
Coronary artery disorders									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	0		
Male	6 (3.0)	6	2.3	4 (2.2)	4	1.7	4 (1.9)	4	1.5
Angina pectoris									
Female	0			0			0		
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	2 (0.9)	2	0.7
Coronary artery disease									
Female	0			0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Myocardial infarction									
Female	0			0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Acute myocardial infarction									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Angina unstable									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Myocardial ischaemia									
Female	0			1 (0.5)	1	0.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Arteriosclerosis coronary artery									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Cardiac disorders, signs and symptoms NEC									
Female	2 (1.0)	2	0.7	2 (0.9)	3	1.0	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	2 (0.9)	2	0.7
Palpitations									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	1 (0.5)	1	0.4
Cardiovascular disorder									
Female	0			1 (0.5)	2	0.7	1 (0.5)	1	0.4
Male	0			0			0		
Hypertensive heart disease									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Heart failures									
Female	0			0			2 (1.1)	3	1.2
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Cardiac failure congestive									
Female	0			0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Cardiac failure acute									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Left ventricular failure									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Myocardial disorders									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Cardiac hypertrophy									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Left ventricular hypertrophy									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Ear and labyrinth disorders									
Female	4 (2.0)	6	2.2	11 (5.0)	11	3.7	10 (5.3)	12	4.7
Male	7 (3.5)	8	3.1	9 (5.0)	9	3.8	2 (0.9)	2	0.7
Inner ear and VIIIth cranial nerve disorders									
Female	2 (1.0)	4	1.5	5 (2.3)	5	1.7	8 (4.2)	9	3.5
Male	6 (3.0)	7	2.7	5 (2.8)	5	2.1	0		
Vertigo									
Female	1 (0.5)	2	0.7	4 (1.8)	4	1.3	6 (3.2)	7	2.8
Male	2 (1.0)	3	1.1	3 (1.7)	3	1.3	0		
Vertigo positional									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			2 (1.1)	2	0.8	0		
Motion sickness									
Female	1 (0.5)	2	0.7	0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	0			0		
Tinnitus									
Female	0			0			1 (0.5)	1	0.4
Male	3 (1.5)	3	1.1	0			0		
Aural disorders NEC									
Female	1 (0.5)	1	0.4	4 (1.8)	4	1.3	3 (1.6)	3	1.2
Male	0			2 (1.1)	2	0.8	0		
Ear pain									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	2 (1.1)	2	0.8
Male	0			2 (1.1)	2	0.8	0		
Ear pruritus									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Ear discomfort									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Hearing disorders									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			2 (1.1)	2	0.8	1 (0.5)	1	0.4
Hypoacusis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			1 (0.6)	1	0.4	0		
Deafness bilateral									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Deafness unilateral									
Female	1 (0.5)	1	0.4	0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			0		
Mixed deafness									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
External ear disorders (excl congenital)									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Cerumen impaction									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			1 (0.5)	1	0.4
Excessive cerumen production									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Blood and lymphatic system disorders									
Female	5 (2.5)	5	1.9	10 (4.5)	10	3.4	3 (1.6)	3	1.2
Male	4 (2.0)	4	1.5	2 (1.1)	3	1.3	7 (3.3)	8	2.9
Anaemias nonhaemolytic and marrow depression									
Female	5 (2.5)	5	1.9	9 (4.1)	9	3.0	1 (0.5)	1	0.4
Male	3 (1.5)	3	1.1	1 (0.6)	2	0.8	5 (2.4)	5	1.8
Anaemia									
Female	2 (1.0)	2	0.7	8 (3.6)	8	2.7	0		
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	4 (1.9)	4	1.5
Pancytopenia									
Female	0			0			0		

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			1 (0.6)	1	0.4	0		
Iron deficiency anaemia									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Hypochromic anaemia									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Microcytic anaemia									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Normocytic anaemia									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Spleen, lymphatic and reticuloendothelial system disorders									
Female	0			0			1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	2 (0.9)	2	0.7
Splenomegaly									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Lymphadenopathy									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Platelet disorders									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Thrombocytosis									

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
White blood cell disorders									
Female	0			0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Leukocytosis									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Lymphopenia									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Reproductive system and breast disorders									
Female	6 (3.0)	10	3.7	10 (4.5)	10	3.4	5 (2.6)	7	2.8
Male	9 (4.5)	10	3.8	2 (1.1)	2	0.8	4 (1.9)	4	1.5
Menstrual cycle and uterine bleeding disorders									
Female	2 (1.0)	2	0.7	3 (1.4)	3	1.0	1 (0.5)	2	0.8
Male	0			0			0		
Dysmenorrhoea									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Metrorrhagia									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Oligomenorrhoea									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Menorrhagia									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Menstruation irregular									
Female	1 (0.5)	1	0.4	0			1 (0.5)	2	0.8
Male	0			0			0		
Vulvovaginal disorders (excl infections and inflammations)									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	2 (1.1)	2	0.8
Male	0			0			0		
Vulva cyst									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Vulval disorder									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Vulvovaginal pruritus									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Vaginal disorder									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Vaginal haemorrhage									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Vulvovaginal dryness									
Female	0			0			1 (0.5)	1	0.4

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			0		
Sexual function and fertility disorders									
Female	0			0			0		
Male	2 (1.0)	2	0.8	2 (1.1)	2	0.8	1 (0.5)	1	0.4
Erectile dysfunction									
Female	0			0			0		
Male	2 (1.0)	2	0.8	2 (1.1)	2	0.8	1 (0.5)	1	0.4
Breast disorders									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			0		
Breast mass									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			0		
Breast cyst									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Breast pain									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Menopause related conditions									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			0		
Atrophic vulvovaginitis									
Female	0			1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			0		
Reproductive tract disorders NEC									

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	0		
Male	0			0			0		
Pruritus genital									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	0		
Male	0			0			0		
Pelvic pain									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Uterine, pelvic and broad ligament disorders									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	0			0			0		
Uterine polyp									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Adenomyosis									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Endometriosis									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Male reproductive tract infections and inflammations									
Female	0			0			0		
Male	4 (2.0)	4	1.5	0			1 (0.5)	1	0.4
Balanoposthitis									
Female	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	3 (1.5)	3	1.1	0			0		
Prostatitis									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Ovarian and fallopian tube disorders									
Female	2 (1.0)	2	0.7	0			0		
Male	0			0			0		
Haemorrhagic ovarian cyst									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Ovarian cyst									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Penile and scrotal disorders (excl infections and inflammations)									
Female	0			0			0		
Male	1 (0.5)	2	0.8	0			0		
Penile erosion									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Peyronie's disease									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Prostatic disorders (excl infections and inflammations)									
Female	0			0			0		
Male	2 (1.0)	2	0.8	0			1 (0.5)	1	0.4

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Benign prostatic hyperplasia									
Female	0			0			0		
Male	2 (1.0)	2	0.8	0			1 (0.5)	1	0.4
Testicular and epididymal disorders									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Testicular disorder									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Hepatobiliary disorders									
Female	6 (3.0)	6	2.2	3 (1.4)	5	1.7	2 (1.1)	3	1.2
Male	4 (2.0)	5	1.9	7 (3.9)	8	3.4	7 (3.3)	11	4.0
Hepatic and hepatobiliary disorders									
Female	4 (2.0)	4	1.5	3 (1.4)	3	1.0	2 (1.1)	2	0.8
Male	2 (1.0)	2	0.8	5 (2.8)	6	2.5	7 (3.3)	8	2.9
Hepatic steatosis									
Female	2 (1.0)	2	0.7	1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	3 (1.7)	3	1.3	3 (1.4)	3	1.1
Hepatic lesion									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Nonalcoholic fatty liver disease									
Female	1 (0.5)	1	0.4	0			0		
Male	0			1 (0.6)	1	0.4	0		
Portal vein thrombosis									
Female	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Hepatic cyst									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			1 (0.5)	1	0.4
Non-alcoholic steatohepatitis									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Drug-induced liver injury									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Hepatic cirrhosis									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Hepatomegaly									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Liver disorder									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Portal hypertension									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Gallbladder disorders									
Female	2 (1.0)	2	0.7	1 (0.5)	2	0.7	1 (0.5)	1	0.4
Male	2 (1.0)	3	1.1	2 (1.1)	2	0.8	2 (0.9)	3	1.1
Gallbladder polyp									
Female	1 (0.5)	1	0.4	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	2 (1.1)	2	0.8	0		
Cholecystitis chronic									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Cholelithiasis									
Female	1 (0.5)	1	0.4	1 (0.5)	1	0.3	1 (0.5)	1	0.4
Male	2 (1.0)	2	0.8	0			2 (0.9)	2	0.7
Cholecystitis acute									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Neoplasms benign, malignant and unspecified (incl cysts and polyps)									
Female	8 (4.0)	10	3.7	3 (1.4)	3	1.0	5 (2.6)	6	2.4
Male	5 (2.5)	6	2.3	6 (3.3)	7	3.0	7 (3.3)	8	2.9
Leukaemias									
Female	0			0			0		
Male	0			2 (1.1)	2	0.8	0		
Chronic lymphocytic leukaemia									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Myeloid leukaemia									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Gastrointestinal neoplasms benign									
Female	2 (1.0)	3	1.1	1 (0.5)	1	0.3	2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Benign duodenal neoplasm									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Gastrointestinal tract adenoma									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Colon adenoma									
Female	2 (1.0)	3	1.1	0			2 (1.1)	2	0.8
Male	1 (0.5)	1	0.4	0			0		
Cutaneous neoplasms benign									
Female	0			0			1 (0.5)	1	0.4
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Anogenital warts									
Female	0			0			0		
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	0		
Melanocytic naevus									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Lymphomas non-Hodgkin's unspecified histology									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Gastrointestinal lymphoma									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Miscellaneous and site unspecified neoplasms malignant and unspecified									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Squamous cell carcinoma									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Respiratory and mediastinal neoplasms malignant and unspecified									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	1 (0.5)	1	0.4
Nasal cavity cancer									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Keratinising squamous cell carcinoma of nasopharynx									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Skeletal neoplasms benign									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Osteochondroma									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Soft tissue neoplasms benign									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Lipoma									
Female	0			1 (0.5)	1	0.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Breast neoplasms malignant and unspecified (incl nipple)									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Invasive ductal breast carcinoma									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Endocrine neoplasms benign									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Pituitary tumour benign									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Endocrine neoplasms malignant and unspecified									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Neuroendocrine tumour									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Gastrointestinal neoplasms malignant and unspecified									
Female	4 (2.0)	4	1.5	0			0		
Male	1 (0.5)	1	0.4	0			2 (0.9)	2	0.7
Adenocarcinoma gastric									
Female	1 (0.5)	1	0.4	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Male	0			0			0		
Adenocarcinoma of colon									
Female	1	(0.5)	1 0.4	0			0		
Male	0			0			0		
Gastric cancer									
Female	0			0			0		
Male	0			0			1	(0.5)	1 0.4
Gastric cancer stage IV									
Female	0			0			0		
Male	0			0			1	(0.5)	1 0.4
Gastrointestinal stromal tumour									
Female	0			0			0		
Male	1	(0.5)	1 0.4	0			0		
Gastrointestinal submucosal tumour									
Female	1	(0.5)	1 0.4	0			0		
Male	0			0			0		
Oral neoplasm									
Female	1	(0.5)	1 0.4	0			0		
Male	0			0			0		
Hepatobiliary neoplasms malignant and unspecified									
Female	0			0			0		
Male	0			0			1	(0.5)	1 0.4
Hepatocellular carcinoma									
Female	0			0			0		
Male	0			0			1	(0.5)	1 0.4
Metastases									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Metastases to liver									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Reproductive neoplasms female benign									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Uterine leiomyoma									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Reproductive neoplasms female malignant and unspecified									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Uterine cancer									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Reproductive neoplasms male malignant and unspecified									
Female	0			0			0		
Male	0			0			3 (1.4)	3	1.1
Prostate cancer									
Female	0			0			0		
Male	0			0			3 (1.4)	3	1.1
Skin neoplasms malignant and unspecified									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			2 (1.1)	2	0.8
Male	0			0			0		
Basal cell carcinoma									
Female	0			0			2 (1.1)	2	0.8
Male	0			0			0		
Immune system disorders									
Female	0			4 (1.8)	4	1.3	3 (1.6)	3	1.2
Male	6 (3.0)	6	2.3	2 (1.1)	2	0.8	3 (1.4)	4	1.5
Allergic conditions									
Female	0			4 (1.8)	4	1.3	3 (1.6)	3	1.2
Male	5 (2.5)	5	1.9	2 (1.1)	2	0.8	3 (1.4)	4	1.5
Seasonal allergy									
Female	0			3 (1.4)	3	1.0	1 (0.5)	1	0.4
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	3 (1.4)	4	1.5
Allergy to arthropod sting									
Female	0			0			1 (0.5)	1	0.4
Male	0			1 (0.6)	1	0.4	0		
Hypersensitivity									
Female	0			1 (0.5)	1	0.3	0		
Male	1 (0.5)	1	0.4	0			0		
Allergy to chemicals									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Drug hypersensitivity									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Multiple allergies									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Immune disorders NEC									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Immunisation reaction									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Endocrine disorders									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	2 (1.1)	2	0.8
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	2 (0.9)	2	0.7
Thyroid gland disorders									
Female	1 (0.5)	1	0.4	3 (1.4)	3	1.0	2 (1.1)	2	0.8
Male	2 (1.0)	2	0.8	1 (0.6)	1	0.4	2 (0.9)	2	0.7
Hypothyroidism									
Female	1 (0.5)	1	0.4	2 (0.9)	2	0.7	0		
Male	0			0			0		
Primary hyperthyroidism									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Thyroid cyst									
Female	0			1 (0.5)	1	0.3	0		
Male	0			0			0		
Autoimmune thyroiditis									
Female	0			0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	0			0		
Goitre									
Female	0			0			0		
Male	0			0			1 (0.5)	1	0.4
Silent thyroiditis									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Thyroid mass									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			1 (0.5)	1	0.4
Surgical and medical procedures									
Female	2 (1.0)	2	0.7	0			2 (1.1)	3	1.2
Male	1 (0.5)	1	0.4	1 (0.6)	1	0.4	3 (1.4)	3	1.1
Endocrine gland therapeutic procedures									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Thyroidectomy									
Female	0			0			0		
Male	0			1 (0.6)	1	0.4	0		
Bone and joint therapeutic procedures									
Female	1 (0.5)	1	0.4	0			1 (0.5)	1	0.4
Male	0			0			0		
Bone graft									
Female	1 (0.5)	1	0.4	0			0		
Male	0			0			0		
Joint injection									

Adverse events with onset prior to randomisation are not included.
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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Female	0			0			1	(0.5)	1 0.4
Male	0			0			0		
Cardiac therapeutic procedures									
Female	1	(0.5)	1 0.4	0			0		
Male	0			0			0		
Cardiac pacemaker replacement									
Female	1	(0.5)	1 0.4	0			0		
Male	0			0			0		
Eye therapeutic procedures									
Female	0			0			0		
Male	0			0			1	(0.5)	1 0.4
Cataract operation									
Female	0			0			0		
Male	0			0			1	(0.5)	1 0.4
Head and neck therapeutic procedures									
Female	0			0			0		
Male	1	(0.5)	1 0.4	0			0		
Tooth extraction									
Female	0			0			0		
Male	1	(0.5)	1 0.4	0			0		
Male genital tract therapeutic procedures									
Female	0			0			0		
Male	0			0			1	(0.5)	1 0.4
Sperm aspiration									
Female	0			0			0		
Male	0			0			1	(0.5)	1 0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Therapeutic procedures and supportive care NEC									
Female	0			0			2	(1.1)	2 0.8
Male	0			0			1	(0.5)	1 0.4
Cyst removal									
Female	0			0			1	(0.5)	1 0.4
Male	0			0			0		
Nerve block									
Female	0			0			1	(0.5)	1 0.4
Male	0			0			0		
Stent placement									
Female	0			0			0		
Male	0			0			1	(0.5)	1 0.4
Congenital, familial and genetic disorders									
Female	0			0			0		
Male	1	(0.5)	1 0.4	0			2	(0.9)	2 0.7
Reproductive tract and breast disorders congenital									
Female	0			0			0		
Male	0			0			2	(0.9)	2 0.7
Phimosis									
Female	0			0			0		
Male	0			0			2	(0.9)	2 0.7
Respiratory disorders congenital									
Female	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (0.5)	1	0.4	0			0		
Laryngeal web									
Female	0			0			0		
Male	1 (0.5)	1	0.4	0			0		
Pregnancy, puerperium and perinatal conditions									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Abortions and stillbirth									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Abortion spontaneous									
Female	0			0			1 (0.5)	1	0.4
Male	0			0			0		
Social circumstances									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	0			0		
Economic and housing issues									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	0			0		
Stress at work									
Female	1 (0.5)	1	0.4	0			0		
Male	1 (0.5)	1	0.4	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

5 Adverse events by sex - overview - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
Female	36	49.7			85	120.1			26	37.1		
Male	64	86.5			114	154.9			75	104.8		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Events												
Female	31	(86.1)	175	352.2	78	(91.8)	425	353.9	22	(84.6)	74	199.7
Male	51	(79.7)	308	356.0	93	(81.6)	409	264.0	58	(77.3)	161	153.7
Serious												
Yes												
Female	2	(5.6)	2	4.0	5	(5.9)	6	5.0	0			
Male	5	(7.8)	8	9.2	5	(4.4)	6	3.9	7	(9.3)	7	6.7
No												
Female	31	(86.1)	173	348.2	78	(91.8)	419	348.9	22	(84.6)	74	199.7
Male	51	(79.7)	300	346.7	92	(80.7)	403	260.1	56	(74.7)	154	147.0
Severity												
Severe												
Female	0				1	(1.2)	2	1.7	0			
Male	3	(4.7)	3	3.5	2	(1.8)	2	1.3	5	(6.7)	5	4.8
Moderate												
Female	4	(11.1)	19	38.2	13	(15.3)	18	15.0	5	(19.2)	7	18.9
Male	10	(15.6)	44	50.9	12	(10.5)	24	15.5	6	(8.0)	6	5.7
Mild												
Female	31	(86.1)	156	314.0	78	(91.8)	405	337.3	21	(80.8)	67	180.8
Male	48	(75.0)	261	301.6	90	(78.9)	383	247.2	55	(73.3)	150	143.2

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by sex - overview - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Relationship to trial product									
Missing									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Probable									
Female	14 (38.9)	20	40.3	22 (25.9)	79	65.8	2 (7.7)	2	5.4
Male	11 (17.2)	41	47.4	33 (28.9)	79	51.0	8 (10.7)	14	13.4
Possible									
Female	20 (55.6)	44	88.6	38 (44.7)	91	75.8	4 (15.4)	5	13.5
Male	35 (54.7)	146	168.7	46 (40.4)	115	74.2	6 (8.0)	12	11.5
Unlikely									
Female	30 (83.3)	111	223.4	70 (82.4)	255	212.3	21 (80.8)	67	180.8
Male	43 (67.2)	121	139.8	82 (71.9)	214	138.1	53 (70.7)	135	128.8
Outcome									
Recovered									
Female	29 (80.6)	133	267.7	74 (87.1)	362	301.5	21 (80.8)	57	153.8
Male	49 (76.6)	276	319.0	90 (78.9)	367	236.9	54 (72.0)	129	123.1
Recovering									
Female	4 (11.1)	7	14.1	10 (11.8)	13	10.8	1 (3.8)	1	2.7
Male	5 (7.8)	9	10.4	6 (5.3)	8	5.2	4 (5.3)	4	3.8
Not Recovered									
Female	18 (50.0)	35	70.4	30 (35.3)	50	41.6	11 (42.3)	16	43.2
Male	17 (26.6)	23	26.6	24 (21.1)	34	21.9	15 (20.0)	28	26.7
Leading to									
Permanent treatment discontinuation									
Female	2 (5.6)	5	10.1	1 (1.2)	2	1.7	0		
Male	1 (1.6)	1	1.2	4 (3.5)	7	4.5	1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by sex - overview - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Leading to									
Temporary interruption of trial product									
Female	3 (8.3)	4	8.1	5 (5.9)	5	4.2	1 (3.8)	1	2.7
Male	4 (6.3)	5	5.8	9 (7.9)	21	13.6	4 (5.3)	4	3.8
Dose reduction of trial product									
Female	0			7 (8.2)	10	8.3	0		
Male	3 (4.7)	3	3.5	7 (6.1)	9	5.8	0		

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

6 Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N		PYE		N		PYE		N		PYE	
Female	36		49.7		85		120.1		26		37.1	
Male	64		86.5		114		154.9		75		104.8	
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Adverse events												
Female	31	(86.1)	175	352.2	78	(91.8)	425	353.9	22	(84.6)	74	199.7
Male	51	(79.7)	308	356.0	93	(81.6)	409	264.0	58	(77.3)	161	153.7
Gastrointestinal disorders												
Female	28	(77.8)	70	140.9	54	(63.5)	171	142.4	10	(38.5)	11	29.7
Male	36	(56.3)	186	215.0	64	(56.1)	172	111.0	20	(26.7)	32	30.5
Gastrointestinal motility and defaecation conditions												
Female	16	(44.4)	21	42.3	36	(42.4)	60	50.0	5	(19.2)	5	13.5
Male	25	(39.1)	63	72.8	42	(36.8)	59	38.1	4	(5.3)	4	3.8
Constipation												
Female	10	(27.8)	12	24.2	24	(28.2)	27	22.5	2	(7.7)	2	5.4
Male	9	(14.1)	10	11.6	28	(24.6)	33	21.3	1	(1.3)	1	1.0
Diarrhoea												
Female	7	(19.4)	9	18.1	17	(20.0)	30	25.0	3	(11.5)	3	8.1
Male	15	(23.4)	50	57.8	15	(13.2)	22	14.2	3	(4.0)	3	2.9
Gastrooesophageal reflux disease												
Female	0				2	(2.4)	2	1.7	0			
Male	2	(3.1)	2	2.3	4	(3.5)	4	2.6	0			
Gastrointestinal motility disorder												

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Irritable bowel syndrome									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Gastrointestinal signs and symptoms									
Female	21 (58.3)	39	78.5	32 (37.6)	79	65.8	1 (3.8)	1	2.7
Male	18 (28.1)	112	129.4	39 (34.2)	90	58.1	10 (13.3)	16	15.3
Nausea									
Female	10 (27.8)	11	22.1	16 (18.8)	29	24.1	0		
Male	8 (12.5)	16	18.5	19 (16.7)	37	23.9	4 (5.3)	4	3.8
Vomiting									
Female	4 (11.1)	4	8.1	8 (9.4)	14	11.7	1 (3.8)	1	2.7
Male	6 (9.4)	30	34.7	9 (7.9)	15	9.7	1 (1.3)	1	1.0
Abdominal discomfort									
Female	5 (13.9)	5	10.1	5 (5.9)	7	5.8	0		
Male	6 (9.4)	7	8.1	7 (6.1)	9	5.8	1 (1.3)	1	1.0
Abdominal pain									
Female	2 (5.6)	3	6.0	4 (4.7)	5	4.2	0		
Male	1 (1.6)	1	1.2	8 (7.0)	11	7.1	0		
Abdominal pain upper									
Female	3 (8.3)	5	10.1	8 (9.4)	11	9.2	0		
Male	0			2 (1.8)	2	1.3	1 (1.3)	1	1.0
Dyspepsia									
Female	2 (5.6)	2	4.0	4 (4.7)	7	5.8	0		
Male	4 (6.3)	15	17.3	5 (4.4)	7	4.5	1 (1.3)	4	3.8
Abdominal distension									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	3 (8.3)	3	6.0	2 (2.4)	3	2.5	0		
Male	4 (6.3)	5	5.8	5 (4.4)	5	3.2	2 (2.7)	3	2.9
Faeces soft									
Female	0			1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Eructation									
Female	2 (5.6)	2	4.0	0			0		
Male	2 (3.1)	19	22.0	2 (1.8)	2	1.3	0		
Abdominal tenderness									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Faeces hard									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Flatulence									
Female	0			0			0		
Male	1 (1.6)	18	20.8	1 (0.9)	1	0.6	0		
Abdominal pain lower									
Female	1 (2.8)	2	4.0	0			0		
Male	0			0			1 (1.3)	2	1.9
Epigastric discomfort									
Female	2 (5.6)	2	4.0	0			0		
Male	0			0			0		
Dental and gingival conditions									
Female	3 (8.3)	3	6.0	8 (9.4)	9	7.5	2 (7.7)	2	5.4
Male	3 (4.7)	3	3.5	6 (5.3)	6	3.9	4 (5.3)	4	3.8
Dental caries									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	2 (5.6)	2	4.0	6 (7.1)	7	5.8	2 (7.7)	2	5.4
Male	2 (3.1)	2	2.3	5 (4.4)	5	3.2	3 (4.0)	3	2.9
Toothache									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	0			1 (0.9)	1	0.6	1 (1.3)	1	1.0
Tooth impacted									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Dental cyst									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Gastrointestinal conditions NEC									
Female	2 (5.6)	2	4.0	7 (8.2)	8	6.7	0		
Male	2 (3.1)	2	2.3	3 (2.6)	4	2.6	1 (1.3)	1	1.0
Gastrointestinal disorder									
Female	1 (2.8)	1	2.0	3 (3.5)	4	3.3	0		
Male	1 (1.6)	1	1.2	1 (0.9)	2	1.3	0		
Gastric disorder									
Female	1 (2.8)	1	2.0	3 (3.5)	3	2.5	0		
Male	1 (1.6)	1	1.2	0			0		
Food poisoning									
Female	0			1 (1.2)	1	0.8	0		
Male	0			2 (1.8)	2	1.3	0		
Barrett's oesophagus									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gastrointestinal inflammatory conditions									
Female	1 (2.8)	1	2.0	4 (4.7)	5	4.2	3 (11.5)	3	8.1
Male	0			6 (5.3)	6	3.9	2 (2.7)	2	1.9
Enterocolitis									
Female	1 (2.8)	1	2.0	2 (2.4)	2	1.7	0		
Male	0			2 (1.8)	2	1.3	1 (1.3)	1	1.0
Gastritis									
Female	0			1 (1.2)	1	0.8	2 (7.7)	2	5.4
Male	0			2 (1.8)	2	1.3	1 (1.3)	1	1.0
Chronic gastritis									
Female	0			1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	0			0			0		
Enteritis									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Colitis									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Colitis ischaemic									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Benign neoplasms gastrointestinal									
Female	1 (2.8)	1	2.0	3 (3.5)	4	3.3	0		
Male	2 (3.1)	2	2.3	3 (2.6)	3	1.9	2 (2.7)	2	1.9
Large intestine polyp									
Female	1 (2.8)	1	2.0	2 (2.4)	2	1.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (1.6)	1	1.2	2 (1.8)	2	1.3	2 (2.7)	2	1.9
Gastric polyps									
Female	0			2 (2.4)	2	1.7	0		
Male	0			1 (0.9)	1	0.6	0		
Rectal polyp									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Oral soft tissue conditions									
Female	0			3 (3.5)	3	2.5	0		
Male	0			0			0		
Stomatitis									
Female	0			2 (2.4)	2	1.7	0		
Male	0			0			0		
Angular cheilitis									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Gastrointestinal haemorrhages NEC									
Female	0			1 (1.2)	1	0.8	0		
Male	0			1 (0.9)	1	0.6	0		
Mallory-Weiss syndrome									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Anal haemorrhage									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Diverticular disorders									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (1.6)	1	1.2	0			0		
Diverticulum intestinal									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	0			0		
Gastrointestinal vascular conditions									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	0			1 (1.3)	1	1.0
Haemorrhoids									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	0			1 (1.3)	1	1.0
Anal and rectal conditions NEC									
Female	1 (2.8)	1	2.0	0			0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Anal fissure									
Female	1 (2.8)	1	2.0	0			0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Gastrointestinal ulceration and perforation									
Female	0			0			0		
Male	0			1 (0.9)	2	1.3	1 (1.3)	1	1.0
Erosive duodenitis									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Gastritis erosive									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gastrointestinal stenosis and obstruction									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Intestinal obstruction									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Salivary gland conditions									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Parotid gland enlargement									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Infections and infestations									
Female	17 (47.2)	26	52.3	42 (49.4)	82	68.3	13 (50.0)	20	54.0
Male	25 (39.1)	38	43.9	38 (33.3)	71	45.8	22 (29.3)	33	31.5
Infections - pathogen unspecified									
Female	17 (47.2)	25	50.3	38 (44.7)	73	60.8	12 (46.2)	18	48.6
Male	22 (34.4)	33	38.1	33 (28.9)	59	38.1	22 (29.3)	33	31.5
Nasopharyngitis									
Female	10 (27.8)	16	32.2	26 (30.6)	37	30.8	7 (26.9)	8	21.6
Male	14 (21.9)	20	23.1	27 (23.7)	44	28.4	11 (14.7)	16	15.3
Gastroenteritis									
Female	1 (2.8)	1	2.0	4 (4.7)	4	3.3	1 (3.8)	1	2.7
Male	6 (9.4)	7	8.1	7 (6.1)	9	5.8	0		
Bronchitis									

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			6 (7.1)	9	7.5	0		
Male	3 (4.7)	3	3.5	0			0		
Cystitis									
Female	1 (2.8)	1	2.0	3 (3.5)	3	2.5	0		
Male	0			0			1 (1.3)	2	1.9
Pharyngitis									
Female	1 (2.8)	1	2.0	2 (2.4)	3	2.5	1 (3.8)	1	2.7
Male	2 (3.1)	2	2.3	1 (0.9)	1	0.6	3 (4.0)	4	3.8
Conjunctivitis									
Female	0			2 (2.4)	3	2.5	1 (3.8)	1	2.7
Male	0			0			1 (1.3)	1	1.0
Rhinitis									
Female	0			1 (1.2)	1	0.8	2 (7.7)	2	5.4
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Tonsillitis									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	0			1 (0.9)	1	0.6	3 (4.0)	4	3.8
Acute sinusitis									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Enteritis infectious									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Folliculitis									
Female	0			1 (1.2)	2	1.7	0		
Male	0			0			0		
Gingivitis									

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Hordeolum									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	0			0			0		
Pelvic inflammatory disease									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Pyelonephritis									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	0			0			0		
Sinusitis									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	0			0			3 (4.0)	3	2.9
Urinary tract infection									
Female	1 (2.8)	1	2.0	1 (1.2)	3	2.5	0		
Male	0			0			0		
Diverticulitis									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Pyelonephritis acute									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Urethritis									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Periodontitis									

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	1 (2.8)	1	2.0	0			1 (3.8)	1	2.7
Male	0			0			0		
Pyoderma									
Female	0			0			0		
Male	0			0			1 (1.3)	2	1.9
Upper respiratory tract infection									
Female	0			0			1 (3.8)	2	5.4
Male	0			0			1 (1.3)	1	1.0
Vaginal infection									
Female	0			0			1 (3.8)	1	2.7
Male	0			0			0		
Viral infectious disorders									
Female	1 (2.8)	1	2.0	7 (8.2)	7	5.8	1 (3.8)	1	2.7
Male	4 (6.3)	4	4.6	6 (5.3)	7	4.5	0		
Influenza									
Female	0			5 (5.9)	5	4.2	1 (3.8)	1	2.7
Male	2 (3.1)	2	2.3	3 (2.6)	3	1.9	0		
Herpes zoster									
Female	0			0			0		
Male	1 (1.6)	1	1.2	3 (2.6)	3	1.9	0		
Gastroenteritis viral									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	0			1 (0.9)	1	0.6	0		
Herpes simplex									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Infectious mononucleosis									

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Bacterial infectious disorders									
Female	0			1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	3 (2.6)	4	2.6	0		
Cellulitis									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Alpha haemolytic streptococcal infection									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Erysipelas									
Female	0			0			0		
Male	0			1 (0.9)	2	1.3	0		
Furuncle									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Helicobacter infection									
Female	0			0			1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	0			0		
Fungal infectious disorders									
Female	0			1 (1.2)	1	0.8	0		
Male	0			1 (0.9)	1	0.6	0		
Vulvovaginal candidiasis									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Tinea pedis									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Musculoskeletal and connective tissue disorders									
Female	12 (33.3)	17	34.2	22 (25.9)	30	25.0	8 (30.8)	10	27.0
Male	12 (18.8)	17	19.6	21 (18.4)	22	14.2	16 (21.3)	24	22.9
Musculoskeletal and connective tissue disorders NEC									
Female	6 (16.7)	8	16.1	11 (12.9)	12	10.0	3 (11.5)	3	8.1
Male	4 (6.3)	6	6.9	11 (9.6)	11	7.1	10 (13.3)	12	11.5
Back pain									
Female	5 (13.9)	7	14.1	9 (10.6)	10	8.3	2 (7.7)	2	5.4
Male	3 (4.7)	5	5.8	10 (8.8)	10	6.5	7 (9.3)	9	8.6
Neck pain									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			1 (1.3)	1	1.0
Pain in extremity									
Female	0			1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	0			2 (2.7)	2	1.9
Musculoskeletal discomfort									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Musculoskeletal pain									
Female	0			0			1 (3.8)	1	2.7
Male	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Musculoskeletal stiffness									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Joint disorders									
Female	6 (16.7)	7	14.1	8 (9.4)	8	6.7	4 (15.4)	5	13.5
Male	9 (14.1)	10	11.6	5 (4.4)	5	3.2	7 (9.3)	11	10.5
Arthralgia									
Female	4 (11.1)	5	10.1	3 (3.5)	3	2.5	1 (3.8)	2	5.4
Male	5 (7.8)	5	5.8	2 (1.8)	2	1.3	5 (6.7)	7	6.7
Periarthritis									
Female	0			3 (3.5)	3	2.5	0		
Male	2 (3.1)	2	2.3	1 (0.9)	1	0.6	1 (1.3)	1	1.0
Osteoarthritis									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	2 (7.7)	2	5.4
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Spinal osteoarthritis									
Female	0			1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	0			0		
Rotator cuff syndrome									
Female	0			0			0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	1 (1.3)	1	1.0
Arthritis									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Articular calcification									
Female	0			0			0		
Male	0			0			1 (1.3)	2	1.9

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Muscle disorders									
Female	1 (2.8)	1	2.0	4 (4.7)	4	3.3	1 (3.8)	1	2.7
Male	0			5 (4.4)	5	3.2	0		
Myalgia									
Female	1 (2.8)	1	2.0	3 (3.5)	3	2.5	1 (3.8)	1	2.7
Male	0			1 (0.9)	1	0.6	0		
Muscle spasms									
Female	0			1 (1.2)	1	0.8	0		
Male	0			2 (1.8)	2	1.3	0		
Fibromyalgia									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Rhabdomyolysis									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Tendon, ligament and cartilage disorders									
Female	1 (2.8)	1	2.0	3 (3.5)	4	3.3	0		
Male	0			0			0		
Tendonitis									
Female	1 (2.8)	1	2.0	2 (2.4)	2	1.7	0		
Male	0			0			0		
Trigger finger									
Female	0			1 (1.2)	2	1.7	0		
Male	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)									
Female	0			1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	1 (1.3)	1	1.0
Spinal stenosis									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Intervertebral disc protrusion									
Female	0			0			0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	1 (1.3)	1	1.0
Synovial and bursal disorders									
Female	0			1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	0			0			0		
Bursitis									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Synovitis									
Female	0			0			1 (3.8)	1	2.7
Male	0			0			0		
Nervous system disorders									
Female	4 (11.1)	6	12.1	15 (17.6)	21	17.5	2 (7.7)	2	5.4
Male	4 (6.3)	5	5.8	20 (17.5)	31	20.0	4 (5.3)	4	3.8
Neurological disorders NEC									
Female	3 (8.3)	5	10.1	10 (11.8)	13	10.8	1 (3.8)	1	2.7
Male	3 (4.7)	3	3.5	12 (10.5)	20	12.9	2 (2.7)	2	1.9

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Dizziness									
Female	2 (5.6)	4	8.1	8 (9.4)	10	8.3	0		
Male	1 (1.6)	1	1.2	6 (5.3)	9	5.8	0		
Hypoaesthesia									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	2 (1.8)	3	1.9	0		
Dysaesthesia									
Female	0			1 (1.2)	2	1.7	0		
Male	0			0			0		
Dizziness postural									
Female	0			0			0		
Male	0			1 (0.9)	2	1.3	0		
Dysgeusia									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Neuralgia									
Female	0			0			0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Neurological symptom									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Paraesthesia									
Female	0			0			1 (3.8)	1	2.7
Male	0			1 (0.9)	1	0.6	0		
Somnolence									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Taste disorder									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Intercostal neuralgia									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Sensory loss									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Headaches									
Female	1 (2.8)	1	2.0	4 (4.7)	5	4.2	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	6 (5.3)	7	4.5	2 (2.7)	2	1.9
Headache									
Female	1 (2.8)	1	2.0	4 (4.7)	5	4.2	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	6 (5.3)	7	4.5	2 (2.7)	2	1.9
Spinal cord and nerve root disorders									
Female	0			0			0		
Male	1 (1.6)	1	1.2	3 (2.6)	3	1.9	0		
Sciatica									
Female	0			0			0		
Male	1 (1.6)	1	1.2	3 (2.6)	3	1.9	0		
Central nervous system vascular disorders									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Lacunar infarction									
Female	0			1 (1.2)	1	0.8	0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			0		
Neuromuscular disorders									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Autonomic nervous system imbalance									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Peripheral neuropathies									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Carpal tunnel syndrome									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Cranial nerve disorders (excl neoplasms)									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Parosmia									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Skin and subcutaneous tissue disorders									
Female	9 (25.0)	16	32.2	20 (23.5)	26	21.7	5 (19.2)	8	21.6
Male	4 (6.3)	6	6.9	4 (3.5)	4	2.6	6 (8.0)	6	5.7
Epidermal and dermal conditions									
Female	6 (16.7)	9	18.1	15 (17.6)	17	14.2	5 (19.2)	7	18.9
Male	4 (6.3)	4	4.6	2 (1.8)	2	1.3	3 (4.0)	3	2.9

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Eczema									
Female	3 (8.3)	3	6.0	3 (3.5)	3	2.5	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	1 (1.3)	1	1.0
Pruritus									
Female	0			3 (3.5)	3	2.5	2 (7.7)	3	8.1
Male	1 (1.6)	1	1.2	0			0		
Dermatitis									
Female	0			2 (2.4)	3	2.5	0		
Male	0			0			0		
Eczema asteatotic									
Female	0			1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Dermatitis atopic									
Female	0			1 (1.2)	2	1.7	0		
Male	0			0			0		
Dermatitis contact									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	0			0			2 (2.7)	2	1.9
Dyshidrotic eczema									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Erythema									
Female	0			1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	0			0		
Rash									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Stasis dermatitis									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Drug eruption									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Dry skin									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Pain of skin									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Rash pruritic									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Seborrhoeic dermatitis									
Female	0			0			1 (3.8)	1	2.7
Male	0			0			0		
Xanthelasma									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Skin appendage conditions									
Female	3 (8.3)	3	6.0	5 (5.9)	5	4.2	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	2 (1.8)	2	1.3	1 (1.3)	1	1.0
Alopecia									
Female	2 (5.6)	2	4.0	2 (2.4)	2	1.7	0		
Male	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Alopecia areata									
Female	0			2 (2.4)	2	1.7	0		
Male	0			0			0		
Miliaria									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	0			0			1 (1.3)	1	1.0
Acne									
Female	0			0			0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Ingrowing nail									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Angioedema and urticaria									
Female	2 (5.6)	3	6.0	2 (2.4)	2	1.7	0		
Male	1 (1.6)	1	1.2	0			2 (2.7)	2	1.9
Urticaria									
Female	2 (5.6)	3	6.0	2 (2.4)	2	1.7	0		
Male	1 (1.6)	1	1.2	0			2 (2.7)	2	1.9
Cornification and dystrophic skin disorders									
Female	1 (2.8)	1	2.0	2 (2.4)	2	1.7	0		
Male	0			0			0		
Hyperkeratosis									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	0			0			0		
Xeroderma									
Female	0			1 (1.2)	1	0.8	0		

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			0		
Injury, poisoning and procedural complications									
Female	6 (16.7)	7	14.1	12 (14.1)	12	10.0	5 (19.2)	6	16.2
Male	9 (14.1)	12	13.9	13 (11.4)	14	9.0	7 (9.3)	8	7.6
Injuries NEC									
Female	2 (5.6)	3	6.0	8 (9.4)	8	6.7	4 (15.4)	4	10.8
Male	4 (6.3)	7	8.1	9 (7.9)	10	6.5	5 (6.7)	6	5.7
Contusion									
Female	1 (2.8)	1	2.0	2 (2.4)	2	1.7	0		
Male	1 (1.6)	1	1.2	2 (1.8)	2	1.3	0		
Arthropod sting									
Female	0			1 (1.2)	1	0.8	0		
Male	0			2 (1.8)	2	1.3	0		
Ligament sprain									
Female	1 (2.8)	2	4.0	0			1 (3.8)	1	2.7
Male	2 (3.1)	2	2.3	3 (2.6)	3	1.9	1 (1.3)	1	1.0
Tendon rupture									
Female	0			1 (1.2)	1	0.8	0		
Male	0			1 (0.9)	1	0.6	1 (1.3)	1	1.0
Arthropod bite									
Female	0			1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	0			0			0		
Epicondylitis									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Limb injury									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Subcutaneous haematoma									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Post-traumatic neck syndrome									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	2 (2.7)	2	1.9
Tooth fracture									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Limb crushing injury									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Muscle contusion									
Female	0			0			1 (3.8)	1	2.7
Male	0			0			1 (1.3)	1	1.0
Muscle strain									
Female	0			0			0		
Male	1 (1.6)	2	2.3	0			0		
Road traffic accident									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Skin laceration									
Female	0			0			1 (3.8)	1	2.7
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subdural haematoma									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Bone and joint injuries									
Female	2 (5.6)	2	4.0	4 (4.7)	4	3.3	0		
Male	3 (4.7)	3	3.5	0			1 (1.3)	1	1.0
Ankle fracture									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Meniscus injury									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	0			0			0		
Radius fracture									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			1 (1.3)	1	1.0
Rib fracture									
Female	0			1 (1.2)	1	0.8	0		
Male	2 (3.1)	2	2.3	0			0		
Fracture									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Joint injury									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Injuries by physical agents									
Female	2 (5.6)	2	4.0	0			2 (7.7)	2	5.4
Male	1 (1.6)	1	1.2	2 (1.8)	2	1.3	1 (1.3)	1	1.0

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Heat stroke									
Female	0			0			0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Thermal burn									
Female	1 (2.8)	1	2.0	0			1 (3.8)	1	2.7
Male	0			1 (0.9)	1	0.6	0		
Heat illness									
Female	1 (2.8)	1	2.0	0			1 (3.8)	1	2.7
Male	0			0			1 (1.3)	1	1.0
Medication errors and other product use errors and issues									
Female	0			0			0		
Male	1 (1.6)	1	1.2	2 (1.8)	2	1.3	0		
Accidental overdose									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Product administration error									
Female	0			0			0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Respiratory, thoracic and mediastinal disorders									
Female	4 (11.1)	6	12.1	10 (11.8)	11	9.2	5 (19.2)	6	16.2
Male	6 (9.4)	7	8.1	14 (12.3)	16	10.3	8 (10.7)	13	12.4
Respiratory tract signs and symptoms									
Female	2 (5.6)	2	4.0	6 (7.1)	6	5.0	4 (15.4)	4	10.8
Male	4 (6.3)	5	5.8	9 (7.9)	11	7.1	7 (9.3)	11	10.5

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Upper respiratory tract inflammation									
Female	2 (5.6)	2	4.0	5 (5.9)	5	4.2	3 (11.5)	3	8.1
Male	3 (4.7)	4	4.6	6 (5.3)	8	5.2	6 (8.0)	10	9.5
Oropharyngeal pain									
Female	0			1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	1 (1.3)	1	1.0
Hiccups									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Rhinorrhoea									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Upper respiratory tract disorders (excl infections)									
Female	2 (5.6)	2	4.0	4 (4.7)	4	3.3	0		
Male	0			3 (2.6)	3	1.9	1 (1.3)	2	1.9
Rhinitis allergic									
Female	1 (2.8)	1	2.0	4 (4.7)	4	3.3	0		
Male	0			2 (1.8)	2	1.3	1 (1.3)	2	1.9
Epistaxis									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Vasomotor rhinitis									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Respiratory disorders NEC									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	1 (3.8)	1	2.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			1 (0.9)	1	0.6	0		
Dyspnoea									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Cough									
Female	1 (2.8)	1	2.0	0			1 (3.8)	1	2.7
Male	0			1 (0.9)	1	0.6	0		
Bronchial disorders (excl neoplasms)									
Female	1 (2.8)	1	2.0	0			1 (3.8)	1	2.7
Male	2 (3.1)	2	2.3	1 (0.9)	1	0.6	0		
Asthma									
Female	0			0			0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Cough variant asthma									
Female	1 (2.8)	1	2.0	0			1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	0			0		
Metabolism and nutrition disorders									
Female	2 (5.6)	2	4.0	8 (9.4)	8	6.7	2 (7.7)	3	8.1
Male	4 (6.3)	4	4.6	15 (13.2)	16	10.3	6 (8.0)	8	7.6
Appetite and general nutritional disorders									
Female	2 (5.6)	2	4.0	5 (5.9)	5	4.2	0		
Male	3 (4.7)	3	3.5	8 (7.0)	8	5.2	0		
Decreased appetite									
Female	2 (5.6)	2	4.0	5 (5.9)	5	4.2	0		
Male	3 (4.7)	3	3.5	8 (7.0)	8	5.2	0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Purine and pyrimidine metabolism disorders									
Female	0			0			0		
Male	1 (1.6)	1	1.2	4 (3.5)	4	2.6	4 (5.3)	5	4.8
Gout									
Female	0			0			0		
Male	1 (1.6)	1	1.2	2 (1.8)	2	1.3	1 (1.3)	2	1.9
Hyperuricaemia									
Female	0			0			0		
Male	0			2 (1.8)	2	1.3	3 (4.0)	3	2.9
Lipid metabolism disorders									
Female	0			2 (2.4)	2	1.7	0		
Male	0			0			2 (2.7)	2	1.9
Dyslipidaemia									
Female	0			2 (2.4)	2	1.7	0		
Male	0			0			2 (2.7)	2	1.9
Glucose metabolism disorders (incl diabetes mellitus)									
Female	0			1 (1.2)	1	0.8	2 (7.7)	3	8.1
Male	0			1 (0.9)	2	1.3	1 (1.3)	1	1.0
Diabetes mellitus									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			1 (1.3)	1	1.0
Type 2 diabetes mellitus									
Female	0			0			1 (3.8)	1	2.7
Male	0			1 (0.9)	2	1.3	0		
Glucose tolerance impaired									

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			1 (3.8)	2	5.4
Male	0			0			0		
Electrolyte and fluid balance conditions									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Dehydration									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Metabolism disorders NEC									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Hypercreatininaemia									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Eye disorders									
Female	2 (5.6)	2	4.0	8 (9.4)	8	6.7	2 (7.7)	2	5.4
Male	4 (6.3)	5	5.8	9 (7.9)	11	7.1	5 (6.7)	6	5.7
Retina, choroid and vitreous haemorrhages and vascular disorders									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	1 (1.6)	2	2.3	4 (3.5)	4	2.6	2 (2.7)	2	1.9
Diabetic retinopathy									
Female	0			0			0		
Male	1 (1.6)	2	2.3	3 (2.6)	3	1.9	2 (2.7)	2	1.9
Retinal haemorrhage									

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Retinal exudates									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Retinopathy									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Vision disorders									
Female	0			2 (2.4)	2	1.7	0		
Male	0			2 (1.8)	2	1.3	0		
Amblyopia									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Visual acuity reduced									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Optic nerve disorder									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Presbyopia									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Anterior eye structural change, deposit and degeneration									
Female	0			3 (3.5)	3	2.5	0		
Male	0			0			1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Cataract									
Female	0			3 (3.5)	3	2.5	0		
Male	0			0			1 (1.3)	1	1.0
Ocular infections, irritations and inflammations									
Female	0			1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Conjunctivitis allergic									
Female	0			1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	0			0		
Ocular hyperaemia									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Glaucoma and ocular hypertension									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			1 (1.3)	1	1.0
Glaucoma									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Open angle glaucoma									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Eye disorders NEC									
Female	1 (2.8)	1	2.0	0			1 (3.8)	1	2.7
Male	0			1 (0.9)	2	1.3	0		
Lacrimal disorder									
Female	0			0			0		

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			1 (0.9)	1	0.6	0		
Lacrimation increased									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Dry eye									
Female	1 (2.8)	1	2.0	0			1 (3.8)	1	2.7
Male	0			0			0		
Ocular haemorrhages and vascular disorders NEC									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	1 (1.3)	1	1.0
Optic disc haemorrhage									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Conjunctival haemorrhage									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Ocular structural change, deposit and degeneration NEC									
Female	0			0			0		
Male	2 (3.1)	2	2.3	1 (0.9)	1	0.6	1 (1.3)	1	1.0
Retinal tear									
Female	0			0			0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Macular fibrosis									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Rhegmatogenous retinal detachment									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
General disorders and administration site conditions									
Female	0			7 (8.2)	22	18.3	1 (3.8)	1	2.7
Male	3 (4.7)	5	5.8	9 (7.9)	13	8.4	1 (1.3)	1	1.0
General system disorders NEC									
Female	0			5 (5.9)	8	6.7	0		
Male	2 (3.1)	4	4.6	6 (5.3)	10	6.5	1 (1.3)	1	1.0
Malaise									
Female	0			1 (1.2)	2	1.7	0		
Male	1 (1.6)	1	1.2	4 (3.5)	6	3.9	0		
Fatigue									
Female	0			1 (1.2)	1	0.8	0		
Male	0			2 (1.8)	2	1.3	0		
Feeling abnormal									
Female	0			1 (1.2)	1	0.8	0		
Male	0			1 (0.9)	1	0.6	0		
Influenza like illness									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Non-cardiac chest pain									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Oedema peripheral									

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Thirst									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Pain									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Hangover									
Female	0			0			0		
Male	1 (1.6)	3	3.5	0			0		
Hunger									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Administration site reactions									
Female	0			2 (2.4)	13	10.8	0		
Male	0			2 (1.8)	2	1.3	0		
Injection site erythema									
Female	0			2 (2.4)	13	10.8	0		
Male	0			0			0		
Injection site dermatitis									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Injection site discomfort									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Body temperature conditions									

Adverse events with onset prior to randomisation are not included.
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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Pyrexia									
Female	0			1 (1.2)	1	0.8	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Investigations									
Female	3 (8.3)	5	10.1	5 (5.9)	5	4.2	1 (3.8)	2	5.4
Male	10 (15.6)	11	12.7	11 (9.6)	15	9.7	8 (10.7)	9	8.6
Enzyme investigations NEC									
Female	0			0			0		
Male	4 (6.3)	4	4.6	6 (5.3)	7	4.5	2 (2.7)	2	1.9
Blood creatine phosphokinase increased									
Female	0			0			0		
Male	4 (6.3)	4	4.6	6 (5.3)	7	4.5	2 (2.7)	2	1.9
Gastrointestinal investigations									
Female	0			2 (2.4)	2	1.7	0		
Male	5 (7.8)	5	5.8	2 (1.8)	3	1.9	0		
Lipase increased									
Female	0			2 (2.4)	2	1.7	0		
Male	3 (4.7)	3	3.5	2 (1.8)	2	1.3	0		
Amylase increased									
Female	0			0			0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Occult blood positive									
Female	0			0			0		

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (1.6)	1	1.2	0			0		
Cardiac and vascular investigations (excl enzyme tests)									
Female	1 (2.8)	1	2.0	2 (2.4)	2	1.7	0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Blood pressure decreased									
Female	0			2 (2.4)	2	1.7	0		
Male	0			1 (0.9)	1	0.6	0		
Electrocardiogram QRS complex prolonged									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Electrocardiogram QT prolonged									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Hepatobiliary investigations									
Female	0			0			1 (3.8)	1	2.7
Male	0			2 (1.8)	2	1.3	4 (5.3)	4	3.8
Aspartate aminotransferase increased									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Liver function test increased									
Female	0			0			1 (3.8)	1	2.7
Male	0			1 (0.9)	1	0.6	1 (1.3)	1	1.0
Alanine aminotransferase increased									
Female	0			0			0		
Male	0			0			2 (2.7)	2	1.9

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Blood bilirubin increased									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Endocrine investigations (incl sex hormones)									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Blood thyroid stimulating hormone decreased									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Haematology investigations (incl blood groups)									
Female	1 (2.8)	2	4.0	0			0		
Male	0			1 (0.9)	1	0.6	0		
Haemoglobin decreased									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Lymphocyte count decreased									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
White blood cell count increased									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Physical examination and organ system status topics									
Female	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Weight decreased									
Female	0			0			0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	0		
Lipid analyses									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Blood triglycerides increased									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Metabolic, nutritional and blood gas investigations									
Female	0			0			1 (3.8)	1	2.7
Male	0			0			1 (1.3)	1	1.0
Blood uric acid increased									
Female	0			0			1 (3.8)	1	2.7
Male	0			0			0		
Glycosylated haemoglobin increased									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Protein and chemistry analyses NEC									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			1 (1.3)	1	1.0
C-reactive protein increased									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			1 (1.3)	1	1.0

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Water, electrolyte and mineral investigations									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Blood potassium increased									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Vascular disorders									
Female	0			6 (7.1)	6	5.0	2 (7.7)	2	5.4
Male	2 (3.1)	2	2.3	5 (4.4)	5	3.2	2 (2.7)	2	1.9
Decreased and nonspecific blood pressure disorders and shock									
Female	0			2 (2.4)	2	1.7	0		
Male	0			3 (2.6)	3	1.9	0		
Orthostatic hypotension									
Female	0			1 (1.2)	1	0.8	0		
Male	0			2 (1.8)	2	1.3	0		
Hypotension									
Female	0			1 (1.2)	1	0.8	0		
Male	0			1 (0.9)	1	0.6	0		
Vascular hypertensive disorders									
Female	0			2 (2.4)	2	1.7	2 (7.7)	2	5.4
Male	1 (1.6)	1	1.2	2 (1.8)	2	1.3	1 (1.3)	1	1.0
Hypertension									
Female	0			2 (2.4)	2	1.7	2 (7.7)	2	5.4
Male	1 (1.6)	1	1.2	2 (1.8)	2	1.3	1 (1.3)	1	1.0

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Arteriosclerosis, stenosis, vascular insufficiency and necrosis									
Female	0			2 (2.4)	2	1.7	0		
Male	0			0			1 (1.3)	1	1.0
Arteriosclerosis									
Female	0			2 (2.4)	2	1.7	0		
Male	0			0			1 (1.3)	1	1.0
Embolism and thrombosis									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Venous thrombosis limb									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Reproductive system and breast disorders									
Female	2 (5.6)	3	6.0	6 (7.1)	6	5.0	0		
Male	1 (1.6)	1	1.2	3 (2.6)	4	2.6	0		
Menstrual cycle and uterine bleeding disorders									
Female	0			4 (4.7)	4	3.3	0		
Male	0			0			0		
Dysmenorrhoea									
Female	0			2 (2.4)	2	1.7	0		
Male	0			0			0		
Menstrual disorder									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Menstruation irregular									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Prostatic disorders (excl infections and inflammations)									
Female	0			0			0		
Male	1 (1.6)	1	1.2	2 (1.8)	2	1.3	0		
Benign prostatic hyperplasia									
Female	0			0			0		
Male	1 (1.6)	1	1.2	2 (1.8)	2	1.3	0		
Breast disorders									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Breast calcifications									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Menopause related conditions									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Menopausal symptoms									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Male reproductive tract infections and inflammations									
Female	0			0			0		
Male	0			1 (0.9)	2	1.3	0		
Prostatitis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			0			0		
Male	0			1 (0.9)	2	1.3	0		
Uterine, pelvic and broad ligament disorders									
Female	2 (5.6)	3	6.0	0			0		
Male	0			0			0		
Endometrial hyperplasia									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Endometriosis									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Uterine haemorrhage									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Psychiatric disorders									
Female	2 (5.6)	2	4.0	4 (4.7)	4	3.3	0		
Male	2 (3.1)	2	2.3	2 (1.8)	2	1.3	1 (1.3)	1	1.0
Sleep disorders and disturbances									
Female	1 (2.8)	1	2.0	3 (3.5)	3	2.5	0		
Male	2 (3.1)	2	2.3	1 (0.9)	1	0.6	0		
Insomnia									
Female	1 (2.8)	1	2.0	3 (3.5)	3	2.5	0		
Male	2 (3.1)	2	2.3	1 (0.9)	1	0.6	0		
Depressed mood disorders and disturbances									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Depression									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Mood disorders and disturbances NEC									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	1 (1.3)	1	1.0
Emotional disorder									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Listless									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Adjustment disorders (incl subtypes)									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Adjustment disorder									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Hepatobiliary disorders									
Female	1 (2.8)	1	2.0	2 (2.4)	2	1.7	0		
Male	1 (1.6)	1	1.2	3 (2.6)	3	1.9	1 (1.3)	1	1.0
Gallbladder disorders									
Female	0			1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	2 (1.8)	2	1.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Cholelithiasis									
Female	0			1 (1.2)	1	0.8	0		
Male	0			1 (0.9)	1	0.6	0		
Gallbladder polyp									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Hyperplastic cholecystopathy									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Hepatic and hepatobiliary disorders									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	0			1 (0.9)	1	0.6	1 (1.3)	1	1.0
Hepatic function abnormal									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Hepatic cyst									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Alcoholic liver disease									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Hepatic steatosis									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Renal and urinary disorders									
Female	3 (8.3)	4	8.1	2 (2.4)	2	1.7	0		
Male	2 (3.1)	2	2.3	3 (2.6)	3	1.9	5 (6.7)	7	6.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Urolithiases									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	2 (3.1)	2	2.3	1 (0.9)	1	0.6	3 (4.0)	5	4.8
Ureterolithiasis									
Female	0			1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	1 (0.9)	1	0.6	2 (2.7)	4	3.8
Calculus urinary									
Female	1 (2.8)	1	2.0	0			0		
Male	1 (1.6)	1	1.2	0			1 (1.3)	1	1.0
Renal disorders (excl nephropathies)									
Female	0			0			0		
Male	0			2 (1.8)	2	1.3	1 (1.3)	1	1.0
Azotaemia									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Renal cyst									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	1 (1.3)	1	1.0
Urinary tract signs and symptoms									
Female	1 (2.8)	2	4.0	1 (1.2)	1	0.8	0		
Male	0			0			0		
Hyperuricosuria									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Nocturia									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Proteinuria									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Nephropathies									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			1 (1.3)	1	1.0
Diabetic nephropathy									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Nephropathy toxic									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Cardiac disorders									
Female	2 (5.6)	2	4.0	1 (1.2)	1	0.8	0		
Male	0			3 (2.6)	3	1.9	3 (4.0)	3	2.9
Cardiac arrhythmias									
Female	1 (2.8)	1	2.0	0			0		
Male	0			2 (1.8)	2	1.3	2 (2.7)	2	1.9
Tachycardia									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Ventricular extrasystoles									
Female	1 (2.8)	1	2.0	0			0		
Male	0			1 (0.9)	1	0.6	0		
Arrhythmia									
Female	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	0			0			1 (1.3)	1	1.0
Atrial fibrillation									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Cardiac disorders, signs and symptoms NEC									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	0			0			1 (1.3)	1	1.0
Palpitations									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	0			0			1 (1.3)	1	1.0
Coronary artery disorders									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Acute myocardial infarction									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Ear and labyrinth disorders									
Female	3 (8.3)	3	6.0	1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	2 (1.8)	2	1.3	1 (1.3)	1	1.0
Hearing disorders									
Female	0			0			0		
Male	0			2 (1.8)	2	1.3	0		
Deafness									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Deafness neurosensory									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Inner ear and VIIIth cranial nerve disorders									
Female	3 (8.3)	3	6.0	1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	0			1 (1.3)	1	1.0
Vertigo									
Female	2 (5.6)	2	4.0	1 (1.2)	1	0.8	0		
Male	1 (1.6)	1	1.2	0			1 (1.3)	1	1.0
Tinnitus									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Blood and lymphatic system disorders									
Female	1 (2.8)	1	2.0	2 (2.4)	2	1.7	1 (3.8)	1	2.7
Male	1 (1.6)	1	1.2	0			0		
Anaemias nonhaemolytic and marrow depression									
Female	1 (2.8)	1	2.0	2 (2.4)	2	1.7	1 (3.8)	1	2.7
Male	0			0			0		
Iron deficiency anaemia									
Female	1 (2.8)	1	2.0	2 (2.4)	2	1.7	0		
Male	0			0			0		
Anaemia									
Female	0			0			1 (3.8)	1	2.7
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Spleen, lymphatic and reticuloendothelial system disorders									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Lymphadenitis									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Congenital, familial and genetic disorders									
Female	0			2 (2.4)	2	1.7	0		
Male	0			0			0		
Gastrointestinal tract disorders congenital									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Diverticulitis Meckel's									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Skin and subcutaneous tissue disorders congenital									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Birth mark									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Neoplasms benign, malignant and unspecified (incl cysts and polyps)									
Female	0			1 (1.2)	1	0.8	0		
Male	2 (3.1)	2	2.3	1 (0.9)	1	0.6	1 (1.3)	1	1.0
Reproductive neoplasms female benign									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Uterine leiomyoma									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		
Gastrointestinal neoplasms benign									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Intraductal papillary mucinous neoplasm									
Female	0			0			0		
Male	0			1 (0.9)	1	0.6	0		
Hepatobiliary neoplasms malignant and unspecified									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Bile duct adenocarcinoma									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Renal and urinary tract neoplasms malignant and unspecified									
Female	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Male	1 (1.6)	1	1.2	0			0		
Clear cell renal cell carcinoma									
Female	0			0			0		
Male	1 (1.6)	1	1.2	0			0		
Respiratory and mediastinal neoplasms malignant and unspecified									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Lung neoplasm malignant									
Female	0			0			0		
Male	0			0			1 (1.3)	1	1.0
Immune system disorders									
Female	2 (5.6)	2	4.0	1 (1.2)	1	0.8	0		
Male	0			0			1 (1.3)	1	1.0
Allergic conditions									
Female	2 (5.6)	2	4.0	1 (1.2)	1	0.8	0		
Male	0			0			1 (1.3)	1	1.0
Seasonal allergy									
Female	1 (2.8)	1	2.0	1 (1.2)	1	0.8	0		
Male	0			0			1 (1.3)	1	1.0
Food allergy									
Female	1 (2.8)	1	2.0	0			0		
Male	0			0			0		
Surgical and medical procedures									
Female	0			1 (1.2)	1	0.8	0		
Male	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by sex, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Gastrointestinal therapeutic procedures												
Female	0				1	(1.2)	1	0.8	0			
Male	0				0				0			
Large intestinal polypectomy												
Female	0				1	(1.2)	1	0.8	0			
Male	0				0				0			
Endocrine disorders												
Female	0				0				0			
Male	0				1	(0.9)	1	0.6	0			
Thyroid gland disorders												
Female	0				0				0			
Male	0				1	(0.9)	1	0.6	0			
Hyperthyroidism												
Female	0				0				0			
Male	0				1	(0.9)	1	0.6	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

7 Adverse events by age at baseline - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
<65	1198	1562.8			607	766.3		
>=65	108	143.3			48	63.2		
Subjects with events	N	(%)	E	R	N	(%)	E	R
Events								
<65	1074	(89.6)	8943	572.3	524	(86.3)	3016	393.6
>=65	97	(89.8)	715	498.9	42	(87.5)	286	452.4
Serious								
Yes								
<65	109	(9.1)	136	8.7	37	(6.1)	48	6.3
>=65	19	(17.6)	28	19.5	5	(10.4)	5	7.9
No								
<65	1072	(89.5)	8807	563.5	520	(85.7)	2968	387.3
>=65	97	(89.8)	687	479.4	40	(83.3)	281	444.4
Severity								
Severe								
<65	125	(10.4)	215	13.8	39	(6.4)	63	8.2
>=65	18	(16.7)	27	18.8	5	(10.4)	5	7.9
Moderate								
<65	666	(55.6)	2400	153.6	280	(46.1)	760	99.2
>=65	57	(52.8)	212	147.9	31	(64.6)	103	162.9
Mild								
<65	992	(82.8)	6328	404.9	469	(77.3)	2193	286.2
>=65	87	(80.6)	476	332.1	38	(79.2)	178	281.5

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by age at baseline - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Relationship to trial product								
Missing								
<65	22	(1.8)	28	1.8	6	(1.0)	7	0.9
>=65	2	(1.9)	2	1.4	1	(2.1)	1	1.6
Probable								
<65	529	(44.2)	2021	129.3	136	(22.4)	303	39.5
>=65	42	(38.9)	127	88.6	11	(22.9)	27	42.7
Possible								
<65	668	(55.8)	2516	161.0	206	(33.9)	524	68.4
>=65	58	(53.7)	184	128.4	17	(35.4)	31	49.0
Unlikely								
<65	948	(79.1)	4378	280.1	495	(81.5)	2182	284.7
>=65	84	(77.8)	402	280.5	41	(85.4)	227	359.0
Outcome								
Fatal								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Recovered								
<65	1046	(87.3)	7846	502.1	506	(83.4)	2487	324.5
>=65	94	(87.0)	593	413.8	39	(81.3)	223	352.7
Recovering								
<65	56	(4.7)	86	5.5	25	(4.1)	37	4.8
>=65	3	(2.8)	5	3.5	0			
Recovered With Sequelae								
<65	7	(0.6)	12	0.8	2	(0.3)	2	0.3
>=65	4	(3.7)	7	4.9	2	(4.2)	3	4.7
Not Recovered								
<65	471	(39.3)	996	63.7	239	(39.4)	489	63.8

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by age at baseline - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Outcome								
Not Recovered								
>=65	42	(38.9)	110	76.8	26	(54.2)	59	93.3
Unknown								
<65	2	(0.2)	3	0.2	0			
>=65	0				1	(2.1)	1	1.6
Leading to								
Permanent treatment discontinuation								
<65	80	(6.7)	111	7.1	19	(3.1)	22	2.9
>=65	12	(11.1)	12	8.4	1	(2.1)	1	1.6
Temporary interruption of trial product								
<65	114	(9.5)	244	15.6	25	(4.1)	43	5.6
>=65	12	(11.1)	21	14.7	1	(2.1)	1	1.6
Dose reduction of trial product								
<65	112	(9.3)	203	13.0	4	(0.7)	9	1.2
>=65	12	(11.1)	22	15.4	0			

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

8 Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
<65	1198	1562.8			607	766.3		
>=65	108	143.3			48	63.2		
Subjects with events	N	(%)	E	R	N	(%)	E	R
Adverse events								
<65	1074	(89.6)	8943	572.3	524	(86.3)	3016	393.6
>=65	97	(89.8)	715	498.9	42	(87.5)	286	452.4
Gastrointestinal disorders								
<65	889	(74.2)	4027	257.7	291	(47.9)	690	90.0
>=65	80	(74.1)	282	196.8	23	(47.9)	49	77.5
Gastrointestinal signs and symptoms								
<65	762	(63.6)	2548	163.0	186	(30.6)	365	47.6
>=65	62	(57.4)	166	115.8	15	(31.3)	30	47.4
Nausea								
<65	533	(44.5)	986	63.1	110	(18.1)	140	18.3
>=65	44	(40.7)	82	57.2	4	(8.3)	6	9.5
Vomiting								
<65	307	(25.6)	604	38.6	39	(6.4)	47	6.1
>=65	17	(15.7)	32	22.3	4	(8.3)	5	7.9
Dyspepsia								
<65	124	(10.4)	165	10.6	20	(3.3)	26	3.4
>=65	11	(10.2)	14	9.8	3	(6.3)	4	6.3
Eructation								
<65	104	(8.7)	131	8.4	2	(0.3)	2	0.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	8 (7.4)	8	5.6	1 (2.1)	1	1.6
Abdominal pain						
<65	127 (10.6)	172	11.0	34 (5.6)	38	5.0
>=65	3 (2.8)	3	2.1	2 (4.2)	3	4.7
Abdominal pain upper						
<65	122 (10.2)	173	11.1	30 (4.9)	32	4.2
>=65	3 (2.8)	3	2.1	5 (10.4)	5	7.9
Abdominal distension						
<65	91 (7.6)	129	8.3	30 (4.9)	41	5.4
>=65	5 (4.6)	6	4.2	1 (2.1)	1	1.6
Flatulence						
<65	58 (4.8)	77	4.9	18 (3.0)	19	2.5
>=65	7 (6.5)	7	4.9	3 (6.3)	3	4.7
Abdominal discomfort						
<65	50 (4.2)	71	4.5	8 (1.3)	8	1.0
>=65	6 (5.6)	8	5.6	1 (2.1)	1	1.6
Regurgitation						
<65	2 (0.2)	3	0.2	0		
>=65	1 (0.9)	1	0.7	0		
Faeces discoloured						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Abdominal pain lower						
<65	12 (1.0)	12	0.8	4 (0.7)	4	0.5
>=65	0			0		
Faeces hard						
<65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	1 (0.9)	1	0.7	0		
Epigastric discomfort						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Faeces soft						
<65	3 (0.3)	4	0.3	4 (0.7)	4	0.5
>=65	0			1 (2.1)	1	1.6
Gastrointestinal pain						
<65	3 (0.3)	4	0.3	0		
>=65	0			0		
Breath odour						
<65	2 (0.2)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Dysphagia						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Gastrointestinal sounds abnormal						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Retching						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Abdominal tenderness						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Abnormal faeces						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Aerophagia								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Oesophageal pain								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Gastrointestinal motility and defaecation conditions								
<65	576	(48.1)	1179	75.4	155	(25.5)	225	29.4
>=65	50	(46.3)	92	64.2	11	(22.9)	14	22.1
Diarrhoea								
<65	384	(32.1)	726	46.5	99	(16.3)	130	17.0
>=65	28	(25.9)	40	27.9	5	(10.4)	8	12.7
Constipation								
<65	280	(23.4)	353	22.6	57	(9.4)	68	8.9
>=65	26	(24.1)	37	25.8	5	(10.4)	5	7.9
Gastrooesophageal reflux disease								
<65	69	(5.8)	78	5.0	19	(3.1)	20	2.6
>=65	13	(12.0)	14	9.8	1	(2.1)	1	1.6
Frequent bowel movements								
<65	4	(0.3)	4	0.3	3	(0.5)	3	0.4
>=65	1	(0.9)	1	0.7	0			
Irritable bowel syndrome								
<65	6	(0.5)	7	0.4	1	(0.2)	2	0.3
>=65	0				0			
Dyschezia								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Impaired gastric emptying						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Bowel movement irregularity						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Change of bowel habit						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Defaecation urgency						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Gastrointestinal hypermotility						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Gastrointestinal motility disorder						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Infrequent bowel movements						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Oesophageal achalasia						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Gastrointestinal inflammatory conditions						
<65	68 (5.7)	91	5.8	11 (1.8)	12	1.6
>=65	3 (2.8)	3	2.1	1 (2.1)	1	1.6
Gastritis						
<65	49 (4.1)	66	4.2	5 (0.8)	6	0.8
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Colitis						
<65	6 (0.5)	8	0.5	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Oesophagitis						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Reflux gastritis						
<65	4 (0.3)	4	0.3	1 (0.2)	1	0.1
>=65	0			0		
Chronic gastritis						
<65	2 (0.2)	2	0.1	2 (0.3)	2	0.3
>=65	0			0		
Duodenitis						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Enteritis						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Gastrointestinal inflammation						
<65	2 (0.2)	2	0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Colitis ischaemic								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Crohn's disease								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Eosinophilic oesophagitis								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Gastroenteritis eosinophilic								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Epiploic appendagitis								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Inflammatory bowel disease								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Gastrointestinal conditions NEC								
<65	45	(3.8)	63	4.0	12	(2.0)	16	2.1
>=65	3	(2.8)	4	2.8	0			
Gastrointestinal disorder								
<65	3	(0.3)	4	0.3	4	(0.7)	4	0.5
>=65	2	(1.9)	3	2.1	0			
Hyperchlorhydria								
<65	20	(1.7)	37	2.4	3	(0.5)	5	0.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Food poisoning						
<65	18 (1.5)	18	1.2	4 (0.7)	6	0.8
>=65	0			0		
Anal fistula						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Barrett's oesophagus						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Functional gastrointestinal disorder						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Gastric mucosal hypertrophy						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Dental and gingival conditions						
<65	24 (2.0)	28	1.8	27 (4.4)	30	3.9
>=65	3 (2.8)	4	2.8	2 (4.2)	2	3.2
Toothache						
<65	16 (1.3)	19	1.2	16 (2.6)	17	2.2
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Dental caries						
<65	2 (0.2)	2	0.1	10 (1.6)	10	1.3
>=65	2 (1.9)	3	2.1	0		
Gingival bleeding						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Gingival disorder								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Gingival pain								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Noninfective gingivitis								
<65	1	(<0.1)	1	<0.1	1	(0.2)	1	0.1
>=65	0				0			
Periodontal disease								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Tooth impacted								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Tooth loss								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Dental necrosis								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Dental pulp disorder								
<65	0				0			
>=65	0				1	(2.1)	1	1.6
Tooth disorder								
<65	0				1	(0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Salivary gland conditions						
<65	24 (2.0)	24	1.5	8 (1.3)	9	1.2
>=65	3 (2.8)	3	2.1	0		
Dry mouth						
<65	22 (1.8)	22	1.4	7 (1.2)	8	1.0
>=65	3 (2.8)	3	2.1	0		
Salivary gland calculus						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Salivary gland cyst						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Salivary gland enlargement						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Benign neoplasms gastrointestinal						
<65	7 (0.6)	7	0.4	5 (0.8)	5	0.7
>=65	3 (2.8)	3	2.1	0		
Large intestine polyp						
<65	6 (0.5)	6	0.4	4 (0.7)	4	0.5
>=65	3 (2.8)	3	2.1	0		
Gastric polyps						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Gastrointestinal vascular conditions						
<65	27 (2.3)	28	1.8	5 (0.8)	5	0.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	1 (0.9)	2	1.4	0		
Haemorrhoids						
<65	26 (2.2)	27	1.7	3 (0.5)	3	0.4
>=65	0			0		
Haemorrhoidal haemorrhage						
<65	0			1 (0.2)	1	0.1
>=65	1 (0.9)	2	1.4	0		
Haemorrhoids thrombosed						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Gastrointestinal haemorrhages NEC						
<65	13 (1.1)	14	0.9	6 (1.0)	7	0.9
>=65	2 (1.9)	2	1.4	0		
Rectal haemorrhage						
<65	6 (0.5)	6	0.4	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Lower gastrointestinal haemorrhage						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Haematochezia						
<65	7 (0.6)	7	0.4	3 (0.5)	4	0.5
>=65	0			0		
Haematemesis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Melaena						
<65	0			1 (0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Upper gastrointestinal haemorrhage						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Abdominal hernias and other abdominal wall conditions						
<65	8 (0.7)	9	0.6	3 (0.5)	3	0.4
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Hiatus hernia						
<65	6 (0.5)	7	0.4	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Abdominal hernia						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			1 (2.1)	1	1.6
Umbilical hernia						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	0			0		
Diverticular disorders						
<65	6 (0.5)	6	0.4	5 (0.8)	5	0.7
>=65	1 (0.9)	1	0.7	0		
Diverticulum						
<65	6 (0.5)	6	0.4	5 (0.8)	5	0.7
>=65	1 (0.9)	1	0.7	0		
Gastrointestinal ulceration and perforation						
<65	4 (0.3)	4	0.3	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Oesophageal ulcer						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Duodenal ulcer						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Gastric ulcer						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Large intestine perforation						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Peptic ulcer						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Oral soft tissue conditions						
<65	8 (0.7)	9	0.6	6 (1.0)	6	0.8
>=65	0			0		
Lip swelling						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Aphthous ulcer						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Cheilitis						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Lip disorder						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Mouth ulceration						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	0			0		
Odynophagia						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Paraesthesia oral						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Stomatitis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Oral mucosal eruption						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Anal and rectal conditions NEC						
<65	7 (0.6)	9	0.6	0		
>=65	0			0		
Anal fissure						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Proctalgia						
<65	2 (0.2)	3	0.2	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Anal pruritus						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Anorectal discomfort						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Rectal fissure						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Gastrointestinal stenosis and obstruction						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			1 (2.1)	1	1.6
Ileus						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Oesophageal stenosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Volvulus						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Intestinal obstruction						
<65	0			0		
>=65	0			1 (2.1)	1	1.6
Exocrine pancreas conditions						
<65	2 (0.2)	2	0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Pancreatitis acute								
<65	2	(0.2)	2	0.1	0			
>=65	0				0			
Malabsorption conditions								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Coeliac disease								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Peritoneal and retroperitoneal conditions								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Pneumoperitoneum								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Tongue conditions								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Glossodynia								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Infections and infestations								
<65	658	(54.9)	1502	96.1	346	(57.0)	750	97.9
>=65	56	(51.9)	113	78.8	26	(54.2)	52	82.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Infections - pathogen unspecified						
<65	577 (48.2)	1160	74.2	294 (48.4)	576	75.2
>=65	49 (45.4)	87	60.7	20 (41.7)	34	53.8
Nasopharyngitis						
<65	264 (22.0)	455	29.1	128 (21.1)	205	26.8
>=65	17 (15.7)	25	17.4	5 (10.4)	11	17.4
Upper respiratory tract infection						
<65	104 (8.7)	141	9.0	72 (11.9)	104	13.6
>=65	10 (9.3)	17	11.9	8 (16.7)	12	19.0
Gastroenteritis						
<65	79 (6.6)	96	6.1	27 (4.4)	34	4.4
>=65	6 (5.6)	8	5.6	3 (6.3)	4	6.3
Urinary tract infection						
<65	61 (5.1)	75	4.8	28 (4.6)	34	4.4
>=65	7 (6.5)	8	5.6	0		
Sinusitis						
<65	66 (5.5)	79	5.1	34 (5.6)	38	5.0
>=65	5 (4.6)	5	3.5	2 (4.2)	2	3.2
Bronchitis						
<65	41 (3.4)	45	2.9	23 (3.8)	26	3.4
>=65	6 (5.6)	7	4.9	2 (4.2)	2	3.2
Pneumonia						
<65	7 (0.6)	9	0.6	8 (1.3)	8	1.0
>=65	4 (3.7)	5	3.5	0		
Cystitis						
<65	18 (1.5)	20	1.3	3 (0.5)	3	0.4
>=65	1 (0.9)	1	0.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Acute sinusitis						
<65	10 (0.8)	11	0.7	8 (1.3)	9	1.2
>=65	1 (0.9)	1	0.7	0		
Tooth infection						
<65	10 (0.8)	11	0.7	4 (0.7)	4	0.5
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Rhinitis						
<65	19 (1.6)	25	1.6	9 (1.5)	14	1.8
>=65	0			0		
Pulpitis dental						
<65	4 (0.3)	4	0.3	0		
>=65	1 (0.9)	1	0.7	0		
Laryngitis						
<65	14 (1.2)	14	0.9	4 (0.7)	5	0.7
>=65	0			0		
Pharyngitis						
<65	13 (1.1)	13	0.8	9 (1.5)	9	1.2
>=65	0			0		
Abdominal wall abscess						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Tonsillitis						
<65	12 (1.0)	15	1.0	10 (1.6)	12	1.6
>=65	0			0		
Device related infection						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Diverticulitis						
<65	0			2 (0.3)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Eyelid infection						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Large intestine infection						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Osteomyelitis						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Perirectal abscess						
<65	0			0		
>=65	1 (0.9)	2	1.4	0		
Vaginal infection						
<65	11 (0.9)	13	0.8	0		
>=65	0			0		
Ear infection						
<65	9 (0.8)	11	0.7	3 (0.5)	3	0.4
>=65	0			0		
Lower respiratory tract infection						
<65	9 (0.8)	10	0.6	12 (2.0)	16	2.1
>=65	0			0		
Tooth abscess						
<65	8 (0.7)	8	0.5	8 (1.3)	9	1.2
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Conjunctivitis						
<65	7 (0.6)	7	0.4	3 (0.5)	3	0.4
>=65	0			0		
Otitis media						
<65	6 (0.5)	6	0.4	2 (0.3)	2	0.3
>=65	0			0		
Appendicitis						
<65	5 (0.4)	5	0.3	1 (0.2)	1	0.1
>=65	0			0		
Eye infection						
<65	5 (0.4)	5	0.3	0		
>=65	0			0		
Folliculitis						
<65	5 (0.4)	5	0.3	1 (0.2)	1	0.1
>=65	0			0		
Gastrointestinal infection						
<65	5 (0.4)	7	0.4	3 (0.5)	3	0.4
>=65	0			0		
Breast abscess						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Chronic sinusitis						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Gingivitis						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hordeolum						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Infected bite						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	0			1 (2.1)	1	1.6
Kidney infection						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Pharyngotonsillitis						
<65	3 (0.3)	3	0.2	1 (0.2)	2	0.3
>=65	0			0		
Pyelonephritis						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Subcutaneous abscess						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	0			0		
Abscess						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Atypical pneumonia						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Diarrhoea infectious						
<65	2 (0.2)	2	0.1	1 (0.2)	2	0.3
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Infection						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Localised infection						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			1 (2.1)	1	1.6
Omphalitis						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Otitis externa						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Periodontitis						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Postoperative wound infection						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Abdominal abscess						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Abscess limb						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Appendicitis perforated						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Bartholinitis						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Carbuncle						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Endometritis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Epididymitis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Fracture infection						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Groin abscess						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Haematoma infection						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Mastitis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Nail infection						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Oophoritis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Oral infection						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Parasitic gastroenteritis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Paronychia						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Parotitis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Peritonitis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Prostate infection						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Purulence						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Respiratory tract infection						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Salpingitis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Sepsis syndrome						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Skin infection						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Arthritis infective						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Cervicitis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Empyema						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Gastric infection						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Infected dermal cyst						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Lymphangitis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Neutropenic sepsis								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Otitis media acute								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Peritonsillar abscess								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Peritonsillitis								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Root canal infection								
<65	0				2	(0.3)	2	0.3
>=65	0				0			
Septic shock								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Tracheitis								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Wound infection								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Viral infectious disorders								
<65	182	(15.2)	235	15.0	96	(15.8)	126	16.4
>=65	12	(11.1)	13	9.1	7	(14.6)	10	15.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Influenza						
<65	86 (7.2)	108	6.9	59 (9.7)	72	9.4
>=65	3 (2.8)	4	2.8	4 (8.3)	7	11.1
Gastroenteritis viral						
<65	40 (3.3)	42	2.7	14 (2.3)	15	2.0
>=65	2 (1.9)	2	1.4	0		
Gastrointestinal viral infection						
<65	6 (0.5)	7	0.4	1 (0.2)	1	0.1
>=65	2 (1.9)	2	1.4	0		
Viral upper respiratory tract infection						
<65	6 (0.5)	6	0.4	3 (0.5)	4	0.5
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Herpes simplex						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Viral infection						
<65	14 (1.2)	20	1.3	8 (1.3)	8	1.0
>=65	0			0		
Herpes zoster						
<65	12 (1.0)	13	0.8	11 (1.8)	11	1.4
>=65	0			0		
Gastroenteritis astroviral						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Parainfluenzae virus infection						
<65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	1 (0.9)	1	0.7	0		
Respiratory syncytial virus infection						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Ear infection viral						
<65	5 (0.4)	5	0.3	1 (0.2)	1	0.1
>=65	0			0		
Gastroenteritis norovirus						
<65	5 (0.4)	6	0.4	0		
>=65	0			0		
Oral herpes						
<65	4 (0.3)	5	0.3	1 (0.2)	1	0.1
>=65	0			0		
Dengue fever						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	0			0		
Viral pharyngitis						
<65	3 (0.3)	3	0.2	0		
>=65	0			1 (2.1)	1	1.6
Herpes virus infection						
<65	2 (0.2)	2	0.1	0		
>=65	0			1 (2.1)	1	1.6
Respiratory tract infection viral						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Chronic hepatitis B						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Cytomegalovirus infection								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Genital herpes zoster								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Hepatitis E								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Infectious mononucleosis								
<65	1	(<0.1)	1	<0.1	1	(0.2)	1	0.1
>=65	0				0			
Oral viral infection								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Papilloma viral infection								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Varicella								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Vestibular neuronitis								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Viral sinusitis								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Bronchitis viral						
<65	0			2 (0.3)	2	0.3
>=65	0			0		
Conjunctivitis viral						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Hand-foot-and-mouth disease						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Meningitis viral						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Viral rhinitis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Bacterial infectious disorders						
<65	50 (4.2)	55	3.5	23 (3.8)	25	3.3
>=65	7 (6.5)	8	5.6	4 (8.3)	6	9.5
Cellulitis						
<65	5 (0.4)	5	0.3	6 (1.0)	7	0.9
>=65	4 (3.7)	4	2.8	1 (2.1)	1	1.6
Staphylococcal infection						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	2 (1.9)	2	1.4	1 (2.1)	1	1.6
Pharyngitis streptococcal						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	10 (0.8)	10	0.6	6 (1.0)	6	0.8
>=65	1 (0.9)	1	0.7	0		
Ear infection bacterial						
<65	5 (0.4)	5	0.3	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Helicobacter infection						
<65	6 (0.5)	6	0.4	2 (0.3)	2	0.3
>=65	0			0		
Bacterial vaginosis						
<65	5 (0.4)	8	0.5	1 (0.2)	1	0.1
>=65	0			1 (2.1)	1	1.6
Erysipelas						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Furuncle						
<65	3 (0.3)	4	0.3	1 (0.2)	1	0.1
>=65	0			0		
Helicobacter gastritis						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Bacterial colitis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Bacterial vulvovaginitis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Genital infection bacterial						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Lyme disease								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Pharyngitis bacterial								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Salmonellosis								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Sinusitis bacterial								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Skin bacterial infection								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Syphilis								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Tonsillitis bacterial								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Typhoid fever								
<65	1	(<0.1)	1	<0.1	1	(0.2)	1	0.1
>=65	0				0			
Bacteriuria								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<65	0				0			
>=65	0				1	(2.1)	1	1.6
Gastric ulcer helicobacter								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Listeriosis								
<65	0				0			
>=65	0				1	(2.1)	1	1.6
Staphylococcal sepsis								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Streptococcal urinary tract infection								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Upper respiratory tract infection bacterial								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Fungal infectious disorders								
<65	40	(3.3)	48	3.1	20	(3.3)	22	2.9
>=65	5	(4.6)	5	3.5	2	(4.2)	2	3.2
Fungal infection								
<65	9	(0.8)	10	0.6	5	(0.8)	5	0.7
>=65	1	(0.9)	1	0.7	0			
Body tinea								
<65	1	(<0.1)	1	<0.1	1	(0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	1 (0.9)	1	0.7	0		
Fungal skin infection						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Onychomycosis						
<65	1 (<0.1)	1	<0.1	4 (0.7)	5	0.7
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Tinea cruris						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Vulvovaginal mycotic infection						
<65	11 (0.9)	13	0.8	2 (0.3)	2	0.3
>=65	0			0		
Tinea pedis						
<65	6 (0.5)	6	0.4	1 (0.2)	1	0.1
>=65	0			0		
Vulvovaginal candidiasis						
<65	5 (0.4)	8	0.5	3 (0.5)	3	0.4
>=65	0			0		
Dermatophytosis						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Skin candida						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Candida infection						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Dermatophytosis of nail								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Tinea capitis								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Tinea infection								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Oral candidiasis								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Otitis externa fungal								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Protozoal infectious disorders								
<65	2	(0.2)	2	0.1	1	(0.2)	1	0.1
>=65	0				0			
Trichomoniasis								
<65	2	(0.2)	2	0.1	0			
>=65	0				0			
Toxoplasmosis								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Chlamydial infectious disorders								
<65	1	(<0.1)	1	<0.1	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Chlamydial infection								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Ectoparasitic disorders								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Acarodermatitis								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Musculoskeletal and connective tissue disorders								
<65	301	(25.1)	494	31.6	165	(27.2)	261	34.1
>=65	37	(34.3)	64	44.7	21	(43.8)	43	68.0
Musculoskeletal and connective tissue disorders NEC								
<65	167	(13.9)	223	14.3	88	(14.5)	115	15.0
>=65	20	(18.5)	21	14.7	11	(22.9)	17	26.9
Back pain								
<65	97	(8.1)	111	7.1	50	(8.2)	52	6.8
>=65	10	(9.3)	10	7.0	4	(8.3)	4	6.3
Pain in extremity								
<65	41	(3.4)	45	2.9	20	(3.3)	22	2.9
>=65	3	(2.8)	3	2.1	4	(8.3)	6	9.5
Musculoskeletal pain								
<65	28	(2.3)	28	1.8	12	(2.0)	14	1.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	3 (2.8)	3	2.1	4 (8.3)	4	6.3
Neck pain						
<65	16 (1.3)	18	1.2	9 (1.5)	9	1.2
>=65	3 (2.8)	3	2.1	0		
Musculoskeletal stiffness						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Dupuytren's contracture						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Musculoskeletal chest pain						
<65	8 (0.7)	8	0.5	5 (0.8)	5	0.7
>=65	0			0		
Flank pain						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Plantar fasciitis						
<65	3 (0.3)	3	0.2	5 (0.8)	6	0.8
>=65	0			1 (2.1)	1	1.6
Axillary mass						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Musculoskeletal discomfort						
<65	1 (<0.1)	2	0.1	0		
>=65	0			0		
Groin pain						
<65	0			2 (0.3)	2	0.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Limb mass						
<65	0			0		
>=65	0			1 (2.1)	2	3.2
Muscle contracture						
<65	0			3 (0.5)	3	0.4
>=65	0			0		
Neck mass						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Joint disorders						
<65	112 (9.3)	141	9.0	65 (10.7)	80	10.4
>=65	21 (19.4)	28	19.5	10 (20.8)	14	22.1
Arthralgia						
<65	71 (5.9)	80	5.1	38 (6.3)	41	5.4
>=65	10 (9.3)	12	8.4	5 (10.4)	6	9.5
Osteoarthritis						
<65	16 (1.3)	20	1.3	14 (2.3)	16	2.1
>=65	7 (6.5)	8	5.6	4 (8.3)	4	6.3
Rotator cuff syndrome						
<65	3 (0.3)	3	0.2	5 (0.8)	5	0.7
>=65	3 (2.8)	3	2.1	0		
Spinal osteoarthritis						
<65	11 (0.9)	12	0.8	0		
>=65	1 (0.9)	1	0.7	0		
Arthritis						
<65	7 (0.6)	7	0.4	5 (0.8)	5	0.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Joint swelling						
<65	6 (0.5)	6	0.4	3 (0.5)	3	0.4
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Joint stiffness						
<65	2 (0.2)	2	0.1	0		
>=65	1 (0.9)	1	0.7	0		
Vertebral foraminal stenosis						
<65	2 (0.2)	3	0.2	0		
>=65	1 (0.9)	1	0.7	0		
Facet joint syndrome						
<65	2 (0.2)	3	0.2	0		
>=65	0			0		
Arthropathy						
<65	1 (<0.1)	2	0.1	0		
>=65	0			1 (2.1)	1	1.6
Periarthritis						
<65	1 (<0.1)	1	<0.1	1 (0.2)	2	0.3
>=65	0			0		
Spondylitis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Vertebral osteophyte						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Chondromalacia						
<65	0			1 (0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Haemarthrosis						
<65	0			0		
>=65	0			1 (2.1)	1	1.6
Joint noise						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Joint range of motion decreased						
<65	0			2 (0.3)	2	0.3
>=65	0			0		
Joint space narrowing						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Polyarthritis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Rheumatoid arthritis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Spondyloarthropathy						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Muscle disorders						
<65	53 (4.4)	59	3.8	21 (3.5)	27	3.5
>=65	5 (4.6)	5	3.5	2 (4.2)	2	3.2
Myalgia						
<65	21 (1.8)	24	1.5	8 (1.3)	13	1.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	2 (1.9)	2	1.4	0		
Muscle spasms						
<65	17 (1.4)	17	1.1	8 (1.3)	9	1.2
>=65	2 (1.9)	2	1.4	2 (4.2)	2	3.2
Fibromyalgia						
<65	3 (0.3)	3	0.2	3 (0.5)	3	0.4
>=65	1 (0.9)	1	0.7	0		
Muscular weakness						
<65	5 (0.4)	6	0.4	1 (0.2)	1	0.1
>=65	0			0		
Myofascial pain syndrome						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Muscle disorder						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Muscle fatigue						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Muscle tightness						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Muscle twitching						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Myalgia intercostal						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Myosclerosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Torticollis						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)						
<65	15 (1.3)	20	1.3	9 (1.5)	11	1.4
>=65	4 (3.7)	4	2.8	2 (4.2)	2	3.2
Scoliosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	2 (1.9)	2	1.4	0		
Finger deformity						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Spinal stenosis						
<65	0			1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Intervertebral disc protrusion						
<65	8 (0.7)	8	0.5	3 (0.5)	4	0.5
>=65	0			1 (2.1)	1	1.6
Intervertebral disc degeneration						
<65	5 (0.4)	7	0.4	2 (0.3)	2	0.3
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Cervical spinal stenosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Intervertebral disc displacement						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Kyphoscoliosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Spondylolisthesis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Foot deformity						
<65	0			2 (0.3)	2	0.3
>=65	0			1 (2.1)	1	1.6
Intervertebral disc annular tear						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Kyphosis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Tendon, ligament and cartilage disorders						
<65	22 (1.8)	24	1.5	11 (1.8)	12	1.6
>=65	3 (2.8)	3	2.1	2 (4.2)	3	4.7
Costochondritis						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	2	(1.9)	2	1.4	0			
Tendonitis								
<65	12	(1.0)	13	0.8	7	(1.2)	8	1.0
>=65	1	(0.9)	1	0.7	2	(4.2)	3	4.7
Tenosynovitis								
<65	3	(0.3)	3	0.2	1	(0.2)	1	0.1
>=65	0				0			
Tendon disorder								
<65	2	(0.2)	2	0.1	0			
>=65	0				0			
Osteochondrosis								
<65	1	(<0.1)	1	<0.1	1	(0.2)	1	0.1
>=65	0				0			
Posterior tibial tendon dysfunction								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Tendon discomfort								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Tendon pain								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Trigger finger								
<65	1	(<0.1)	1	<0.1	2	(0.3)	2	0.3
>=65	0				0			
Synovial and bursal disorders								
<65	15	(1.3)	15	1.0	3	(0.5)	3	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	1 (0.9)	1	0.7	2 (4.2)	2	3.2
Bursitis						
<65	9 (0.8)	9	0.6	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	2 (4.2)	2	3.2
Synovial cyst						
<65	5 (0.4)	5	0.3	1 (0.2)	1	0.1
>=65	0			0		
Synovitis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Bursal fluid accumulation						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Bone disorders (excl congenital and fractures)						
<65	10 (0.8)	11	0.7	11 (1.8)	11	1.4
>=65	1 (0.9)	1	0.7	3 (6.3)	3	4.7
Exostosis						
<65	0			3 (0.5)	3	0.4
>=65	1 (0.9)	1	0.7	0		
Osteopenia						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			1 (2.1)	1	1.6
Pain in jaw						
<65	2 (0.2)	2	0.1	2 (0.3)	2	0.3
>=65	0			0		
Bone cyst						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	1 (<0.1)	2	0.1	0		
>=65	0			0		
Coccydynia						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Metatarsalgia						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			1 (2.1)	1	1.6
Osteonecrosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Osteoporosis						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	0			1 (2.1)	1	1.6
Pubic pain						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Connective tissue disorders (excl congenital)						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Myofascitis						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Sjogren's syndrome						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Systemic lupus erythematosus								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Systemic scleroderma								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Nervous system disorders								
<65	360	(30.1)	712	45.6	129	(21.3)	200	26.1
>=65	31	(28.7)	46	32.1	12	(25.0)	22	34.8
Neurological disorders NEC								
<65	160	(13.4)	222	14.2	42	(6.9)	56	7.3
>=65	21	(19.4)	26	18.1	5	(10.4)	12	19.0
Dizziness								
<65	87	(7.3)	118	7.6	21	(3.5)	33	4.3
>=65	11	(10.2)	12	8.4	2	(4.2)	2	3.2
Syncope								
<65	7	(0.6)	7	0.4	2	(0.3)	2	0.3
>=65	4	(3.7)	4	2.8	0			
Paraesthesia								
<65	10	(0.8)	14	0.9	4	(0.7)	4	0.5
>=65	3	(2.8)	3	2.1	1	(2.1)	1	1.6
Dysgeusia								
<65	17	(1.4)	23	1.5	3	(0.5)	3	0.4
>=65	1	(0.9)	1	0.7	1	(2.1)	8	12.7
Lethargy								
<65	5	(0.4)	5	0.3	3	(0.5)	3	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	2 (1.9)	2	1.4	0		
Hypoaesthesia						
<65	6 (0.5)	6	0.4	2 (0.3)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Neuralgia						
<65	4 (0.3)	4	0.3	2 (0.3)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Burning sensation						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Dysaesthesia						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Taste disorder						
<65	9 (0.8)	11	0.7	1 (0.2)	1	0.1
>=65	0			0		
Somnolence						
<65	7 (0.6)	9	0.6	1 (0.2)	1	0.1
>=65	0			0		
Hyperaesthesia						
<65	4 (0.3)	6	0.4	0		
>=65	0			0		
Dizziness postural						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Allodynia						
<65	2 (0.2)	2	0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
>=65	0			0		
Balance disorder						
<65	2	(0.2)	2 0.1	0		
>=65	0			0		
Presyncope						
<65	2	(0.2)	2 0.1	0		
>=65	0			0		
Ageusia						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Aphasia						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Dysarthria						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Hyporeflexia						
<65	1	(<0.1)	1 <0.1	1	(0.2)	1 0.1
>=65	0			1	(2.1)	1 1.6
Loss of consciousness						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Restless legs syndrome						
<65	1	(<0.1)	2 0.1	2	(0.3)	2 0.3
>=65	0			0		
Sensory disturbance						
<65	1	(<0.1)	1 <0.1	1	(0.2)	1 0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Vertigo CNS origin								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Sensory loss								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Headaches								
<65	216	(18.0)	436	27.9	84	(13.8)	113	14.7
>=65	13	(12.0)	15	10.5	5	(10.4)	5	7.9
Headache								
<65	185	(15.4)	372	23.8	75	(12.4)	99	12.9
>=65	13	(12.0)	15	10.5	5	(10.4)	5	7.9
Migraine								
<65	32	(2.7)	52	3.3	9	(1.5)	11	1.4
>=65	0				0			
Sinus headache								
<65	5	(0.4)	5	0.3	1	(0.2)	1	0.1
>=65	0				0			
Tension headache								
<65	4	(0.3)	4	0.3	1	(0.2)	1	0.1
>=65	0				0			
Migraine with aura								
<65	2	(0.2)	2	0.1	1	(0.2)	1	0.1
>=65	0				0			
Occipital neuralgia								
<65	1	(<0.1)	1	<0.1	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Spinal cord and nerve root disorders						
<65	18 (1.5)	20	1.3	11 (1.8)	11	1.4
>=65	2 (1.9)	2	1.4	3 (6.3)	3	4.7
Sciatica						
<65	13 (1.1)	15	1.0	5 (0.8)	5	0.7
>=65	1 (0.9)	1	0.7	3 (6.3)	3	4.7
Cervicobrachial syndrome						
<65	1 (<0.1)	1	<0.1	4 (0.7)	4	0.5
>=65	1 (0.9)	1	0.7	0		
Cervical radiculopathy						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Lumbar radiculopathy						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Lumbosacral radiculopathy						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Spinal cord compression						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Movement disorders (incl parkinsonism)						
<65	4 (0.3)	4	0.3	2 (0.3)	3	0.4
>=65	2 (1.9)	2	1.4	0		
Tremor						
<65	4 (0.3)	4	0.3	2 (0.3)	3	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	1 (0.9)	1	0.7	0		
Essential tremor						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Mental impairment disorders						
<65	4 (0.3)	4	0.3	3 (0.5)	4	0.5
>=65	1 (0.9)	1	0.7	0		
Dementia Alzheimer's type						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Memory impairment						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Amnesia						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Disturbance in attention						
<65	1 (<0.1)	1	<0.1	3 (0.5)	4	0.5
>=65	0			0		
Peripheral neuropathies						
<65	12 (1.0)	13	0.8	8 (1.3)	9	1.2
>=65	0			0		
Carpal tunnel syndrome						
<65	4 (0.3)	5	0.3	3 (0.5)	3	0.4
>=65	0			0		
Neuropathy peripheral						
<65	4 (0.3)	4	0.3	2 (0.3)	2	0.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Nerve compression								
<65	3	(0.3)	3	0.2	2	(0.3)	2	0.3
>=65	0				0			
Peripheral sensory neuropathy								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Peroneal nerve palsy								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Radial nerve compression								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Cranial nerve disorders (excl neoplasms)								
<65	4	(0.3)	4	0.3	0			
>=65	0				0			
Anosmia								
<65	2	(0.2)	2	0.1	0			
>=65	0				0			
Cranial nerve disorder								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Parosmia								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Sleep disturbances (incl subtypes)								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	4 (0.3)	4	0.3	1 (0.2)	1	0.1
>=65	0			0		
Poor quality sleep						
<65	4 (0.3)	4	0.3	1 (0.2)	1	0.1
>=65	0			0		
Central nervous system vascular disorders						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			1 (2.1)	1	1.6
Cerebral infarction						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Ischaemic stroke						
<65	0			0		
>=65	0			1 (2.1)	1	1.6
Increased intracranial pressure and hydrocephalus						
<65	1 (<0.1)	2	0.1	0		
>=65	0			0		
Idiopathic intracranial hypertension						
<65	1 (<0.1)	2	0.1	0		
>=65	0			0		
Neurological disorders of the eye						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Visual field defect						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Neuromuscular disorders								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Autonomic nervous system imbalance								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Demyelinating disorders								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Multiple sclerosis								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Seizures (incl subtypes)								
<65	0				1	(0.2)	1	0.1
>=65	0				1	(2.1)	1	1.6
Partial seizures								
<65	0				0			
>=65	0				1	(2.1)	1	1.6
Psychogenic seizure								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
General disorders and administration site conditions								
<65	271	(22.6)	434	27.8	122	(20.1)	207	27.0
>=65	20	(18.5)	31	21.6	9	(18.8)	15	23.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
General system disorders NEC						
<65	210 (17.5)	299	19.1	80 (13.2)	106	13.8
>=65	15 (13.9)	25	17.4	6 (12.5)	7	11.1
Fatigue						
<65	97 (8.1)	113	7.2	28 (4.6)	29	3.8
>=65	7 (6.5)	7	4.9	0		
Asthenia						
<65	30 (2.5)	47	3.0	10 (1.6)	11	1.4
>=65	5 (4.6)	6	4.2	1 (2.1)	1	1.6
Early satiety						
<65	24 (2.0)	24	1.5	2 (0.3)	2	0.3
>=65	2 (1.9)	2	1.4	0		
Malaise						
<65	14 (1.2)	16	1.0	4 (0.7)	5	0.7
>=65	2 (1.9)	3	2.1	0		
Pain						
<65	20 (1.7)	21	1.3	7 (1.2)	7	0.9
>=65	1 (0.9)	2	1.4	0		
Influenza like illness						
<65	16 (1.3)	17	1.1	13 (2.1)	13	1.7
>=65	1 (0.9)	1	0.7	0		
Chills						
<65	6 (0.5)	6	0.4	0		
>=65	1 (0.9)	1	0.7	2 (4.2)	2	3.2
Hunger						
<65	5 (0.4)	5	0.3	3 (0.5)	3	0.4
>=65	1 (0.9)	1	0.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Oedema peripheral						
<65	3 (0.3)	3	0.2	8 (1.3)	8	1.0
>=65	1 (0.9)	1	0.7	0		
Peripheral swelling						
<65	1 (<0.1)	1	<0.1	4 (0.7)	4	0.5
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Chest discomfort						
<65	9 (0.8)	9	0.6	1 (0.2)	1	0.1
>=65	0			1 (2.1)	2	3.2
Non-cardiac chest pain						
<65	7 (0.6)	7	0.4	4 (0.7)	4	0.5
>=65	0			0		
Chest pain						
<65	3 (0.3)	3	0.2	6 (1.0)	6	0.8
>=65	0			1 (2.1)	1	1.6
Thirst						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Feeling cold						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Feeling hot						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Hernia						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Ill-defined disorder						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Sensation of foreign body						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Swelling						
<65	2 (0.2)	2	0.1	2 (0.3)	2	0.3
>=65	0			0		
Swelling face						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Axillary pain						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Crying						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Fat tissue increased						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Hangover						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Inflammation						
<65	1 (<0.1)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Pseudocyst								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Sense of oppression								
<65	1	(<0.1)	2	0.1	0			
>=65	0				0			
Sluggishness								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Discomfort								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Facial pain								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Granuloma								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Gravitational oedema								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Temperature intolerance								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Administration site reactions								
<65	63	(5.3)	96	6.1	39	(6.4)	75	9.8
>=65	2	(1.9)	3	2.1	5	(10.4)	7	11.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Injection site bruising						
<65	27 (2.3)	30	1.9	24 (4.0)	32	4.2
>=65	1 (0.9)	1	0.7	2 (4.2)	2	3.2
Injection site pruritus						
<65	8 (0.7)	8	0.5	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Injection site pain						
<65	19 (1.6)	24	1.5	13 (2.1)	17	2.2
>=65	0			3 (6.3)	4	6.3
Infusion site extravasation						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Injection site mass						
<65	4 (0.3)	4	0.3	3 (0.5)	3	0.4
>=65	0			0		
Injection site erythema						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	0			0		
Injection site haematoma						
<65	3 (0.3)	8	0.5	3 (0.5)	11	1.4
>=65	0			1 (2.1)	1	1.6
Injection site reaction						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Application site haematoma						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Injection site haemorrhage						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Injection site inflammation						
<65	2 (0.2)	4	0.3	0		
>=65	0			0		
Injection site paraesthesia						
<65	2 (0.2)	2	0.1	2 (0.3)	2	0.3
>=65	0			0		
Injection site induration						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Injection site swelling						
<65	1 (<0.1)	1	<0.1	1 (0.2)	2	0.3
>=65	0			0		
Injection site urticaria						
<65	1 (<0.1)	2	0.1	0		
>=65	0			0		
Vessel puncture site bruise						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Vessel puncture site rash						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Application site bruise						
<65	0			1 (0.2)	1	0.1
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Puncture site pain						
<65	0			1 (0.2)	2	0.3
>=65	0			0		
Body temperature conditions						
<65	26 (2.2)	32	2.0	16 (2.6)	20	2.6
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Pyrexia						
<65	26 (2.2)	32	2.0	16 (2.6)	20	2.6
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Tissue disorders NEC						
<65	4 (0.3)	4	0.3	5 (0.8)	5	0.7
>=65	1 (0.9)	1	0.7	0		
Cyst						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Nodule						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Dysplasia						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Fat necrosis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Hyperplasia						
<65	0			1 (0.2)	1	0.1
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Complications associated with device						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Vascular stent occlusion						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Injury associated with device						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Therapeutic and nontherapeutic effects (excl toxicity)						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Withdrawal syndrome						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Injury, poisoning and procedural complications						
<65	166 (13.9)	229	14.7	108 (17.8)	152	19.8
>=65	22 (20.4)	35	24.4	13 (27.1)	24	38.0
Injuries NEC						
<65	112 (9.3)	143	9.2	88 (14.5)	113	14.7
>=65	14 (13.0)	25	17.4	8 (16.7)	17	26.9
Fall						
<65	12 (1.0)	12	0.8	10 (1.6)	15	2.0
>=65	7 (6.5)	7	4.9	2 (4.2)	4	6.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Muscle strain						
<65	14 (1.2)	15	1.0	14 (2.3)	14	1.8
>=65	3 (2.8)	3	2.1	1 (2.1)	1	1.6
Skin abrasion						
<65	2 (0.2)	5	0.3	2 (0.3)	2	0.3
>=65	3 (2.8)	3	2.1	1 (2.1)	1	1.6
Skin laceration						
<65	7 (0.6)	7	0.4	7 (1.2)	7	0.9
>=65	2 (1.9)	2	1.4	1 (2.1)	2	3.2
Contusion						
<65	14 (1.2)	16	1.0	12 (2.0)	15	2.0
>=65	1 (0.9)	3	2.1	3 (6.3)	4	6.3
Ligament sprain						
<65	21 (1.8)	24	1.5	18 (3.0)	19	2.5
>=65	0			1 (2.1)	1	1.6
Arthropod bite						
<65	8 (0.7)	8	0.5	6 (1.0)	6	0.8
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Tooth fracture						
<65	4 (0.3)	4	0.3	3 (0.5)	3	0.4
>=65	1 (0.9)	1	0.7	0		
Concussion						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Ligament rupture						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Eye burns						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Eyelid injury						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Foreign body in eye						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Arthropod sting						
<65	6 (0.5)	6	0.4	2 (0.3)	2	0.3
>=65	0			0		
Limb injury						
<65	6 (0.5)	6	0.4	2 (0.3)	2	0.3
>=65	0			2 (4.2)	2	3.2
Epicondylitis						
<65	4 (0.3)	4	0.3	5 (0.8)	5	0.7
>=65	0			0		
Animal bite						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Back injury						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Muscle rupture						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
Road traffic accident						
<65	3	(0.3)	3 0.2	0		
>=65	0			0		
Injury						
<65	2	(0.2)	2 0.1	0		
>=65	0			0		
Wound						
<65	2	(0.2)	2 0.1	2	(0.3)	2 0.3
>=65	0			0		
Bone contusion						
<65	1	(<0.1)	1 <0.1	2	(0.3)	2 0.3
>=65	0			0		
Eyelid contusion						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Face injury						
<65	1	(<0.1)	1 <0.1	1	(0.2)	1 0.1
>=65	0			0		
Head injury						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			1	(2.1)	1 1.6
Ligament injury						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Muscle injury						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Musculoskeletal injury						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Nerve injury						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Post-traumatic neck syndrome						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Post-traumatic pain						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Skeletal injury						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Soft tissue foreign body						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Subdural haematoma						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Tendon injury						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Chest injury						
<65	0			1 (0.2)	1	0.1
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Corneal abrasion						
<65	0			2 (0.3)	2	0.3
>=65	0			0		
Eye injury						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Gun shot wound						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Post concussion syndrome						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Scar						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Tendon rupture						
<65	0			2 (0.3)	3	0.4
>=65	0			0		
Procedural related injuries and complications NEC						
<65	23 (1.9)	31	2.0	9 (1.5)	10	1.3
>=65	4 (3.7)	4	2.8	2 (4.2)	3	4.7
Procedural pain						
<65	11 (0.9)	12	0.8	6 (1.0)	7	0.9
>=65	1 (0.9)	1	0.7	1 (2.1)	2	3.2
Injection related reaction						
<65	3 (0.3)	3	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	1 (0.9)	1	0.7	0		
Post procedural haemorrhage						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Procedural haemorrhage						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Post procedural complication						
<65	4 (0.3)	5	0.3	0		
>=65	0			0		
Administration related reaction						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Procedural nausea						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Anaemia postoperative						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Anaphylactic transfusion reaction						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Post procedural constipation						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Suture related complication						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
>=65	0			0		
Urinary retention postoperative						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Vaccination complication						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			1	(2.1)	1 1.6
Procedural vomiting						
<65	0			1	(0.2)	1 0.1
>=65	0			0		
Seroma						
<65	0			1	(0.2)	1 0.1
>=65	0			0		
Bone and joint injuries						
<65	32	(2.7)	35 2.2	19	(3.1)	20 2.6
>=65	3	(2.8)	4 2.8	3	(6.3)	3 4.7
Hand fracture						
<65	2	(0.2)	2 0.1	1	(0.2)	1 0.1
>=65	1	(0.9)	1 0.7	0		
Facial bones fracture						
<65	0			0		
>=65	1	(0.9)	1 0.7	0		
Femur fracture						
<65	0			0		
>=65	1	(0.9)	2 1.4	0		
Foot fracture						
<65	5	(0.4)	7 0.4	5	(0.8)	5 0.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Joint injury						
<65	5 (0.4)	5	0.3	1 (0.2)	1	0.1
>=65	0			0		
Meniscus injury						
<65	4 (0.3)	4	0.3	4 (0.7)	5	0.7
>=65	0			0		
Joint dislocation						
<65	3 (0.3)	3	0.2	0		
>=65	0			1 (2.1)	1	1.6
Radius fracture						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Rib fracture						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Ankle fracture						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	0			0		
Fractured coccyx						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Spinal compression fracture						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Stress fracture						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			1 (2.1)	1	1.6
Thoracic vertebral fracture						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Tibia fracture						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Upper limb fracture						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Wrist fracture						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Fibula fracture						
<65	0			0		
>=65	0			1 (2.1)	1	1.6
Torus fracture						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Medication errors and other product use errors and issues						
<65	9 (0.8)	9	0.6	2 (0.3)	3	0.4
>=65	1 (0.9)	1	0.7	0		
Incorrect dose administered						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Accidental overdose						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	7 (0.6)	7	0.4	2 (0.3)	3	0.4
>=65	0			0		
Medication error						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Overdoses and underdoses NEC						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Overdose						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Injuries by physical agents						
<65	6 (0.5)	6	0.4	4 (0.7)	4	0.5
>=65	0			1 (2.1)	1	1.6
Sunburn						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Heat exhaustion						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Heat illness						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Hypobarism						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Thermal burn						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<65	1	(<0.1)	1	<0.1	2	(0.3)	2	0.3
>=65	0				0			
Burns second degree								
<65	0				2	(0.3)	2	0.3
>=65	0				1	(2.1)	1	1.6
Exposures, chemical injuries and poisoning								
<65	2	(0.2)	2	0.1	0			
>=65	0				0			
Exposure to toxic agent								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Reactive gastropathy								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Skin and subcutaneous tissue disorders								
<65	167	(13.9)	222	14.2	69	(11.4)	87	11.4
>=65	21	(19.4)	27	18.8	6	(12.5)	9	14.2
Epidermal and dermal conditions								
<65	92	(7.7)	115	7.4	48	(7.9)	59	7.7
>=65	13	(12.0)	14	9.8	4	(8.3)	6	9.5
Pruritus								
<65	13	(1.1)	14	0.9	6	(1.0)	6	0.8
>=65	4	(3.7)	4	2.8	0			
Rash								
<65	24	(2.0)	28	1.8	16	(2.6)	20	2.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	2 (1.9)	2	1.4	1 (2.1)	3	4.7
Dry skin						
<65	5 (0.4)	5	0.3	2 (0.3)	2	0.3
>=65	3 (2.8)	3	2.1	1 (2.1)	1	1.6
Erythema						
<65	1 (<0.1)	1	<0.1	4 (0.7)	4	0.5
>=65	2 (1.9)	2	1.4	0		
Eczema						
<65	12 (1.0)	12	0.8	4 (0.7)	4	0.5
>=65	1 (0.9)	1	0.7	0		
Skin lesion						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Decubitus ulcer						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Skin burning sensation						
<65	6 (0.5)	12	0.8	1 (0.2)	1	0.1
>=65	0			1 (2.1)	1	1.6
Dermatitis contact						
<65	5 (0.4)	7	0.4	4 (0.7)	4	0.5
>=65	0			0		
Dermatitis						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	0			0		
Pain of skin						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Psoriasis						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Rash pruritic						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Skin irritation						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Blister						
<65	2 (0.2)	2	0.1	4 (0.7)	4	0.5
>=65	0			1 (2.1)	1	1.6
Dermatitis allergic						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Skin disorder						
<65	2 (0.2)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Dermatitis atopic						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Macule						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Papule						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Perioral dermatitis								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Pityriasis rosea								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Prurigo								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Rash maculo-papular								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Skin discolouration								
<65	1	(<0.1)	1	<0.1	2	(0.3)	2	0.3
>=65	0				0			
Skin odour abnormal								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Xanthelasma								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Drug eruption								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Photosensitivity reaction								
<65	0				1	(0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Rash erythematous								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Rash macular								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Skin reaction								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Skin appendage conditions								
<65	74	(6.2)	84	5.4	17	(2.8)	18	2.3
>=65	8	(7.4)	8	5.6	2	(4.2)	3	4.7
Alopecia								
<65	50	(4.2)	52	3.3	5	(0.8)	5	0.7
>=65	3	(2.8)	3	2.1	0			
Hyperhidrosis								
<65	6	(0.5)	6	0.4	7	(1.2)	7	0.9
>=65	2	(1.9)	2	1.4	1	(2.1)	1	1.6
Cold sweat								
<65	2	(0.2)	2	0.1	0			
>=65	1	(0.9)	1	0.7	0			
Ingrowing nail								
<65	2	(0.2)	2	0.1	0			
>=65	1	(0.9)	1	0.7	1	(2.1)	2	3.2
Hair growth abnormal								
<65	1	(<0.1)	1	<0.1	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	1 (0.9)	1	0.7	0		
Acne						
<65	4 (0.3)	4	0.3	2 (0.3)	2	0.3
>=65	0			0		
Hirsutism						
<65	3 (0.3)	4	0.3	1 (0.2)	1	0.1
>=65	0			0		
Hidradenitis						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Miliaria						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Rosacea						
<65	2 (0.2)	3	0.2	2 (0.3)	2	0.3
>=65	0			0		
Diffuse alopecia						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Hypertrichosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Nail bed inflammation						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Nail discolouration						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Night sweats						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Onychoclasis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Cornification and dystrophic skin disorders						
<65	4 (0.3)	5	0.3	0		
>=65	3 (2.8)	4	2.8	0		
Actinic keratosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	2 (1.9)	3	2.1	0		
Hyperkeratosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Lichenoid keratosis						
<65	1 (<0.1)	2	0.1	0		
>=65	0			0		
Skin striae						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Angioedema and urticaria						
<65	12 (1.0)	12	0.8	6 (1.0)	6	0.8
>=65	1 (0.9)	1	0.7	0		
Urticaria						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<65	11	(0.9)	11	0.7	5	(0.8)	5	0.7
>=65	1	(0.9)	1	0.7	0			
Cold urticaria								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Angioedema								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Pigmentation disorders								
<65	3	(0.3)	3	0.2	0			
>=65	0				0			
Ephelides								
<65	2	(0.2)	2	0.1	0			
>=65	0				0			
Skin hyperpigmentation								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Cutaneous neoplasms benign								
<65	2	(0.2)	2	0.1	1	(0.2)	1	0.1
>=65	0				0			
Dermal cyst								
<65	2	(0.2)	2	0.1	1	(0.2)	1	0.1
>=65	0				0			
Skin vascular abnormalities								
<65	1	(<0.1)	1	<0.1	1	(0.2)	1	0.1
>=65	0				0			
Ecchymosis								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<65	1	(<0.1)	1	<0.1	1	(0.2)	1	0.1
>=65	0				0			
Skin and subcutaneous tissue disorders NEC								
<65	0				2	(0.3)	2	0.3
>=65	0				0			
Erythema nodosum								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Skin ulcer								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Metabolism and nutrition disorders								
<65	187	(15.6)	249	15.9	73	(12.0)	97	12.7
>=65	12	(11.1)	18	12.6	10	(20.8)	11	17.4
Appetite and general nutritional disorders								
<65	133	(11.1)	162	10.4	26	(4.3)	34	4.4
>=65	8	(7.4)	10	7.0	2	(4.2)	2	3.2
Decreased appetite								
<65	118	(9.8)	131	8.4	20	(3.3)	24	3.1
>=65	6	(5.6)	8	5.6	2	(4.2)	2	3.2
Food craving								
<65	7	(0.6)	7	0.4	2	(0.3)	2	0.3
>=65	1	(0.9)	1	0.7	0			
Increased appetite								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	5 (0.4)	6	0.4	2 (0.3)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Hyperphagia						
<65	7 (0.6)	8	0.5	2 (0.3)	4	0.5
>=65	0			0		
Food aversion						
<65	4 (0.3)	6	0.4	0		
>=65	0			0		
Lack of satiety						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	0			0		
Malnutrition						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Vitamin related disorders						
<65	20 (1.7)	26	1.7	10 (1.6)	12	1.6
>=65	2 (1.9)	2	1.4	0		
Vitamin D deficiency						
<65	15 (1.3)	15	1.0	8 (1.3)	8	1.0
>=65	2 (1.9)	2	1.4	0		
Vitamin B12 deficiency						
<65	6 (0.5)	6	0.4	0		
>=65	0			0		
Folate deficiency						
<65	2 (0.2)	2	0.1	2 (0.3)	2	0.3
>=65	0			0		
Vitamin A deficiency						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Vitamin B complex deficiency						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	0			0		
Vitamin B2 deficiency						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Lipid metabolism disorders						
<65	18 (1.5)	19	1.2	17 (2.8)	18	2.3
>=65	2 (1.9)	2	1.4	3 (6.3)	3	4.7
Hypercholesterolaemia						
<65	3 (0.3)	3	0.2	4 (0.7)	4	0.5
>=65	2 (1.9)	2	1.4	2 (4.2)	2	3.2
Dyslipidaemia						
<65	10 (0.8)	10	0.6	8 (1.3)	9	1.2
>=65	0			1 (2.1)	1	1.6
Hypertriglyceridaemia						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Cholesterosis						
<65	1 (<0.1)	2	0.1	0		
>=65	0			0		
Hyperlipidaemia						
<65	1 (<0.1)	1	<0.1	4 (0.7)	4	0.5
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Electrolyte and fluid balance conditions						
<65	7 (0.6)	10	0.6	4 (0.7)	4	0.5
>=65	2 (1.9)	2	1.4	2 (4.2)	2	3.2
Hyperkalaemia						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Hyponatraemia						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Hypokalaemia						
<65	3 (0.3)	5	0.3	2 (0.3)	2	0.3
>=65	0			0		
Dehydration						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			2 (4.2)	2	3.2
Electrolyte imbalance						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Polydipsia						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Fluid retention						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Glucose metabolism disorders (incl diabetes mellitus)						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	9 (0.8)	16	1.0	18 (3.0)	22	2.9
>=65	1 (0.9)	1	0.7	3 (6.3)	3	4.7
Hypoglycaemia						
<65	6 (0.5)	12	0.8	5 (0.8)	7	0.9
>=65	1 (0.9)	1	0.7	0		
Glucose tolerance impaired						
<65	1 (<0.1)	1	<0.1	3 (0.5)	3	0.4
>=65	0			1 (2.1)	1	1.6
Postprandial hypoglycaemia						
<65	1 (<0.1)	2	0.1	0		
>=65	0			0		
Type 2 diabetes mellitus						
<65	1 (<0.1)	1	<0.1	5 (0.8)	6	0.8
>=65	0			1 (2.1)	1	1.6
Diabetes mellitus						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Hyperglycaemia						
<65	0			1 (0.2)	1	0.1
>=65	0			1 (2.1)	1	1.6
Impaired fasting glucose						
<65	0			3 (0.5)	3	0.4
>=65	0			0		
Insulin resistance						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Metabolism disorders NEC						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Hyperlipasaemia						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Iron and trace metal metabolism disorders						
<65	5 (0.4)	5	0.3	4 (0.7)	4	0.5
>=65	0			0		
Iron deficiency						
<65	5 (0.4)	5	0.3	4 (0.7)	4	0.5
>=65	0			0		
Purine and pyrimidine metabolism disorders						
<65	4 (0.3)	5	0.3	3 (0.5)	3	0.4
>=65	0			1 (2.1)	1	1.6
Gout						
<65	4 (0.3)	5	0.3	2 (0.3)	2	0.3
>=65	0			1 (2.1)	1	1.6
Hyperuricaemia						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Food intolerance syndromes						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Dairy intolerance						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Food intolerance								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Lactose intolerance								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Bone, calcium, magnesium and phosphorus metabolism disorders								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Hypomagnesaemia								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Protein and amino acid metabolism disorders NEC								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Hypoalbuminaemia								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Respiratory, thoracic and mediastinal disorders								
<65	159	(13.3)	209	13.4	97	(16.0)	124	16.2
>=65	14	(13.0)	16	11.2	7	(14.6)	10	15.8
Respiratory disorders NEC								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	54 (4.5)	63	4.0	48 (7.9)	53	6.9
>=65	7 (6.5)	7	4.9	3 (6.3)	3	4.7
Cough						
<65	37 (3.1)	42	2.7	32 (5.3)	34	4.4
>=65	3 (2.8)	3	2.1	1 (2.1)	1	1.6
Haemoptysis						
<65	0			0		
>=65	2 (1.9)	2	1.4	0		
Sleep apnoea syndrome						
<65	5 (0.4)	5	0.3	3 (0.5)	3	0.4
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Dyspnoea exertional						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Dyspnoea						
<65	8 (0.7)	8	0.5	8 (1.3)	8	1.0
>=65	0			0		
Productive cough						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	0			0		
Respiratory disorder						
<65	2 (0.2)	2	0.1	4 (0.7)	4	0.5
>=65	0			0		
Hyperventilation						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Respiratory tract congestion						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Acute respiratory failure								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Pulmonary mass								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Respiratory tract signs and symptoms								
<65	71	(5.9)	77	4.9	32	(5.3)	36	4.7
>=65	4	(3.7)	4	2.8	1	(2.1)	1	1.6
Oropharyngeal pain								
<65	45	(3.8)	50	3.2	23	(3.8)	26	3.4
>=65	3	(2.8)	3	2.1	0			
Rhinorrhoea								
<65	5	(0.4)	5	0.3	1	(0.2)	1	0.1
>=65	1	(0.9)	1	0.7	0			
Upper respiratory tract inflammation								
<65	5	(0.4)	6	0.4	4	(0.7)	4	0.5
>=65	0				0			
Hiccups								
<65	3	(0.3)	3	0.2	0			
>=65	0				0			
Upper-airway cough syndrome								
<65	3	(0.3)	3	0.2	0			
>=65	0				0			
Catarrh								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Dysphonia						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Diaphragmalgia						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Oropharyngeal discomfort						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Paranasal sinus discomfort						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	0			0		
Pleuritic pain						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Sinus pain						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Yawning						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Upper respiratory tract congestion						
<65	0			0		
>=65	0			1 (2.1)	1	1.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Upper respiratory tract disorders (excl infections)						
<65	49 (4.1)	51	3.3	16 (2.6)	19	2.5
>=65	2 (1.9)	2	1.4	2 (4.2)	2	3.2
Nasal congestion						
<65	10 (0.8)	10	0.6	5 (0.8)	5	0.7
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Epistaxis						
<65	6 (0.5)	6	0.4	0		
>=65	1 (0.9)	1	0.7	0		
Sinus congestion						
<65	13 (1.1)	13	0.8	4 (0.7)	6	0.8
>=65	0			1 (2.1)	1	1.6
Rhinitis allergic						
<65	11 (0.9)	11	0.7	6 (1.0)	7	0.9
>=65	0			0		
Nasal polyps						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Nasal septum deviation						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Paranasal sinus hypersecretion						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Tonsillar hypertrophy						
<65	2 (0.2)	2	0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Nasal dryness						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Paranasal cyst						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Vocal cord polyp						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Nasal adhesions						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Bronchial disorders (excl neoplasms)						
<65	12 (1.0)	12	0.8	10 (1.6)	12	1.6
>=65	2 (1.9)	2	1.4	3 (6.3)	4	6.3
Asthma						
<65	10 (0.8)	10	0.6	7 (1.2)	9	1.2
>=65	1 (0.9)	1	0.7	2 (4.2)	2	3.2
Chronic obstructive pulmonary disease						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Wheezing						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Allergic bronchitis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	0			0		
>=65	0			1 (2.1)	2	3.2
Lower respiratory tract disorders (excl obstruction and infection)						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Atelectasis						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Pulmonary fibrosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Pleural disorders						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Pleural effusion						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Pleurisy						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Pulmonary vascular disorders						
<65	2 (0.2)	2	0.1	2 (0.3)	2	0.3
>=65	0			0		
Pulmonary embolism						
<65	2 (0.2)	2	0.1	2 (0.3)	2	0.3
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Psychiatric disorders						
<65	118 (9.8)	152	9.7	76 (12.5)	105	13.7
>=65	6 (5.6)	8	5.6	7 (14.6)	8	12.7
Anxiety disorders and symptoms						
<65	43 (3.6)	45	2.9	30 (4.9)	31	4.0
>=65	3 (2.8)	3	2.1	1 (2.1)	1	1.6
Anxiety						
<65	29 (2.4)	30	1.9	19 (3.1)	19	2.5
>=65	3 (2.8)	3	2.1	1 (2.1)	1	1.6
Stress						
<65	8 (0.7)	8	0.5	6 (1.0)	6	0.8
>=65	0			0		
Panic attack						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	0			0		
Acute stress disorder						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Burnout syndrome						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Nervousness						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Post-traumatic stress disorder						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Agitation						
<65	0			2 (0.3)	2	0.3
>=65	0			0		
Generalised anxiety disorder						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Sleep disorders and disturbances						
<65	38 (3.2)	40	2.6	25 (4.1)	29	3.8
>=65	2 (1.9)	2	1.4	4 (8.3)	4	6.3
Insomnia						
<65	27 (2.3)	28	1.8	14 (2.3)	15	2.0
>=65	1 (0.9)	1	0.7	4 (8.3)	4	6.3
Abnormal dreams						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Sleep disorder						
<65	6 (0.5)	6	0.4	7 (1.2)	8	1.0
>=65	0			0		
Initial insomnia						
<65	3 (0.3)	4	0.3	1 (0.2)	1	0.1
>=65	0			0		
Middle insomnia						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Nightmare						
<65	1 (<0.1)	1	<0.1	2 (0.3)	3	0.4
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Sleep terror						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Depressed mood disorders and disturbances						
<65	31 (2.6)	37	2.4	26 (4.3)	28	3.7
>=65	2 (1.9)	2	1.4	1 (2.1)	1	1.6
Depressed mood						
<65	13 (1.1)	14	0.9	9 (1.5)	9	1.2
>=65	1 (0.9)	1	0.7	0		
Depression						
<65	15 (1.3)	17	1.1	14 (2.3)	15	2.0
>=65	0			0		
Negative thoughts						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Major depression						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Anhedonia						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Tearfulness						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Depressive symptom						
<65	0			1 (0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Persistent depressive disorder						
<65	0			2 (0.3)	2	0.3
>=65	0			1 (2.1)	1	1.6
Mood disorders and disturbances NEC						
<65	8 (0.7)	8	0.5	3 (0.5)	3	0.4
>=65	1 (0.9)	1	0.7	0		
Apathy						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Irritability						
<65	4 (0.3)	4	0.3	2 (0.3)	2	0.3
>=65	0			0		
Affective disorder						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Mood swings						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Changes in physical activity						
<65	4 (0.3)	4	0.3	0		
>=65	0			0		
Restlessness						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Tic						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Sexual dysfunctions, disturbances and gender identity disorders						
<65	4 (0.3)	4	0.3	1 (0.2)	1	0.1
>=65	0			0		
Libido decreased						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Libido increased						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Suicidal and self-injurious behaviours NEC						
<65	4 (0.3)	4	0.3	3 (0.5)	5	0.7
>=65	0			0		
Suicidal ideation						
<65	4 (0.3)	4	0.3	2 (0.3)	4	0.5
>=65	0			0		
Suicide attempt						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Adjustment disorders (incl subtypes)						
<65	3 (0.3)	3	0.2	2 (0.3)	2	0.3
>=65	0			2 (4.2)	2	3.2
Adjustment disorder						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			1 (2.1)	1	1.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
Adjustment disorder with depressed mood						
<65	1	(<0.1)	1 <0.1	2	(0.3)	2 0.3
>=65	0			1	(2.1)	1 1.6
Grief reaction						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Cognitive and attention disorders and disturbances						
<65	2	(0.2)	3 0.2	1	(0.2)	1 0.1
>=65	0			0		
Attention deficit/hyperactivity disorder						
<65	1	(<0.1)	1 <0.1	1	(0.2)	1 0.1
>=65	0			0		
Mental fatigue						
<65	1	(<0.1)	2 0.1	0		
>=65	0			0		
Deliria (incl confusion)						
<65	1	(<0.1)	2 0.1	1	(0.2)	1 0.1
>=65	0			0		
Disorientation						
<65	1	(<0.1)	2 0.1	1	(0.2)	1 0.1
>=65	0			0		
Manic and bipolar mood disorders and disturbances						
<65	1	(<0.1)	1 <0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
>=65	0			0		
Bipolar disorder						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Psychiatric and behavioural symptoms NEC						
<65	1	(<0.1)	1 <0.1	2	(0.3)	2 0.3
>=65	0			0		
Abulia						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Psychiatric symptom						
<65	0			2	(0.3)	2 0.3
>=65	0			0		
Psychiatric disorders NEC						
<65	0			1	(0.2)	1 0.1
>=65	0			0		
Alcoholic hangover						
<65	0			1	(0.2)	1 0.1
>=65	0			0		
Somatic symptom and related disorders						
<65	0			1	(0.2)	1 0.1
>=65	0			0		
Conversion disorder						
<65	0			1	(0.2)	1 0.1
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Investigations						
<65	85 (7.1)	110	7.0	47 (7.7)	65	8.5
>=65	8 (7.4)	8	5.6	2 (4.2)	2	3.2
Protein and chemistry analyses NEC						
<65	11 (0.9)	11	0.7	5 (0.8)	5	0.7
>=65	2 (1.9)	2	1.4	0		
C-reactive protein increased						
<65	11 (0.9)	11	0.7	5 (0.8)	5	0.7
>=65	2 (1.9)	2	1.4	0		
Gastrointestinal investigations						
<65	12 (1.0)	14	0.9	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Pancreatic enzymes increased						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Lipase increased						
<65	11 (0.9)	11	0.7	1 (0.2)	1	0.1
>=65	0			1 (2.1)	1	1.6
Amylase increased						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Gastric pH						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Physical examination and organ system status topics						
<65	6 (0.5)	6	0.4	3 (0.5)	4	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	1 (0.9)	1	0.7	0		
Weight decreased						
<65	2 (0.2)	2	0.1	0		
>=65	1 (0.9)	1	0.7	0		
Weight increased						
<65	2 (0.2)	2	0.1	2 (0.3)	2	0.3
>=65	0			0		
Body mass index decreased						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Respiratory rate increased						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Body temperature increased						
<65	0			1 (0.2)	2	0.3
>=65	0			0		
Hepatobiliary investigations						
<65	16 (1.3)	17	1.1	11 (1.8)	15	2.0
>=65	0			0		
Gamma-glutamyltransferase increased						
<65	7 (0.6)	7	0.4	3 (0.5)	3	0.4
>=65	0			0		
Hepatic enzyme increased						
<65	6 (0.5)	6	0.4	2 (0.3)	2	0.3
>=65	0			0		
Alanine aminotransferase increased						
<65	1 (<0.1)	1	<0.1	3 (0.5)	3	0.4

Adverse events with onset prior to randomisation are not included.
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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Aspartate aminotransferase increased						
<65	1 (<0.1)	1	<0.1	4 (0.7)	4	0.5
>=65	0			0		
Blood bilirubin increased						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	0			0		
Transaminases increased						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Microbiology and serology investigations						
<65	3 (0.3)	3	0.2	0		
>=65	1 (0.9)	1	0.7	0		
Helicobacter test positive						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
HIV test positive						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Human papilloma virus test positive						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Haematology investigations (incl blood groups)						
<65	2 (0.2)	2	0.1	2 (0.3)	5	0.7
>=65	1 (0.9)	1	0.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Haematology test abnormal						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Haemoglobin decreased						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Haematocrit increased						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Haemoglobin increased						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Red blood cell count increased						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Red cell distribution width increased						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Cytogenetic investigations						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Prostatic specific antigen increased						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Metabolic, nutritional and blood gas investigations						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	1 (<0.1)	1	<0.1	4 (0.7)	4	0.5
>=65	1 (0.9)	1	0.7	0		
Blood uric acid increased						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Blood glucose increased						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	0			0		
Glycosylated haemoglobin increased						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Vitamin D decreased						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Cardiac and vascular investigations (excl enzyme tests)						
<65	10 (0.8)	12	0.8	7 (1.2)	7	0.9
>=65	0			0		
Heart rate increased						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
QRS axis abnormal						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Blood pressure abnormal						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Blood pressure decreased						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Blood pressure increased						
<65	1 (<0.1)	1	<0.1	6 (1.0)	6	0.8
>=65	0			0		
Cardiac murmur						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Electrocardiogram ST segment depression						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Electrocardiogram T wave amplitude decreased						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Electrocardiogram T wave inversion						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Pulse abnormal						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Electrocardiogram T wave abnormal						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Lipid analyses						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<65	9	(0.8)	16	1.0	4	(0.7)	5	0.7
>=65	0				0			
High density lipoprotein decreased								
<65	5	(0.4)	5	0.3	0			
>=65	0				0			
Blood cholesterol increased								
<65	4	(0.3)	4	0.3	1	(0.2)	1	0.1
>=65	0				0			
Low density lipoprotein increased								
<65	3	(0.3)	3	0.2	2	(0.3)	2	0.3
>=65	0				0			
Lipids increased								
<65	2	(0.2)	2	0.1	1	(0.2)	1	0.1
>=65	0				0			
Blood triglycerides increased								
<65	1	(<0.1)	1	<0.1	1	(0.2)	1	0.1
>=65	0				0			
Very low density lipoprotein increased								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Endocrine investigations (incl sex hormones)								
<65	8	(0.7)	10	0.6	3	(0.5)	3	0.4
>=65	0				0			
Blood calcitonin increased								
<65	4	(0.3)	4	0.3	1	(0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Blood thyroid stimulating hormone decreased						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Blood thyroid stimulating hormone abnormal						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Thyroxine free increased						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Thyroxine increased						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Blood thyroid stimulating hormone increased						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Enzyme investigations NEC						
<65	6 (0.5)	6	0.4	8 (1.3)	8	1.0
>=65	0			0		
Blood creatine phosphokinase increased						
<65	5 (0.4)	5	0.3	7 (1.2)	7	0.9
>=65	0			0		
Enzyme level increased						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Blood alkaline phosphatase increased						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Renal and urinary tract investigations and urinalyses						
<65	4 (0.3)	4	0.3	3 (0.5)	3	0.4
>=65	0			0		
Blood creatinine increased						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Glomerular filtration rate decreased						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	0			0		
White blood cells urine						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Blood urine present						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Investigations, imaging and histopathology procedures NEC						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Precancerous cells present						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Smear test								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Endoscopy								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Reproductive organ and breast investigations (excl hormone analyses)								
<65	2	(0.2)	2	0.1	0			
>=65	0				0			
Biopsy breast								
<65	2	(0.2)	2	0.1	0			
>=65	0				0			
Water, electrolyte and mineral investigations								
<65	2	(0.2)	2	0.1	2	(0.3)	2	0.3
>=65	0				1	(2.1)	1	1.6
Blood calcium decreased								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Blood potassium increased								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Blood iron decreased								
<65	0				1	(0.2)	1	0.1
>=65	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Blood sodium increased								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Serum ferritin decreased								
<65	0				0			
>=65	0				1	(2.1)	1	1.6
Musculoskeletal and soft tissue investigations (excl enzyme tests)								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Arthroscopy								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Immunology and allergy investigations								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Antinuclear antibody positive								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Vascular disorders								
<65	82	(6.8)	88	5.6	38	(6.3)	43	5.6
>=65	8	(7.4)	9	6.3	7	(14.6)	7	11.1
Vascular hypertensive disorders								
<65	40	(3.3)	40	2.6	26	(4.3)	30	3.9
>=65	2	(1.9)	2	1.4	2	(4.2)	2	3.2
Hypertension								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	38 (3.2)	38	2.4	25 (4.1)	29	3.8
>=65	2 (1.9)	2	1.4	2 (4.2)	2	3.2
Essential hypertension						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Hypertensive emergency						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Hypertensive crisis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Decreased and nonspecific blood pressure disorders and shock						
<65	16 (1.3)	18	1.2	1 (0.2)	1	0.1
>=65	3 (2.8)	3	2.1	1 (2.1)	1	1.6
Hypotension						
<65	7 (0.6)	8	0.5	1 (0.2)	1	0.1
>=65	3 (2.8)	3	2.1	1 (2.1)	1	1.6
Orthostatic hypotension						
<65	8 (0.7)	9	0.6	0		
>=65	0			0		
Circulatory collapse						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Vascular disorders NEC						
<65	7 (0.6)	8	0.5	4 (0.7)	4	0.5
>=65	2 (1.9)	2	1.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hot flush						
<65	6 (0.5)	6	0.4	3 (0.5)	3	0.4
>=65	2 (1.9)	2	1.4	0		
Flushing						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Vascular haemorrhagic disorders						
<65	5 (0.4)	5	0.3	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	3 (6.3)	3	4.7
Haematoma						
<65	5 (0.4)	5	0.3	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	3 (6.3)	3	4.7
Venous varices						
<65	5 (0.4)	5	0.3	0		
>=65	1 (0.9)	1	0.7	0		
Varicose vein						
<65	5 (0.4)	5	0.3	0		
>=65	1 (0.9)	1	0.7	0		
Arteriosclerosis, stenosis, vascular insufficiency and necrosis						
<65	7 (0.6)	7	0.4	4 (0.7)	4	0.5
>=65	0			0		
Peripheral venous disease						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Peripheral coldness						
<65	2 (0.2)	2	0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Aortic arteriosclerosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Arteriosclerosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Raynaud's phenomenon						
<65	0			3 (0.5)	3	0.4
>=65	0			0		
Embolism and thrombosis						
<65	3 (0.3)	3	0.2	3 (0.5)	3	0.4
>=65	0			0		
Thrombosis						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Thrombophlebitis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Deep vein thrombosis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Thrombophlebitis superficial						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Vascular infections and inflammations						
<65	2 (0.2)	2	0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Arteritis								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Phlebitis								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Lymphatic vessel disorders								
<65	0				0			
>=65	0				1	(2.1)	1	1.6
Lymphoedema								
<65	0				0			
>=65	0				1	(2.1)	1	1.6
Eye disorders								
<65	34	(2.8)	43	2.8	19	(3.1)	24	3.1
>=65	10	(9.3)	15	10.5	5	(10.4)	7	11.1
Anterior eye structural change, deposit and degeneration								
<65	4	(0.3)	5	0.3	2	(0.3)	3	0.4
>=65	3	(2.8)	3	2.1	1	(2.1)	1	1.6
Cataract								
<65	4	(0.3)	5	0.3	1	(0.2)	2	0.3
>=65	2	(1.9)	2	1.4	0			
Xerophthalmia								
<65	0				0			
>=65	1	(0.9)	1	0.7	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Ectropion						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Pterygium						
<65	0			0		
>=65	0			1 (2.1)	1	1.6
Ocular infections, irritations and inflammations						
<65	6 (0.5)	8	0.5	6 (1.0)	8	1.0
>=65	2 (1.9)	2	1.4	1 (2.1)	2	3.2
Eye discharge						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Ocular hyperaemia						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Eye pruritus						
<65	2 (0.2)	2	0.1	0		
>=65	0			1 (2.1)	1	1.6
Conjunctival irritation						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Conjunctivitis allergic						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Eczema eyelids						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Eye allergy								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Meibomian gland dysfunction								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Swelling of eyelid								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Blepharitis								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Conjunctival hyperaemia								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Erythema of eyelid								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Eye inflammation								
<65	0				1	(0.2)	2	0.3
>=65	0				0			
Eye irritation								
<65	0				0			
>=65	0				1	(2.1)	1	1.6
Keratitis								
<65	0				1	(0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Ulcerative keratitis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Glaucoma and ocular hypertension						
<65	2 (0.2)	2	0.1	0		
>=65	2 (1.9)	2	1.4	1 (2.1)	2	3.2
Glaucoma						
<65	2 (0.2)	2	0.1	0		
>=65	2 (1.9)	2	1.4	1 (2.1)	2	3.2
Vision disorders						
<65	13 (1.1)	15	1.0	3 (0.5)	3	0.4
>=65	1 (0.9)	2	1.4	1 (2.1)	1	1.6
Diplopia						
<65	2 (0.2)	2	0.1	0		
>=65	1 (0.9)	2	1.4	0		
Vision blurred						
<65	6 (0.5)	6	0.4	0		
>=65	0			1 (2.1)	1	1.6
Myopia						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Anisometropia						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Astigmatism						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
>=65	0			0		
Photopsia						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Visual impairment						
<65	1	(<0.1)	1 <0.1	1	(0.2)	1 0.1
>=65	0			0		
Scintillating scotoma						
<65	0			1	(0.2)	1 0.1
>=65	0			0		
Ocular haemorrhages and vascular disorders NEC						
<65	1	(<0.1)	1 <0.1	1	(0.2)	1 0.1
>=65	2	(1.9)	2 1.4	0		
Optic ischaemic neuropathy						
<65	1	(<0.1)	1 <0.1	0		
>=65	1	(0.9)	1 0.7	0		
Eyelid haematoma						
<65	0			0		
>=65	1	(0.9)	1 0.7	0		
Conjunctival haemorrhage						
<65	0			1	(0.2)	1 0.1
>=65	0			0		
Ocular structural change, deposit and degeneration NEC						
<65	1	(<0.1)	1 <0.1	2	(0.3)	2 0.3
>=65	2	(1.9)	3 2.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Macular degeneration						
<65	1 (<0.1)	1	<0.1	0		
>=65	2 (1.9)	3	2.1	0		
Vitreous detachment						
<65	0			2 (0.3)	2	0.3
>=65	0			0		
Eye disorders NEC						
<65	7 (0.6)	7	0.4	5 (0.8)	5	0.7
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Dry eye						
<65	3 (0.3)	3	0.2	3 (0.5)	3	0.4
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Eyelid disorder						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Eye pain						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Lacrimation increased						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Ocular discomfort						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Retina, choroid and vitreous haemorrhages and vascular disorders						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
>=65	0			0		
Retinopathy						
<65	2	(0.2)	2 0.1	0		
>=65	0			0		
Retinal aneurysm						
<65	0			1	(0.2)	1 0.1
>=65	0			0		
Ocular neuromuscular disorders						
<65	1	(<0.1)	1 <0.1	1	(0.2)	1 0.1
>=65	0			0		
Blepharospasm						
<65	1	(<0.1)	1 <0.1	1	(0.2)	1 0.1
>=65	0			0		
Ocular sensory symptoms NEC						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Asthenopia						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Cardiac disorders						
<65	45	(3.8)	51 3.3	27	(4.4)	36 4.7
>=65	9	(8.3)	11 7.7	6	(12.5)	8 12.7
Cardiac arrhythmias						
<65	26	(2.2)	31 2.0	13	(2.1)	17 2.2
>=65	6	(5.6)	7 4.9	4	(8.3)	4 6.3
Atrial fibrillation						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	3 (0.3)	6	0.4	3 (0.5)	4	0.5
>=65	3 (2.8)	3	2.1	0		
Bundle branch block left						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Bradycardia						
<65	0			3 (0.5)	3	0.4
>=65	1 (0.9)	1	0.7	0		
Defect conduction intraventricular						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Nodal rhythm						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Atrioventricular block first degree						
<65	5 (0.4)	5	0.3	3 (0.5)	3	0.4
>=65	0			1 (2.1)	1	1.6
Tachycardia						
<65	5 (0.4)	5	0.3	5 (0.8)	5	0.7
>=65	0			0		
Arrhythmia						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			1 (2.1)	1	1.6
Sinus tachycardia						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Ventricular extrasystoles						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
<65	2	(0.2)	2 0.1	0		
>=65	0			0		
Atrial flutter						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Atrial tachycardia						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Atrioventricular block						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Atrioventricular block second degree						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Bundle branch block right						
<65	1	(<0.1)	1 <0.1	1	(0.2)	1 0.1
>=65	0			1	(2.1)	1 1.6
Cardiac flutter						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Sinus bradycardia						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			1	(2.1)	1 1.6
Supraventricular extrasystoles						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Coronary artery disorders						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	4 (0.3)	4	0.3	6 (1.0)	6	0.8
>=65	3 (2.8)	3	2.1	1 (2.1)	2	3.2
Angina pectoris						
<65	1 (<0.1)	1	<0.1	4 (0.7)	4	0.5
>=65	1 (0.9)	1	0.7	0		
Angina unstable						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Coronary artery stenosis						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Acute myocardial infarction						
<65	2 (0.2)	2	0.1	0		
>=65	0			1 (2.1)	1	1.6
Arteriosclerosis coronary artery						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Coronary artery disease						
<65	0			0		
>=65	0			1 (2.1)	1	1.6
Myocardial infarction						
<65	0			2 (0.3)	2	0.3
>=65	0			0		
Cardiac disorders, signs and symptoms NEC						
<65	11 (0.9)	11	0.7	7 (1.2)	9	1.2
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Palpitations						
<65	9 (0.8)	9	0.6	5 (0.8)	7	0.9
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Cardiovascular disorder						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Hypertensive heart disease						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Cardiac valve disorders						
<65	2 (0.2)	2	0.1	1 (0.2)	2	0.3
>=65	0			0		
Aortic valve incompetence						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Aortic valve sclerosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Mitral valve incompetence						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Tricuspid valve incompetence						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Cardiac neoplasms						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Pericardial cyst						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Myocardial disorders						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	0			1 (2.1)	1	1.6
Left ventricular hypertrophy						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Cardiomegaly						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Cardiomyopathy						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Myocarditis						
<65	0			0		
>=65	0			1 (2.1)	1	1.6
Pericardial disorders						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Pericardial disease						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Reproductive system and breast disorders						
<65	94 (7.8)	120	7.7	32 (5.3)	39	5.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	2	(1.9)	2	1.4	0			
Menstrual cycle and uterine bleeding disorders								
<65	45	(3.8)	53	3.4	7	(1.2)	10	1.3
>=65	0				0			
Menstruation irregular								
<65	14	(1.2)	14	0.9	0			
>=65	0				0			
Menorrhagia								
<65	10	(0.8)	12	0.8	3	(0.5)	3	0.4
>=65	0				0			
Dysmenorrhoea								
<65	7	(0.6)	8	0.5	1	(0.2)	3	0.4
>=65	0				0			
Metrorrhagia								
<65	7	(0.6)	7	0.4	1	(0.2)	1	0.1
>=65	0				0			
Menstrual disorder								
<65	5	(0.4)	5	0.3	0			
>=65	0				0			
Dysfunctional uterine bleeding								
<65	3	(0.3)	3	0.2	0			
>=65	0				0			
Amenorrhoea								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Menstruation delayed								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Oligomenorrhoea						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Premenstrual syndrome						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Premenstrual pain						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Breast disorders						
<65	15 (1.3)	18	1.2	7 (1.2)	8	1.0
>=65	2 (1.9)	2	1.4	0		
Breast mass						
<65	7 (0.6)	7	0.4	1 (0.2)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Breast cyst						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Breast disorder						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Breast pain						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Fibrocystic breast disease						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	2 (0.2)	2	0.1	2 (0.3)	2	0.3
>=65	0			0		
Breast inflammation						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Nipple pain						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Breast fibrosis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Breast haematoma						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Uterine, pelvic and broad ligament disorders						
<65	11 (0.9)	11	0.7	2 (0.3)	2	0.3
>=65	0			0		
Uterine haemorrhage						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Adenomyosis						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Endometriosis						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Uterine polyp						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Uterine enlargement						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Vaginal prolapse						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Menopause related conditions						
<65	9 (0.8)	9	0.6	4 (0.7)	5	0.7
>=65	0			0		
Atrophic vulvovaginitis						
<65	4 (0.3)	4	0.3	2 (0.3)	2	0.3
>=65	0			0		
Menopausal symptoms						
<65	4 (0.3)	4	0.3	1 (0.2)	1	0.1
>=65	0			0		
Postmenopausal haemorrhage						
<65	1 (<0.1)	1	<0.1	1 (0.2)	2	0.3
>=65	0			0		
Ovarian and fallopian tube disorders						
<65	9 (0.8)	9	0.6	3 (0.5)	3	0.4
>=65	0			0		
Ovarian cyst						
<65	7 (0.6)	7	0.4	2 (0.3)	2	0.3
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hydrosalpinx						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Polycystic ovaries						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Vulvovaginal disorders (excl infections and inflammations)						
<65	9 (0.8)	9	0.6	5 (0.8)	5	0.7
>=65	0			0		
Vaginal haemorrhage						
<65	6 (0.5)	6	0.4	2 (0.3)	2	0.3
>=65	0			0		
Vulvovaginal discomfort						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Vulvovaginal dryness						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Vulvovaginal pain						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Vaginal polyp						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Vulvovaginal pruritus						
<65	0			1 (0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
>=65	0			0		
Reproductive tract disorders NEC						
<65	3	(0.3)	3 0.2	1	(0.2)	1 0.1
>=65	0			0		
Pelvic pain						
<65	2	(0.2)	2 0.1	0		
>=65	0			0		
Genital rash						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Genital pain						
<65	0			1	(0.2)	1 0.1
>=65	0			0		
Cervix disorders (excl infections and inflammations)						
<65	2	(0.2)	2 0.1	1	(0.2)	1 0.1
>=65	0			0		
Cervical dysplasia						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Cervical leukoplakia						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Uterine cervical erosion						
<65	0			1	(0.2)	1 0.1
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Sexual function and fertility disorders						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Dyspareunia						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Erectile dysfunction						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Testicular and epididymal disorders						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Testicular mass						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Testicular pain						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Testicular disorder						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Female reproductive tract infections and inflammations						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Uterine inflammation						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Prostatic disorders (excl infections and inflammations)						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Benign prostatic hyperplasia						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Penile and scrotal disorders (excl infections and inflammations)						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Scrotal pain						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Blood and lymphatic system disorders						
<65	28 (2.3)	29	1.9	15 (2.5)	20	2.6
>=65	7 (6.5)	8	5.6	1 (2.1)	1	1.6
Anaemias nonhaemolytic and marrow depression						
<65	17 (1.4)	18	1.2	10 (1.6)	11	1.4
>=65	7 (6.5)	7	4.9	0		
Anaemia						
<65	14 (1.2)	15	1.0	9 (1.5)	10	1.3
>=65	5 (4.6)	5	3.5	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Iron deficiency anaemia						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Blood loss anaemia						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Hypochromic anaemia						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Pernicious anaemia						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Pancytopenia						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Spleen, lymphatic and reticuloendothelial system disorders						
<65	6 (0.5)	6	0.4	3 (0.5)	4	0.5
>=65	1 (0.9)	1	0.7	0		
Lymphadenopathy						
<65	3 (0.3)	3	0.2	1 (0.2)	2	0.3
>=65	1 (0.9)	1	0.7	0		
Hypersplenism						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Splenic haemorrhage						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Splenomegaly								
<65	1	(<0.1)	1	<0.1	2	(0.3)	2	0.3
>=65	0				0			
White blood cell disorders								
<65	3	(0.3)	3	0.2	1	(0.2)	1	0.1
>=65	0				0			
Leukocytosis								
<65	2	(0.2)	2	0.1	1	(0.2)	1	0.1
>=65	0				0			
Eosinophilia								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Platelet disorders								
<65	1	(<0.1)	1	<0.1	3	(0.5)	3	0.4
>=65	0				1	(2.1)	1	1.6
Thrombocytopenia								
<65	1	(<0.1)	1	<0.1	3	(0.5)	3	0.4
>=65	0				1	(2.1)	1	1.6
Red blood cell disorders								
<65	1	(<0.1)	1	<0.1	1	(0.2)	1	0.1
>=65	0				0			
Polycythaemia								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Microcytosis								
<65	0				1	(0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
<65	41 (3.4)	45	2.9	22 (3.6)	22	2.9
>=65	5 (4.6)	7	4.9	3 (6.3)	5	7.9
Cutaneous neoplasms benign						
<65	8 (0.7)	10	0.6	4 (0.7)	4	0.5
>=65	2 (1.9)	4	2.8	2 (4.2)	2	3.2
Melanocytic naevus						
<65	5 (0.4)	5	0.3	2 (0.3)	2	0.3
>=65	2 (1.9)	3	2.1	0		
Acrochordon						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Seborrhoeic keratosis						
<65	2 (0.2)	2	0.1	0		
>=65	0			1 (2.1)	1	1.6
Dysplastic naevus						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Skin papilloma						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Pyogenic granuloma						
<65	0			0		
>=65	0			1 (2.1)	1	1.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Miscellaneous and site unspecified neoplasms malignant and unspecified								
<65	1	(<0.1)	1	<0.1	0			
>=65	1	(0.9)	1	0.7	0			
Squamous cell carcinoma								
<65	0				0			
>=65	1	(0.9)	1	0.7	0			
Neoplasm								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Reproductive neoplasms male malignant and unspecified								
<65	0				0			
>=65	1	(0.9)	1	0.7	0			
Prostate cancer								
<65	0				0			
>=65	1	(0.9)	1	0.7	0			
Soft tissue neoplasms malignant and unspecified								
<65	0				0			
>=65	1	(0.9)	1	0.7	0			
Dermatofibrosarcoma protuberans								
<65	0				0			
>=65	1	(0.9)	1	0.7	0			
Reproductive neoplasms female benign								
<65	6	(0.5)	6	0.4	4	(0.7)	4	0.5
>=65	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Uterine leiomyoma						
<65	5 (0.4)	5	0.3	4 (0.7)	4	0.5
>=65	0			0		
Ovarian adenoma						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Soft tissue neoplasms benign						
<65	5 (0.4)	5	0.3	1 (0.2)	1	0.1
>=65	0			1 (2.1)	1	1.6
Lipoma						
<65	4 (0.3)	4	0.3	1 (0.2)	1	0.1
>=65	0			1 (2.1)	1	1.6
Leiomyoma						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Breast neoplasms malignant and unspecified (incl nipple)						
<65	4 (0.3)	4	0.3	3 (0.5)	3	0.4
>=65	0			0		
Intraductal proliferative breast lesion						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Breast cancer						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Invasive ductal breast carcinoma						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Lobular breast carcinoma in situ								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Phyllodes tumour								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Skin neoplasms malignant and unspecified								
<65	4	(0.3)	4	0.3	3	(0.5)	3	0.4
>=65	0				0			
Basal cell carcinoma								
<65	3	(0.3)	3	0.2	1	(0.2)	1	0.1
>=65	0				0			
Malignant melanoma								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Malignant melanoma in situ								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Neoplasm skin								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Gastrointestinal neoplasms benign								
<65	3	(0.3)	3	0.2	0			
>=65	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Colon adenoma						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Breast neoplasms benign (incl nipple)						
<65	2 (0.2)	2	0.1	2 (0.3)	2	0.3
>=65	0			0		
Benign breast neoplasm						
<65	2 (0.2)	2	0.1	2 (0.3)	2	0.3
>=65	0			0		
Endocrine neoplasms benign						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Benign neoplasm of thyroid gland						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Parathyroid tumour benign						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Hepatic and biliary neoplasms benign						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Haemangioma of liver						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Endocrine neoplasms malignant and unspecified						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Papillary thyroid cancer								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Gastrointestinal neoplasms malignant and unspecified								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Gastrointestinal stromal tumour								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Hepatobiliary neoplasms malignant and unspecified								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Hepatic neoplasm								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Miscellaneous and site unspecified neoplasms benign								
<65	1	(<0.1)	1	<0.1	1	(0.2)	1	0.1
>=65	0				0			
Fibroma								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Adenoma benign								
<65	0				1	(0.2)	1	0.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Reproductive neoplasms female malignant and unspecified								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Cervix carcinoma stage 0								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Skeletal neoplasms benign								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Haemangioma of bone								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Leukaemias								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Hairy cell leukaemia								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Nervous system neoplasms malignant and unspecified NEC								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Glioblastoma								
<65	0				1	(0.2)	1	0.1
>=65	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Ocular neoplasms						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Eyelid haemangioma						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Plasma cell neoplasms						
<65	0			0		
>=65	0			1 (2.1)	1	1.6
Paraproteinaemia						
<65	0			0		
>=65	0			1 (2.1)	1	1.6
Renal and urinary tract neoplasms benign						
<65	0			0		
>=65	0			1 (2.1)	1	1.6
Kidney angiomyolipoma						
<65	0			0		
>=65	0			1 (2.1)	1	1.6
Renal and urinary tract neoplasms malignant and unspecified						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Urinary tract neoplasm						
<65	0			1 (0.2)	1	0.1
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Renal and urinary disorders						
<65	36 (3.0)	44	2.8	19 (3.1)	20	2.6
>=65	5 (4.6)	7	4.9	3 (6.3)	4	6.3
Urinary tract signs and symptoms						
<65	21 (1.8)	24	1.5	8 (1.3)	9	1.2
>=65	5 (4.6)	5	3.5	0		
Dysuria						
<65	8 (0.7)	10	0.6	0		
>=65	1 (0.9)	1	0.7	0		
Chromaturia						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Pollakiuria						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Bladder pain						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Urine odour abnormal						
<65	0			1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Haematuria						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Renal pain						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Stress urinary incontinence						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Micturition urgency						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Nocturia						
<65	1 (<0.1)	1	<0.1	2 (0.3)	2	0.3
>=65	0			0		
Renal colic						
<65	1 (<0.1)	2	0.1	0		
>=65	0			0		
Urine flow decreased						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Polyuria						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Urinary incontinence						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Urinary retention						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Renal disorders (excl nephropathies)						
<65	6 (0.5)	7	0.4	4 (0.7)	4	0.5
>=65	1 (0.9)	2	1.4	3 (6.3)	4	6.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Acute kidney injury						
<65	2 (0.2)	2	0.1	0		
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Chronic kidney disease						
<65	0			0		
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Renal cyst						
<65	2 (0.2)	2	0.1	3 (0.5)	3	0.4
>=65	0			1 (2.1)	1	1.6
Hydronephrosis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Nephrectasia						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Renal impairment						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Hypertensive nephropathy						
<65	0			0		
>=65	0			1 (2.1)	1	1.6
Urolithiases						
<65	11 (0.9)	12	0.8	6 (1.0)	6	0.8
>=65	0			0		
Nephrolithiasis						
<65	8 (0.7)	8	0.5	6 (1.0)	6	0.8
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Calculus urinary						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Ureterolithiasis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Bladder and bladder neck disorders (excl calculi)						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Cystitis noninfective						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Urethral disorders (excl calculi)						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Urethritis noninfective						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Ear and labyrinth disorders						
<65	41 (3.4)	52	3.3	20 (3.3)	25	3.3
>=65	4 (3.7)	4	2.8	4 (8.3)	4	6.3
Aural disorders NEC						
<65	12 (1.0)	13	0.8	2 (0.3)	2	0.3
>=65	3 (2.8)	3	2.1	0		
Ear pain						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	10 (0.8)	11	0.7	2 (0.3)	2	0.3
>=65	2 (1.9)	2	1.4	0		
Ear discomfort						
<65	1 (<0.1)	1	<0.1	0		
>=65	1 (0.9)	1	0.7	0		
Ear congestion						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Inner ear and VIIIth cranial nerve disorders						
<65	21 (1.8)	25	1.6	14 (2.3)	18	2.3
>=65	1 (0.9)	1	0.7	4 (8.3)	4	6.3
Vertigo						
<65	16 (1.3)	16	1.0	9 (1.5)	10	1.3
>=65	1 (0.9)	1	0.7	3 (6.3)	3	4.7
Tinnitus						
<65	3 (0.3)	4	0.3	2 (0.3)	3	0.4
>=65	0			0		
Vertigo positional						
<65	3 (0.3)	4	0.3	2 (0.3)	3	0.4
>=65	0			1 (2.1)	1	1.6
Meniere's disease						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Motion sickness						
<65	0			1 (0.2)	2	0.3
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Middle ear disorders (excl congenital)						
<65	6 (0.5)	7	0.4	2 (0.3)	2	0.3
>=65	0			0		
Eustachian tube dysfunction						
<65	4 (0.3)	5	0.3	1 (0.2)	1	0.1
>=65	0			0		
Eustachian tube disorder						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Tympanic membrane disorder						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Hearing disorders						
<65	4 (0.3)	4	0.3	2 (0.3)	2	0.3
>=65	0			0		
Deafness neurosensory						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Hypoacusis						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Sudden hearing loss						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Deafness						
<65	0			1 (0.2)	1	0.1
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hyperacusis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
External ear disorders (excl congenital)						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Cerumen impaction						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Excessive cerumen production						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Immune system disorders						
<65	26 (2.2)	26	1.7	20 (3.3)	22	2.9
>=65	2 (1.9)	2	1.4	1 (2.1)	1	1.6
Allergic conditions						
<65	25 (2.1)	25	1.6	20 (3.3)	22	2.9
>=65	2 (1.9)	2	1.4	1 (2.1)	1	1.6
Seasonal allergy						
<65	14 (1.2)	14	0.9	13 (2.1)	13	1.7
>=65	1 (0.9)	1	0.7	1 (2.1)	1	1.6
Hypersensitivity						
<65	2 (0.2)	2	0.1	6 (1.0)	6	0.8
>=65	1 (0.9)	1	0.7	0		
Allergy to arthropod bite						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Drug hypersensitivity						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Food allergy						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Allergy to arthropod sting						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Rubber sensitivity						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Mite allergy						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Multiple allergies						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Immune disorders NEC						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Immunisation reaction						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Hepatobiliary disorders								
<65	44	(3.7)	56	3.6	12	(2.0)	12	1.6
>=65	0				1	(2.1)	2	3.2
Gallbladder disorders								
<65	31	(2.6)	38	2.4	4	(0.7)	4	0.5
>=65	0				1	(2.1)	1	1.6
Cholelithiasis								
<65	23	(1.9)	24	1.5	3	(0.5)	3	0.4
>=65	0				1	(2.1)	1	1.6
Cholecystitis								
<65	4	(0.3)	4	0.3	1	(0.2)	1	0.1
>=65	0				0			
Cholecystitis acute								
<65	4	(0.3)	4	0.3	0			
>=65	0				0			
Gallbladder disorder								
<65	3	(0.3)	3	0.2	0			
>=65	0				0			
Cholecystitis chronic								
<65	2	(0.2)	2	0.1	0			
>=65	0				0			
Biliary dyskinesia								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Hepatic and hepatobiliary disorders								
<65	13	(1.1)	16	1.0	8	(1.3)	8	1.0
>=65	0				1	(2.1)	1	1.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hepatic steatosis						
<65	6 (0.5)	6	0.4	6 (1.0)	6	0.8
>=65	0			1 (2.1)	1	1.6
Hepatic cyst						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Hepatic function abnormal						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Granulomatous liver disease						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Hepatic pain						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Hypertransaminasaemia						
<65	1 (<0.1)	3	0.2	0		
>=65	0			0		
Nonalcoholic fatty liver disease						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Portal vein thrombosis						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Bile duct disorders						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Bile duct stone						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Biliary colic						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Surgical and medical procedures						
<65	16 (1.3)	17	1.1	8 (1.3)	8	1.0
>=65	2 (1.9)	2	1.4	0		
Head and neck therapeutic procedures						
<65	5 (0.4)	5	0.3	1 (0.2)	1	0.1
>=65	1 (0.9)	1	0.7	0		
Dental implantation						
<65	0			0		
>=65	1 (0.9)	1	0.7	0		
Dental operation						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Tooth extraction						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Sinus operation						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Nervous system, skull and spine therapeutic procedures						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
<65	0			0		
>=65	1	(0.9)	1 0.7	0		
Intervertebral disc operation						
<65	0			0		
>=65	1	(0.9)	1 0.7	0		
Therapeutic procedures and supportive care NEC						
<65	4	(0.3)	4 0.3	1	(0.2)	1 0.1
>=65	0			0		
Polypectomy						
<65	2	(0.2)	2 0.1	1	(0.2)	1 0.1
>=65	0			0		
Cyst removal						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Spinal anaesthesia						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Skin and subcutaneous tissue therapeutic procedures						
<65	2	(0.2)	2 0.1	0		
>=65	0			0		
Acrochordon excision						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Skin neoplasm excision						
<65	1	(<0.1)	1 <0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=65	0				0			
Bone and joint therapeutic procedures								
<65	1	(<0.1)	1	<0.1	2	(0.3)	2	0.3
>=65	0				0			
Synovial cyst removal								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Bone prosthesis insertion								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Hip surgery								
<65	0				1	(0.2)	1	0.1
>=65	0				0			
Eye therapeutic procedures								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Glaucoma surgery								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Gastrointestinal therapeutic procedures								
<65	1	(<0.1)	1	<0.1	2	(0.3)	2	0.3
>=65	0				0			
Gastric bypass								
<65	1	(<0.1)	1	<0.1	1	(0.2)	1	0.1
>=65	0				0			
Abdominoplasty								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Hepatobiliary therapeutic procedures						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Cholecystectomy						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Obstetric and gynaecological therapeutic procedures						
<65	1 (<0.1)	1	<0.1	1 (0.2)	1	0.1
>=65	0			0		
Abortion induced						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Ovarian operation						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Soft tissue therapeutic procedures						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Lipoma excision						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Endocrine disorders						
<65	14 (1.2)	16	1.0	5 (0.8)	6	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			1 (2.1)	1	1.6
Thyroid gland disorders						
<65	13 (1.1)	15	1.0	5 (0.8)	5	0.7
>=65	0			1 (2.1)	1	1.6
Hypothyroidism						
<65	4 (0.3)	4	0.3	3 (0.5)	3	0.4
>=65	0			1 (2.1)	1	1.6
Goitre						
<65	3 (0.3)	3	0.2	0		
>=65	0			0		
Hyperthyroidism						
<65	3 (0.3)	4	0.3	0		
>=65	0			0		
Thyroid mass						
<65	3 (0.3)	3	0.2	1 (0.2)	1	0.1
>=65	0			0		
Thyroid cyst						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Primary hyperthyroidism						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Adrenal gland disorders						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		
Hyperadrenocorticism						
<65	1 (<0.1)	1	<0.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=65	0			0		
Endocrine disorders of gonadal function						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Hypogonadism						
<65	0			1 (0.2)	1	0.1
>=65	0			0		
Social circumstances						
<65	6 (0.5)	6	0.4	1 (0.2)	1	0.1
>=65	0			0		
Age related factors						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Menopause						
<65	2 (0.2)	2	0.1	0		
>=65	0			0		
Economic and housing issues						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Stress at work						
<65	2 (0.2)	2	0.1	1 (0.2)	1	0.1
>=65	0			0		
Family issues						
<65	1 (<0.1)	1	<0.1	0		
>=65	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
Family stress						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Lifestyle issues						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Bedridden						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Pregnancy, puerperium and perinatal conditions						
<65	5	(0.4)	5 0.3	0		
>=65	0			0		
Abortions and stillbirth						
<65	3	(0.3)	3 0.2	0		
>=65	0			0		
Abortion spontaneous						
<65	2	(0.2)	2 0.1	0		
>=65	0			0		
Abortion						
<65	1	(<0.1)	1 <0.1	0		
>=65	0			0		
Maternal complications of pregnancy						
<65	2	(0.2)	2 0.1	0		
>=65	0			0		
Ectopic pregnancy						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Morning sickness								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Congenital, familial and genetic disorders								
<65	4	(0.3)	4	0.3	0			
>=65	0				1	(2.1)	1	1.6
Metabolic and nutritional disorders congenital								
<65	3	(0.3)	3	0.2	0			
>=65	0				0			
Type V hyperlipidaemia								
<65	2	(0.2)	2	0.1	0			
>=65	0				0			
Gilbert's syndrome								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Musculoskeletal and connective tissue disorders congenital								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Carpus curvus								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Skin and subcutaneous tissue disorders congenital								
<65	0				0			
>=65	0				1	(2.1)	1	1.6
Dermoid cyst								
<65	0				0			
>=65	0				1	(2.1)	1	1.6
Product issues								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Device issues								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			
Device expulsion								
<65	1	(<0.1)	1	<0.1	0			
>=65	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

9 Adverse events by age at baseline - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
<65	319	420.5			315	422.2			317	422.6		
>=65	83	109.3			88	110.9			85	105.7		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Events												
<65	256	(80.3)	1449	344.6	270	(85.7)	1593	377.3	243	(76.7)	1098	259.8
>=65	73	(88.0)	410	375.3	83	(94.3)	604	544.7	66	(77.6)	290	274.4
Serious												
Yes												
<65	21	(6.6)	33	7.8	33	(10.5)	45	10.7	24	(7.6)	36	8.5
>=65	10	(12.0)	20	18.3	7	(8.0)	26	23.4	13	(15.3)	17	16.1
No												
<65	254	(79.6)	1416	336.7	269	(85.4)	1548	366.7	242	(76.3)	1062	251.3
>=65	72	(86.7)	390	356.9	83	(94.3)	578	521.2	65	(76.5)	273	258.3
Severity												
Severe												
<65	15	(4.7)	29	6.9	19	(6.0)	29	6.9	19	(6.0)	25	5.9
>=65	7	(8.4)	14	12.8	8	(9.1)	22	19.8	9	(10.6)	14	13.2
Moderate												
<65	105	(32.9)	230	54.7	129	(41.0)	378	89.5	88	(27.8)	197	46.6
>=65	30	(36.1)	85	77.8	44	(50.0)	130	117.2	30	(35.3)	67	63.4
Mild												
<65	241	(75.5)	1190	283.0	249	(79.0)	1186	280.9	222	(70.0)	876	207.3
>=65	65	(78.3)	311	284.6	79	(89.8)	452	407.6	57	(67.1)	209	197.7

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by age at baseline - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Relationship to trial product												
Missing												
<65	6	(1.9)	6	1.4	6	(1.9)	6	1.4	6	(1.9)	7	1.7
>=65	4	(4.8)	5	4.6	4	(4.5)	4	3.6	0			
Probable												
<65	110	(34.5)	295	70.2	129	(41.0)	355	84.1	51	(16.1)	84	19.9
>=65	23	(27.7)	49	44.8	40	(45.5)	101	91.1	11	(12.9)	16	15.1
Possible												
<65	114	(35.7)	299	71.1	144	(45.7)	381	90.3	73	(23.0)	135	31.9
>=65	39	(47.0)	108	98.8	38	(43.2)	153	138.0	20	(23.5)	35	33.1
Unlikely												
<65	229	(71.8)	849	201.9	226	(71.7)	851	201.6	226	(71.3)	872	206.3
>=65	67	(80.7)	248	227.0	75	(85.2)	346	312.0	63	(74.1)	239	226.1
Outcome												
Fatal												
<65	0				1	(0.3)	1	0.2	0			
>=65	0				0				1	(1.2)	1	0.9
Recovered												
<65	246	(77.1)	1169	278.0	255	(81.0)	1336	316.5	224	(70.7)	846	200.2
>=65	69	(83.1)	334	305.7	78	(88.6)	476	429.3	61	(71.8)	208	196.8
Recovering												
<65	15	(4.7)	28	6.7	13	(4.1)	22	5.2	13	(4.1)	15	3.5
>=65	4	(4.8)	4	3.7	4	(4.5)	4	3.6	4	(4.7)	4	3.8
Recovered With Sequelae												
<65	4	(1.3)	4	1.0	4	(1.3)	4	0.9	1	(0.3)	1	0.2
>=65	1	(1.2)	1	0.9	1	(1.1)	1	0.9	0			
Not Recovered												
<65	113	(35.4)	248	59.0	121	(38.4)	222	52.6	119	(37.5)	233	55.1

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by age at baseline - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Outcome									
Not Recovered									
>=65	34 (41.0)	71	65.0	42 (47.7)	123	110.9	37 (43.5)	77	72.8
Unknown									
<65	0			4 (1.3)	8	1.9	3 (0.9)	3	0.7
>=65	0			0			0		
Leading to									
Permanent treatment discontinuation									
<65	16 (5.0)	19	4.5	15 (4.8)	23	5.4	8 (2.5)	10	2.4
>=65	4 (4.8)	4	3.7	10 (11.4)	11	9.9	6 (7.1)	8	7.6
Temporary interruption of trial product									
<65	21 (6.6)	42	10.0	29 (9.2)	63	14.9	11 (3.5)	12	2.8
>=65	5 (6.0)	5	4.6	8 (9.1)	27	24.3	4 (4.7)	8	7.6
Dose reduction of trial product									
<65	15 (4.7)	25	5.9	24 (7.6)	49	11.6	2 (0.6)	2	0.5
>=65	3 (3.6)	3	2.7	11 (12.5)	17	15.3	1 (1.2)	1	0.9

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

10 Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
<65	319	420.5			315	422.2			317	422.6		
>=65	83	109.3			88	110.9			85	105.7		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Adverse events												
<65	256	(80.3)	1449	344.6	270	(85.7)	1593	377.3	243	(76.7)	1098	259.8
>=65	73	(88.0)	410	375.3	83	(94.3)	604	544.7	66	(77.6)	290	274.4
Gastrointestinal disorders												
<65	186	(58.3)	576	137.0	196	(62.2)	698	165.3	108	(34.1)	202	47.8
>=65	45	(54.2)	148	135.5	60	(68.2)	226	203.8	30	(35.3)	60	56.8
Gastrointestinal signs and symptoms												
<65	153	(48.0)	354	84.2	157	(49.8)	457	108.3	64	(20.2)	99	23.4
>=65	34	(41.0)	78	71.4	43	(48.9)	144	129.9	12	(14.1)	16	15.1
Nausea												
<65	106	(33.2)	165	39.2	108	(34.3)	201	47.6	32	(10.1)	39	9.2
>=65	23	(27.7)	33	30.2	28	(31.8)	48	43.3	5	(5.9)	6	5.7
Vomiting												
<65	45	(14.1)	73	17.4	70	(22.2)	128	30.3	10	(3.2)	11	2.6
>=65	9	(10.8)	20	18.3	18	(20.5)	60	54.1	1	(1.2)	1	0.9
Dyspepsia												
<65	22	(6.9)	22	5.2	19	(6.0)	22	5.2	5	(1.6)	5	1.2
>=65	5	(6.0)	5	4.6	6	(6.8)	8	7.2	0			
Abdominal distension												
<65	7	(2.2)	9	2.1	20	(6.3)	26	6.2	10	(3.2)	10	2.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	2 (2.4)	3	2.7	4 (4.5)	4	3.6	1 (1.2)	3	2.8
Eructation									
<65	7 (2.2)	11	2.6	12 (3.8)	16	3.8	0		
>=65	4 (4.8)	5	4.6	4 (4.5)	5	4.5	1 (1.2)	1	0.9
Abdominal pain upper									
<65	10 (3.1)	10	2.4	13 (4.1)	17	4.0	11 (3.5)	13	3.1
>=65	1 (1.2)	1	0.9	3 (3.4)	4	3.6	0		
Flatulence									
<65	17 (5.3)	21	5.0	13 (4.1)	18	4.3	5 (1.6)	7	1.7
>=65	4 (4.8)	4	3.7	3 (3.4)	3	2.7	2 (2.4)	2	1.9
Abdominal pain									
<65	14 (4.4)	17	4.0	9 (2.9)	11	2.6	4 (1.3)	4	0.9
>=65	3 (3.6)	3	2.7	4 (4.5)	4	3.6	1 (1.2)	1	0.9
Abdominal discomfort									
<65	13 (4.1)	15	3.6	10 (3.2)	10	2.4	5 (1.6)	5	1.2
>=65	2 (2.4)	2	1.8	3 (3.4)	5	4.5	2 (2.4)	2	1.9
Regurgitation									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			2 (2.3)	2	1.8	0		
Gastrointestinal sounds abnormal									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Abdominal pain lower									
<65	2 (0.6)	2	0.5	3 (1.0)	3	0.7	3 (0.9)	3	0.7
>=65	1 (1.2)	1	0.9	0			0		
Abnormal faeces									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Aerophagia									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Epigastric discomfort									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Gastrointestinal pain									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Abdominal rigidity									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Anal incontinence									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Breath odour									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Dysphagia									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			0			0		
Faeces discoloured									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Faeces soft									
<65	2 (0.6)	2	0.5	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Retching									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Gastrointestinal motility and defaecation conditions									
<65	97 (30.4)	186	44.2	103 (32.7)	174	41.2	52 (16.4)	72	17.0
>=65	28 (33.7)	57	52.2	40 (45.5)	65	58.6	18 (21.2)	29	27.4
Diarrhoea									
<65	70 (21.9)	125	29.7	65 (20.6)	108	25.6	36 (11.4)	48	11.4
>=65	19 (22.9)	33	30.2	21 (23.9)	33	29.8	12 (14.1)	18	17.0
Constipation									
<65	34 (10.7)	47	11.2	48 (15.2)	56	13.3	15 (4.7)	17	4.0
>=65	17 (20.5)	23	21.1	22 (25.0)	26	23.4	7 (8.2)	9	8.5
Gastrooesophageal reflux disease									
<65	12 (3.8)	13	3.1	6 (1.9)	7	1.7	6 (1.9)	6	1.4
>=65	1 (1.2)	1	0.9	6 (6.8)	6	5.4	1 (1.2)	1	0.9
Change of bowel habit									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			1 (1.2)	1	0.9
Gastrointestinal motility disorder									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Irritable bowel syndrome									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Gastrointestinal hypermotility									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Gastrooesophageal sphincter insufficiency									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Gastrointestinal conditions NEC									
<65	7 (2.2)	8	1.9	17 (5.4)	20	4.7	3 (0.9)	3	0.7
>=65	0			1 (1.1)	1	0.9	3 (3.5)	3	2.8
Hyperchlorhydria									
<65	5 (1.6)	6	1.4	11 (3.5)	14	3.3	2 (0.6)	2	0.5
>=65	0			0			0		
Gastrointestinal disorder									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			1 (1.1)	1	0.9	0		
Food poisoning									
<65	2 (0.6)	2	0.5	4 (1.3)	4	0.9	0		
>=65	0			0			0		
Barrett's oesophagus									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			1 (1.2)	1	0.9
Gastric disorder									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Gastrointestinal melanosis									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Dental and gingival conditions									
<65	8 (2.5)	9	2.1	6 (1.9)	7	1.7	5 (1.6)	5	1.2
>=65	0			4 (4.5)	4	3.6	2 (2.4)	2	1.9
Toothache									
<65	4 (1.3)	5	1.2	3 (1.0)	3	0.7	0		
>=65	0			2 (2.3)	2	1.8	2 (2.4)	2	1.9
Dental caries									
<65	2 (0.6)	2	0.5	3 (1.0)	3	0.7	5 (1.6)	5	1.2
>=65	0			1 (1.1)	1	0.9	0		
Gingival swelling									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			1 (1.1)	1	0.9	0		
Tooth deposit									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Periodontal disease									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Gastrointestinal inflammatory conditions									
<65	9 (2.8)	9	2.1	16 (5.1)	19	4.5	5 (1.6)	7	1.7
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Gastritis									
<65	6 (1.9)	6	1.4	10 (3.2)	12	2.8	3 (0.9)	5	1.2
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Enteritis									
<65	0			3 (1.0)	3	0.7	1 (0.3)	1	0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Enterocolitis									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			0			0		
Chronic gastritis									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Duodenitis									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Colitis									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			0			0		
Gastrointestinal vascular conditions									
<65	1 (0.3)	2	0.5	5 (1.6)	5	1.2	1 (0.3)	1	0.2
>=65	2 (2.4)	3	2.7	4 (4.5)	4	3.6	1 (1.2)	1	0.9
Haemorrhoids									
<65	0			5 (1.6)	5	1.2	1 (0.3)	1	0.2
>=65	2 (2.4)	3	2.7	4 (4.5)	4	3.6	0		
Haemorrhoids thrombosed									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Varices oesophageal									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			1 (1.2)	1	0.9
Abdominal hernias and other abdominal wall conditions									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			2 (0.6)	2	0.5	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	3 (3.5)	3	2.8
Abdominal hernia									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Hiatus hernia									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Abdominal wall haematoma									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Umbilical hernia									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			1 (1.2)	1	0.9
Inguinal hernia									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Gastrointestinal haemorrhages NEC									
<65	2 (0.6)	2	0.5	3 (1.0)	3	0.7	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	1 (1.2)	1	0.9
Intra-abdominal haemorrhage									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Haematochezia									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			0		
Mallory-Weiss syndrome									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Upper gastrointestinal haemorrhage									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Intra-abdominal haematoma									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Rectal haemorrhage									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Salivary gland conditions									
<65	1 (0.3)	1	0.2	3 (1.0)	4	0.9	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	1 (1.2)	1	0.9
Dry mouth									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	1 (1.2)	1	0.9
Parotid gland enlargement									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Salivary hypersecretion									
<65	0			1 (0.3)	2	0.5	0		
>=65	0			0			0		
Noninfective sialoadenitis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Benign neoplasms gastrointestinal									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	3 (0.9)	3	0.7
>=65	4 (4.8)	5	4.6	1 (1.1)	1	0.9	1 (1.2)	1	0.9
Large intestine polyp									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	3 (3.6)	3	2.7	1 (1.1)	1	0.9	1 (1.2)	1	0.9
Gastric polyps									
<65	0			2 (0.6)	2	0.5	2 (0.6)	2	0.5
>=65	2 (2.4)	2	1.8	0			0		
Oral soft tissue conditions									
<65	0			1 (0.3)	1	0.2	3 (0.9)	3	0.7
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Stomatitis									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Mouth ulceration									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Aphthous ulcer									
<65	0			0			2 (0.6)	2	0.5
>=65	0			0			0		
Lip swelling									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Odynophagia									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gastrointestinal ulceration and perforation									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Gastritis erosive									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Diverticular perforation									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Gastric ulcer									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Anal and rectal conditions NEC									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Anal fissure									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Diverticular disorders									
<65	0			1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	2 (2.4)	2	1.8	0			1 (1.2)	1	0.9
Diverticulum intestinal									
<65	0			1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			0		
Diverticulum									
<65	0			0			2 (0.6)	2	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Exocrine pancreas conditions									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Pancreatitis acute									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Obstructive pancreatitis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Pancreatic cyst									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Gastrointestinal stenosis and obstruction									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Small intestinal obstruction									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Malabsorption conditions									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Malabsorption									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Peritoneal and retroperitoneal conditions									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Retroperitoneal mass									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Tongue conditions									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Glossodynia									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Infections and infestations									
<65	125 (39.2)	241	57.3	136 (43.2)	265	62.8	139 (43.8)	296	70.0
>=65	41 (49.4)	77	70.5	43 (48.9)	80	72.1	36 (42.4)	63	59.6
Infections - pathogen unspecified									
<65	108 (33.9)	193	45.9	122 (38.7)	221	52.4	117 (36.9)	230	54.4
>=65	38 (45.8)	57	52.2	40 (45.5)	68	61.3	30 (35.3)	51	48.2
Nasopharyngitis									
<65	34 (10.7)	49	11.7	54 (17.1)	95	22.5	52 (16.4)	82	19.4
>=65	13 (15.7)	20	18.3	14 (15.9)	20	18.0	7 (8.2)	10	9.5
Upper respiratory tract infection									
<65	25 (7.8)	39	9.3	28 (8.9)	32	7.6	24 (7.6)	34	8.0
>=65	12 (14.5)	15	13.7	14 (15.9)	16	14.4	14 (16.5)	16	15.1
Bronchitis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	8 (2.5)	9	2.1	10 (3.2)	12	2.8	11 (3.5)	13	3.1
>=65	2 (2.4)	2	1.8	4 (4.5)	4	3.6	2 (2.4)	2	1.9
Gastroenteritis									
<65	22 (6.9)	26	6.2	10 (3.2)	11	2.6	11 (3.5)	12	2.8
>=65	2 (2.4)	2	1.8	4 (4.5)	4	3.6	2 (2.4)	3	2.8
Sinusitis									
<65	6 (1.9)	6	1.4	11 (3.5)	16	3.8	8 (2.5)	10	2.4
>=65	0			3 (3.4)	3	2.7	3 (3.5)	3	2.8
Urinary tract infection									
<65	14 (4.4)	18	4.3	10 (3.2)	13	3.1	8 (2.5)	10	2.4
>=65	3 (3.6)	3	2.7	3 (3.4)	3	2.7	4 (4.7)	6	5.7
Cystitis									
<65	2 (0.6)	2	0.5	2 (0.6)	2	0.5	3 (0.9)	5	1.2
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	0		
Conjunctivitis									
<65	3 (0.9)	5	1.2	4 (1.3)	4	0.9	4 (1.3)	5	1.2
>=65	0			1 (1.1)	1	0.9	0		
Tooth infection									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	2 (2.4)	3	2.7	2 (2.3)	2	1.8	0		
Lower respiratory tract infection									
<65	3 (0.9)	3	0.7	2 (0.6)	2	0.5	4 (1.3)	4	0.9
>=65	0			1 (1.1)	1	0.9	2 (2.4)	2	1.9
Pharyngitis									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	6 (1.9)	6	1.4
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Localised infection									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Otitis externa									
<65	4 (1.3)	4	1.0	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Paronychia									
<65	2 (0.6)	2	0.5	4 (1.3)	4	0.9	2 (0.6)	2	0.5
>=65	0			0			0		
Pneumonia									
<65	1 (0.3)	1	0.2	4 (1.3)	5	1.2	4 (1.3)	4	0.9
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Tonsillitis									
<65	2 (0.6)	2	0.5	4 (1.3)	4	0.9	4 (1.3)	4	0.9
>=65	0			0			0		
Breast abscess									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Chronic sinusitis									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Implant site infection									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Mastitis									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Otitis media acute									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (0.3)	1	0.2	0			0		
>=65	0			1 (1.1)	1	0.9	0		
Periodontitis									
<65	1 (0.3)	1	0.2	0			1 (0.3)	2	0.5
>=65	0			1 (1.1)	1	0.9	0		
Respiratory tract infection									
<65	1 (0.3)	1	0.2	0			3 (0.9)	3	0.7
>=65	0			1 (1.1)	1	0.9	2 (2.4)	2	1.9
Tooth abscess									
<65	3 (0.9)	3	0.7	0			0		
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	1 (1.2)	2	1.9
Urosepsis									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Gastrointestinal infection									
<65	1 (0.3)	1	0.2	3 (1.0)	4	0.9	1 (0.3)	1	0.2
>=65	0			0			0		
Acute sinusitis									
<65	3 (0.9)	3	0.7	2 (0.6)	2	0.5	2 (0.6)	4	0.9
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Abscess									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Appendicitis									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Diverticulitis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Infected dermal cyst									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Kidney infection									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			1 (1.2)	1	0.9
Post procedural infection									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Rhinitis									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	4 (1.3)	4	0.9
>=65	0			0			0		
Skin infection									
<65	0			1 (0.3)	2	0.5	1 (0.3)	1	0.2
>=65	0			0			0		
Vulvovaginitis									
<65	1 (0.3)	1	0.2	1 (0.3)	2	0.5	0		
>=65	0			0			0		
Colonic abscess									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Ear infection									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Empyema									

Adverse events with onset prior to randomisation are not included.
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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Eye infection									
<65	1	(0.3)	1 0.2	0			0		
>=65	1	(1.2)	1 0.9	0			0		
Gingival abscess									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Gingivitis									
<65	0			0			3	(0.9)	3 0.7
>=65	0			0			0		
Hordeolum									
<65	1	(0.3)	1 0.2	0			1	(0.3)	1 0.2
>=65	0			0			0		
Joint abscess									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Labyrinthitis									
<65	1	(0.3)	1 0.2	0			0		
>=65	0			0			0		
Laryngitis									
<65	2	(0.6)	3 0.7	0			0		
>=65	1	(1.2)	1 0.9	0			0		
Mastoiditis									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Osteomyelitis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Otitis media									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Otitis media chronic									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Pericoronitis									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Postoperative wound infection									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Pulpitis dental									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Pyelonephritis acute									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Sepsis									
<65	2 (0.6)	2	0.5	0			0		
>=65	1 (1.2)	1	0.9	0			0		
Sialoadenitis									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Sinobronchitis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Subcutaneous abscess									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Tracheitis									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Tracheobronchitis									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Vaginal infection									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Wound infection									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Viral infectious disorders									
<65	26 (8.2)	32	7.6	29 (9.2)	33	7.8	29 (9.1)	35	8.3
>=65	9 (10.8)	9	8.2	7 (8.0)	8	7.2	7 (8.2)	7	6.6
Influenza									
<65	14 (4.4)	16	3.8	14 (4.4)	15	3.6	17 (5.4)	21	5.0
>=65	3 (3.6)	3	2.7	1 (1.1)	1	0.9	1 (1.2)	1	0.9
Herpes zoster									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	2 (0.6)	2	0.5
>=65	2 (2.4)	2	1.8	2 (2.3)	2	1.8	0		
Viral infection									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	3 (0.9)	3	0.7	2 (0.6)	3	0.7	2 (0.6)	3	0.7
>=65	0			2 (2.3)	2	1.8	1 (1.2)	1	0.9
Gastroenteritis viral									
<65	4 (1.3)	4	1.0	5 (1.6)	6	1.4	4 (1.3)	4	0.9
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	3 (3.5)	3	2.8
Herpes virus infection									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Oral herpes									
<65	2 (0.6)	3	0.7	0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Gastroenteritis norovirus									
<65	0			1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			0		
Herpes simplex									
<65	0			1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			0		
Ophthalmic herpes zoster									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Pneumonia influenzal									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Respiratory tract infection viral									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	0			0		
Viral diarrhoea									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Viral pharyngitis									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Chikungunya virus infection									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Ear infection viral									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Rhinovirus infection									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Viral upper respiratory tract infection									
<65	3 (0.9)	4	1.0	0			1 (0.3)	1	0.2
>=65	0			0			0		
Bacterial infectious disorders									
<65	4 (1.3)	4	1.0	5 (1.6)	5	1.2	10 (3.2)	15	3.5
>=65	6 (7.2)	9	8.2	3 (3.4)	3	2.7	2 (2.4)	3	2.8
Cellulitis									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	4 (1.3)	5	1.2
>=65	3 (3.6)	4	3.7	1 (1.1)	1	0.9	0		
Furuncle									
<65	0			0			2 (0.6)	2	0.5
>=65	0			1 (1.1)	1	0.9	0		

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Staphylococcal infection									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	1 (1.2)	2	1.9
Bacterial vaginosis									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Breast cellulitis									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Ear infection bacterial									
<65	0			1 (0.3)	1	0.2	0		
>=65	1 (1.2)	3	2.7	0			0		
Pharyngitis streptococcal									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	3 (0.9)	4	0.9
>=65	0			0			0		
Clostridium difficile colitis									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Helicobacter gastritis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			1 (1.2)	1	0.9
Helicobacter infection									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			0		
Wound infection staphylococcal									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Fungal infectious disorders									
<65	12 (3.8)	12	2.9	6 (1.9)	6	1.4	13 (4.1)	15	3.5
>=65	2 (2.4)	2	1.8	1 (1.1)	1	0.9	2 (2.4)	2	1.9
Vulvovaginal candidiasis									
<65	1 (0.3)	1	0.2	0			3 (0.9)	4	0.9
>=65	0			1 (1.1)	1	0.9	0		
Onychomycosis									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	1 (0.3)	1	0.2
>=65	0			0			0		
Fungal infection									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Fungal skin infection									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Tinea pedis									
<65	0			1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	0			0			1 (1.2)	1	0.9
Vulvovaginal mycotic infection									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	3 (0.9)	3	0.7
>=65	1 (1.2)	1	0.9	0			0		
Balanitis candida									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Candida infection									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Dermatophytosis of nail									
<65	0			0			0		
>=65	0			0			1	(1.2)	1 0.9
Genital candidiasis									
<65	2	(0.6)	2 0.5	0			0		
>=65	0			0			0		
Genital infection fungal									
<65	1	(0.3)	1 0.2	0			0		
>=65	0			0			0		
Skin candida									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Tinea infection									
<65	1	(0.3)	1 0.2	0			2	(0.6)	2 0.5
>=65	0			0			0		
Tinea versicolour									
<65	1	(0.3)	1 0.2	0			0		
>=65	1	(1.2)	1 0.9	0			0		
Ectoparasitic disorders									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Acarodermatitis									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Musculoskeletal and connective tissue disorders									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	82 (25.7)	126	30.0	68 (21.6)	99	23.5	60 (18.9)	92	21.8
>=65	17 (20.5)	21	19.2	30 (34.1)	52	46.9	24 (28.2)	34	32.2
Musculoskeletal and connective tissue disorders NEC									
<65	49 (15.4)	57	13.6	39 (12.4)	46	10.9	24 (7.6)	28	6.6
>=65	8 (9.6)	9	8.2	17 (19.3)	20	18.0	9 (10.6)	10	9.5
Back pain									
<65	27 (8.5)	29	6.9	19 (6.0)	21	5.0	10 (3.2)	11	2.6
>=65	1 (1.2)	1	0.9	8 (9.1)	9	8.1	4 (4.7)	4	3.8
Pain in extremity									
<65	9 (2.8)	9	2.1	10 (3.2)	10	2.4	8 (2.5)	8	1.9
>=65	3 (3.6)	3	2.7	6 (6.8)	6	5.4	2 (2.4)	2	1.9
Neck pain									
<65	1 (0.3)	1	0.2	6 (1.9)	6	1.4	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	1 (1.2)	1	0.9
Musculoskeletal pain									
<65	8 (2.5)	8	1.9	7 (2.2)	7	1.7	3 (0.9)	3	0.7
>=65	0			0			3 (3.5)	3	2.8
Muscle contracture									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Neck mass									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Rheumatic disorder									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Flank pain									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			0		
Musculoskeletal chest pain									
<65	4 (1.3)	5	1.2	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			0		
Axillary mass									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Limb mass									
<65	0			0			0		
>=65	1 (1.2)	2	1.8	0			0		
Musculoskeletal discomfort									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Musculoskeletal stiffness									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Plantar fasciitis									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			0			0		
Joint disorders									
<65	33 (10.3)	40	9.5	31 (9.8)	37	8.8	29 (9.1)	37	8.8
>=65	5 (6.0)	6	5.5	13 (14.8)	20	18.0	12 (14.1)	12	11.4
Arthralgia									
<65	22 (6.9)	25	5.9	15 (4.8)	16	3.8	13 (4.1)	13	3.1
>=65	2 (2.4)	2	1.8	8 (9.1)	13	11.7	7 (8.2)	7	6.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Osteoarthritis									
<65	1 (0.3)	1	0.2	9 (2.9)	11	2.6	9 (2.8)	10	2.4
>=65	1 (1.2)	1	0.9	2 (2.3)	3	2.7	3 (3.5)	3	2.8
Rotator cuff syndrome									
<65	4 (1.3)	5	1.2	1 (0.3)	1	0.2	0		
>=65	1 (1.2)	2	1.8	2 (2.3)	3	2.7	0		
Spinal osteoarthritis									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	6 (1.9)	6	1.4
>=65	0			1 (1.1)	1	0.9	0		
Periarthritis									
<65	3 (0.9)	3	0.7	3 (1.0)	5	1.2	1 (0.3)	1	0.2
>=65	0			0			0		
Arthritis									
<65	2 (0.6)	2	0.5	2 (0.6)	2	0.5	0		
>=65	0			0			1 (1.2)	1	0.9
Joint swelling									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Arthritis climacteric									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Arthropathy									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Femoroacetabular impingement									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gouty arthritis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Joint effusion									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Neuropathic arthropathy									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Psoriatic arthropathy									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Rheumatoid arthritis									
<65	0			0			1 (0.3)	2	0.5
>=65	0			0			0		
Sacroiliitis									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Muscle disorders									
<65	9 (2.8)	13	3.1	7 (2.2)	9	2.1	3 (0.9)	3	0.7
>=65	3 (3.6)	3	2.7	3 (3.4)	3	2.7	5 (5.9)	6	5.7
Muscle spasms									
<65	5 (1.6)	6	1.4	2 (0.6)	2	0.5	0		
>=65	2 (2.4)	2	1.8	3 (3.4)	3	2.7	2 (2.4)	2	1.9
Myalgia									
<65	5 (1.6)	7	1.7	5 (1.6)	7	1.7	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	0			2 (2.4)	3	2.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Diastasis recti abdominis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Muscular weakness									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Tendon, ligament and cartilage disorders									
<65	6 (1.9)	6	1.4	1 (0.3)	1	0.2	8 (2.5)	9	2.1
>=65	0			4 (4.5)	4	3.6	1 (1.2)	1	0.9
Trigger finger									
<65	0			0			2 (0.6)	2	0.5
>=65	0			2 (2.3)	2	1.8	0		
Tendon disorder									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Tendonitis									
<65	1 (0.3)	1	0.2	0			5 (1.6)	5	1.2
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Osteochondrosis									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Costochondritis									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Ligament calcification									
<65	1 (0.3)	1	0.2	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Meniscal degeneration									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Tendon pain									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Synovial and bursal disorders									
<65	2 (0.6)	2	0.5	2 (0.6)	2	0.5	3 (0.9)	3	0.7
>=65	0			2 (2.3)	2	1.8	2 (2.4)	3	2.8
Bursitis									
<65	2 (0.6)	2	0.5	2 (0.6)	2	0.5	3 (0.9)	3	0.7
>=65	0			2 (2.3)	2	1.8	2 (2.4)	3	2.8
Bone disorders (excl congenital and fractures)									
<65	5 (1.6)	5	1.2	1 (0.3)	1	0.2	4 (1.3)	4	0.9
>=65	1 (1.2)	1	0.9	2 (2.3)	3	2.7	0		
Bone lesion									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Osteopenia									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			1 (1.1)	1	0.9	0		
Osteoporosis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Exostosis									

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	0			0		
Bone pain									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Metatarsalgia									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Osteitis									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)									
<65	3 (0.9)	3	0.7	3 (1.0)	3	0.7	7 (2.2)	8	1.9
>=65	2 (2.4)	2	1.8	0			1 (1.2)	1	0.9
Intervertebral disc protrusion									
<65	1 (0.3)	1	0.2	3 (1.0)	3	0.7	2 (0.6)	2	0.5
>=65	0			0			1 (1.2)	1	0.9
Foot deformity									
<65	0			0			1 (0.3)	2	0.5
>=65	1 (1.2)	1	0.9	0			0		
Intervertebral disc degeneration									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Scoliosis									
<65	1 (0.3)	1	0.2	0			2 (0.6)	2	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Spinal flattening									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Spondylolisthesis									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Connective tissue disorders (excl congenital)									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Polymyalgia rheumatica									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Nervous system disorders									
<65	48 (15.0)	78	18.5	55 (17.5)	75	17.8	51 (16.1)	76	18.0
>=65	15 (18.1)	27	24.7	27 (30.7)	43	38.8	12 (14.1)	16	15.1
Neurological disorders NEC									
<65	17 (5.3)	20	4.8	22 (7.0)	25	5.9	24 (7.6)	29	6.9
>=65	11 (13.3)	13	11.9	14 (15.9)	21	18.9	7 (8.2)	9	8.5
Dizziness									
<65	11 (3.4)	13	3.1	10 (3.2)	11	2.6	10 (3.2)	10	2.4
>=65	7 (8.4)	8	7.3	9 (10.2)	9	8.1	3 (3.5)	5	4.7
Dysgeusia									
<65	0			2 (0.6)	2	0.5	1 (0.3)	1	0.2
>=65	0			2 (2.3)	6	5.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Paraesthesia									
<65	2 (0.6)	2	0.5	4 (1.3)	4	0.9	5 (1.6)	6	1.4
>=65	0			1 (1.1)	3	2.7	1 (1.2)	1	0.9
Hypoaesthesia									
<65	0			2 (0.6)	2	0.5	2 (0.6)	2	0.5
>=65	0			1 (1.1)	1	0.9	0		
Hyperaesthesia									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			1 (1.1)	1	0.9	0		
Somnolence									
<65	0			1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	0			1 (1.1)	1	0.9	0		
Dizziness postural									
<65	0			2 (0.6)	2	0.5	0		
>=65	1 (1.2)	2	1.8	0			0		
Syncope									
<65	0			2 (0.6)	2	0.5	0		
>=65	2 (2.4)	2	1.8	0			1 (1.2)	1	0.9
Ageusia									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Aphasia									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Coordination abnormal									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Dysaesthesia									
<65	1	(0.3)	1 0.2	0			0		
>=65	0			0			0		
Head discomfort									
<65	1	(0.3)	1 0.2	0			0		
>=65	0			0			0		
Hypogeusia									
<65	1	(0.3)	1 0.2	0			0		
>=65	0			0			0		
Lethargy									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			1	(1.2)	1 0.9
Loss of consciousness									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Neuralgia									
<65	0			0			2	(0.6)	2 0.5
>=65	0			0			0		
Phantom limb syndrome									
<65	1	(0.3)	1 0.2	0			0		
>=65	0			0			0		
Presyncope									
<65	0			0			2	(0.6)	2 0.5
>=65	0			0			0		
Restless legs syndrome									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Headaches									
<65	30 (9.4)	48	11.4	24 (7.6)	31	7.3	21 (6.6)	29	6.9
>=65	6 (7.2)	8	7.3	13 (14.8)	15	13.5	3 (3.5)	3	2.8
Headache									
<65	27 (8.5)	40	9.5	20 (6.3)	27	6.4	17 (5.4)	24	5.7
>=65	6 (7.2)	8	7.3	11 (12.5)	13	11.7	3 (3.5)	3	2.8
Migraine									
<65	2 (0.6)	2	0.5	2 (0.6)	2	0.5	0		
>=65	0			1 (1.1)	1	0.9	0		
Migraine with aura									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Tension headache									
<65	4 (1.3)	4	1.0	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	0			0			0		
Occipital neuralgia									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Sinus headache									
<65	1 (0.3)	2	0.5	0			1 (0.3)	1	0.2
>=65	0			0			0		
Central nervous system vascular disorders									
<65	0			6 (1.9)	8	1.9	1 (0.3)	2	0.5
>=65	2 (2.4)	2	1.8	2 (2.3)	3	2.7	1 (1.2)	1	0.9
Carotid artery stenosis									
<65	0			1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Spinal epidural haematoma									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Subarachnoid haemorrhage									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Carotid arteriosclerosis									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			0			0		
Cerebrovascular accident									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			0			1 (1.2)	1	0.9
Cerebral artery stenosis									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Cerebral artery thrombosis									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Cerebral infarction									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Ischaemic stroke									
<65	0			0			1 (0.3)	2	0.5
>=65	1 (1.2)	1	0.9	0			0		
Spinal cord and nerve root disorders									
<65	5 (1.6)	5	1.2	2 (0.6)	3	0.7	4 (1.3)	4	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			1 (1.1)	1	0.9	0		
Sciatica									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	0			1 (1.1)	1	0.9	0		
Radiculopathy									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Sacral radiculopathy									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Cervical radiculopathy									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Cervicobrachial syndrome									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Lumbar radiculopathy									
<65	1 (0.3)	1	0.2	0			2 (0.6)	2	0.5
>=65	0			0			0		
Peripheral neuropathies									
<65	4 (1.3)	5	1.2	4 (1.3)	4	0.9	7 (2.2)	8	1.9
>=65	2 (2.4)	2	1.8	0			0		
Carpal tunnel syndrome									
<65	2 (0.6)	3	0.7	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	0			0		
Diabetic neuropathy									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	2 (0.6)	2	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Meralgia paraesthetica									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Neuropathy peripheral									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	2 (0.6)	3	0.7
>=65	0			0			0		
Nerve compression									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Polyneuropathy									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Mental impairment disorders									
<65	0			0			2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	2 (2.4)	2	1.9
Memory impairment									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Amnesia									
<65	0			0			2 (0.6)	2	0.5
>=65	0			0			1 (1.2)	1	0.9
Dementia Alzheimer's type									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Vascular dementia									
<65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=65	1	(1.2)	1 0.9	0			0		
Sleep disturbances (incl subtypes)									
<65	0			0			0		
>=65	0			1	(1.1)	1 0.9	0		
Hypersomnia									
<65	0			0			0		
>=65	0			1	(1.1)	1 0.9	0		
Structural brain disorders									
<65	0			0			0		
>=65	0			1	(1.1)	1 0.9	0		
Cerebral ventricle dilatation									
<65	0			0			0		
>=65	0			1	(1.1)	1 0.9	0		
Cranial nerve disorders (excl neoplasms)									
<65	0			2	(0.6)	2 0.5	0		
>=65	0			0			0		
Anosmia									
<65	0			1	(0.3)	1 0.2	0		
>=65	0			0			0		
Facial paralysis									
<65	0			1	(0.3)	1 0.2	0		
>=65	0			0			0		
Encephalopathies									
<65	0			2	(0.6)	2 0.5	0		
>=65	0			0			0		
Hepatic encephalopathy									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<65	0			1	(0.3)	1 0.2	0		
>=65	0			0			0		
Hyponatraemic encephalopathy									
<65	0			1	(0.3)	1 0.2	0		
>=65	0			0			0		
Movement disorders (incl parkinsonism)									
<65	0			0			0		
>=65	1	(1.2)	1 0.9	0			0		
Tremor									
<65	0			0			0		
>=65	1	(1.2)	1 0.9	0			0		
Neurological disorders of the eye									
<65	0			0			2	(0.6)	2 0.5
>=65	0			0			0		
Visual field defect									
<65	0			0			2	(0.6)	2 0.5
>=65	0			0			0		
Seizures (incl subtypes)									
<65	0			0			0		
>=65	0			0			1	(1.2)	1 0.9
Partial seizures									
<65	0			0			0		
>=65	0			0			1	(1.2)	1 0.9
General disorders and administration site conditions									
<65	40	(12.5)	53 12.6	47	(14.9)	66 15.6	38	(12.0)	53 12.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	11 (13.3)	16	14.6	22 (25.0)	27	24.3	8 (9.4)	8	7.6
General system disorders NEC									
<65	32 (10.0)	41	9.7	39 (12.4)	49	11.6	20 (6.3)	22	5.2
>=65	8 (9.6)	11	10.1	18 (20.5)	19	17.1	8 (9.4)	8	7.6
Fatigue									
<65	14 (4.4)	18	4.3	19 (6.0)	20	4.7	3 (0.9)	3	0.7
>=65	5 (6.0)	8	7.3	9 (10.2)	9	8.1	1 (1.2)	1	0.9
Asthenia									
<65	3 (0.9)	3	0.7	4 (1.3)	5	1.2	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	3 (3.4)	3	2.7	0		
Influenza like illness									
<65	1 (0.3)	1	0.2	3 (1.0)	4	0.9	3 (0.9)	3	0.7
>=65	0			2 (2.3)	2	1.8	0		
Malaise									
<65	1 (0.3)	2	0.5	2 (0.6)	2	0.5	0		
>=65	0			2 (2.3)	2	1.8	1 (1.2)	1	0.9
Non-cardiac chest pain									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	0		
>=65	0			1 (1.1)	1	0.9	0		
Early satiety									
<65	3 (0.9)	3	0.7	4 (1.3)	4	0.9	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	0			0		
Chest discomfort									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			1 (1.1)	1	0.9	2 (2.4)	2	1.9
Thirst decreased									
<65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			1 (1.1)	1	0.9	0		
Pain									
<65	5 (1.6)	5	1.2	3 (1.0)	3	0.7	2 (0.6)	2	0.5
>=65	0			0			1 (1.2)	1	0.9
Oedema peripheral									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	3 (0.9)	3	0.7
>=65	0			0			1 (1.2)	1	0.9
Peripheral swelling									
<65	0			2 (0.6)	2	0.5	3 (0.9)	3	0.7
>=65	0			0			1 (1.2)	1	0.9
Chest pain									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	2 (0.6)	3	0.7
>=65	0			0			1 (1.2)	1	0.9
Face oedema									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Feeling cold									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Hunger									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Swelling									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Chills									
<65	1 (0.3)	1	0.2	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Discomfort									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Inflammation									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Polyp									
<65	1 (0.3)	2	0.5	0			0		
>=65	0			0			0		
Sensation of foreign body									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Thirst									
<65	1 (0.3)	1	0.2	0			0		
>=65	1 (1.2)	1	0.9	0			0		
Administration site reactions									
<65	5 (1.6)	5	1.2	9 (2.9)	14	3.3	10 (3.2)	18	4.3
>=65	1 (1.2)	2	1.8	4 (4.5)	5	4.5	0		
Injection site pain									
<65	3 (0.9)	3	0.7	6 (1.9)	7	1.7	3 (0.9)	7	1.7
>=65	1 (1.2)	1	0.9	1 (1.1)	2	1.8	0		
Injection site erythema									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			1 (1.1)	1	0.9	0		
Injection site bruising									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	5 (1.6)	6	1.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Implant site pain									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Injection site reaction									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			0			0		
Injection site mass									
<65	0			1 (0.3)	2	0.5	1 (0.3)	1	0.2
>=65	0			0			0		
Injection site discomfort									
<65	0			0			2 (0.6)	2	0.5
>=65	0			0			0		
Injection site haemorrhage									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Injection site urticaria									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Body temperature conditions									
<65	6 (1.9)	6	1.4	2 (0.6)	2	0.5	9 (2.8)	12	2.8
>=65	3 (3.6)	3	2.7	2 (2.3)	2	1.8	0		
Pyrexia									
<65	6 (1.9)	6	1.4	2 (0.6)	2	0.5	9 (2.8)	12	2.8
>=65	3 (3.6)	3	2.7	2 (2.3)	2	1.8	0		
Tissue disorders NEC									
<65	1 (0.3)	1	0.2	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			1 (1.1)	1	0.9	0		
Mass									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Nodule									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Therapeutic and nontherapeutic effects (excl toxicity)									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Drug intolerance									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Complications associated with device									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Complication associated with device									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Metabolism and nutrition disorders									
<65	35 (11.0)	49	11.7	40 (12.7)	45	10.7	47 (14.8)	55	13.0
>=65	13 (15.7)	19	17.4	16 (18.2)	21	18.9	6 (7.1)	6	5.7
Appetite and general nutritional disorders									
<65	22 (6.9)	30	7.1	30 (9.5)	34	8.1	14 (4.4)	16	3.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	10 (12.0)	10	9.2	11 (12.5)	12	10.8	2 (2.4)	2	1.9
Decreased appetite									
<65	21 (6.6)	26	6.2	27 (8.6)	29	6.9	13 (4.1)	15	3.5
>=65	8 (9.6)	8	7.3	11 (12.5)	12	10.8	2 (2.4)	2	1.9
Hyperphagia									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			0			0		
Increased appetite									
<65	3 (0.9)	4	1.0	1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			0		
Overweight									
<65	0			1 (0.3)	2	0.5	0		
>=65	0			0			0		
Cachexia									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Obesity									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Electrolyte and fluid balance conditions									
<65	2 (0.6)	2	0.5	3 (1.0)	3	0.7	3 (0.9)	3	0.7
>=65	4 (4.8)	5	4.6	4 (4.5)	4	3.6	0		
Dehydration									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	0		
Hypokalaemia									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			2 (0.6)	2	0.5	0		
>=65	2 (2.4)	3	2.7	1 (1.1)	1	0.9	0		
Hyponatraemia									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Hyperkalaemia									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Lipid metabolism disorders									
<65	4 (1.3)	4	1.0	3 (1.0)	3	0.7	9 (2.8)	9	2.1
>=65	0			2 (2.3)	2	1.8	0		
Hyperlipidaemia									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Hypertriglyceridaemia									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Dyslipidaemia									
<65	2 (0.6)	2	0.5	3 (1.0)	3	0.7	6 (1.9)	6	1.4
>=65	0			0			0		
Hypercholesterolaemia									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Purine and pyrimidine metabolism disorders									
<65	3 (0.9)	4	1.0	1 (0.3)	1	0.2	3 (0.9)	5	1.2
>=65	0			1 (1.1)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gout									
<65	3 (0.9)	4	1.0	1 (0.3)	1	0.2	2 (0.6)	4	0.9
>=65	0			1 (1.1)	1	0.9	0		
Hyperuricaemia									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Vitamin related disorders									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Vitamin B complex deficiency									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Folate deficiency									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Vitamin D deficiency									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Bone, calcium, magnesium and phosphorus metabolism disorders									
<65	2 (0.6)	2	0.5	0			4 (1.3)	4	0.9
>=65	2 (2.4)	2	1.8	1 (1.1)	1	0.9	0		
Hypomagnesaemia									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Hypercalcaemia									
<65	1 (0.3)	1	0.2	0			2 (0.6)	2	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	1 (1.2)	1	0.9	0			0		
Hypercalcitoninaemia									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Hypocalcaemia									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Acid-base disorders									
<65	0			1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			0		
Ketoacidosis									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Lactic acidosis									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Diabetic complications									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Diabetic ketoacidosis									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Diabetic metabolic decompensation									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Glucose metabolism disorders (incl diabetes mellitus)									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	3 (0.9)	4	1.0	1 (0.3)	1	0.2	16 (5.0)	16	3.8
>=65	0			0			4 (4.7)	4	3.8
Diabetes mellitus									
<65	0			1 (0.3)	1	0.2	3 (0.9)	3	0.7
>=65	0			0			3 (3.5)	3	2.8
Diabetes mellitus inadequate control									
<65	1 (0.3)	2	0.5	0			5 (1.6)	5	1.2
>=65	0			0			0		
Hyperglycaemia									
<65	1 (0.3)	1	0.2	0			4 (1.3)	4	0.9
>=65	0			0			1 (1.2)	1	0.9
Hyperinsulinaemia									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Hypoglycaemia									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Type 2 diabetes mellitus									
<65	0			0			3 (0.9)	3	0.7
>=65	0			0			0		
Iron and trace metal metabolism disorders									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Iron deficiency									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Metabolism disorders NEC									
<65	1 (0.3)	2	0.5	0			0		
>=65	0			0			0		
Hyperamylasaemia									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Hyperlipasaemia									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Respiratory, thoracic and mediastinal disorders									
<65	27 (8.5)	34	8.1	29 (9.2)	36	8.5	27 (8.5)	29	6.9
>=65	9 (10.8)	10	9.2	18 (20.5)	26	23.4	9 (10.6)	14	13.2
Respiratory disorders NEC									
<65	12 (3.8)	12	2.9	10 (3.2)	10	2.4	11 (3.5)	11	2.6
>=65	4 (4.8)	5	4.6	8 (9.1)	9	8.1	4 (4.7)	7	6.6
Cough									
<65	6 (1.9)	6	1.4	6 (1.9)	6	1.4	4 (1.3)	4	0.9
>=65	4 (4.8)	5	4.6	3 (3.4)	3	2.7	3 (3.5)	4	3.8
Productive cough									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			3 (3.4)	3	2.7	0		
Pulmonary mass									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	0		
>=65	0			1 (1.1)	1	0.9	0		
Respiratory disorder									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	3 (0.9)	3	0.7
>=65	0			1 (1.1)	1	0.9	0		
Acute respiratory failure									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			1 (1.1)	1	0.9	0		
Sleep apnoea syndrome									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	3 (0.9)	3	0.7
>=65	0			0			1 (1.2)	1	0.9
Dyspnoea									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			1 (1.2)	1	0.9
Hypoxia									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Respiratory tract signs and symptoms									
<65	10 (3.1)	10	2.4	13 (4.1)	13	3.1	6 (1.9)	6	1.4
>=65	3 (3.6)	3	2.7	6 (6.8)	6	5.4	3 (3.5)	3	2.8
Oropharyngeal pain									
<65	6 (1.9)	6	1.4	5 (1.6)	5	1.2	4 (1.3)	4	0.9
>=65	2 (2.4)	2	1.8	2 (2.3)	2	1.8	2 (2.4)	2	1.9
Dysphonia									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			1 (1.1)	1	0.9	0		
Rhinorrhoea									
<65	3 (0.9)	3	0.7	4 (1.3)	4	0.9	0		
>=65	0			0			0		
Dry throat									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Hiccups									
<65	1 (0.3)	1	0.2	0			0		
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Oropharyngeal discomfort									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Aphonia									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Painful respiration									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Upper respiratory tract congestion									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Nasal discomfort									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Upper-airway cough syndrome									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Upper respiratory tract disorders (excl infections)									
<65	4 (1.3)	5	1.2	7 (2.2)	8	1.9	6 (1.9)	6	1.4
>=65	2 (2.4)	2	1.8	3 (3.4)	4	3.6	2 (2.4)	3	2.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Epistaxis									
<65	0			2 (0.6)	3	0.7	4 (1.3)	4	0.9
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	1 (1.2)	1	0.9
Rhinitis allergic									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	0		
>=65	0			1 (1.1)	1	0.9	0		
Nasal congestion									
<65	2 (0.6)	3	0.7	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	1 (1.2)	2	1.9
Sinus congestion									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			0		
Bronchial disorders (excl neoplasms)									
<65	5 (1.6)	5	1.2	3 (1.0)	4	0.9	5 (1.6)	5	1.2
>=65	0			4 (4.5)	5	4.5	1 (1.2)	1	0.9
Asthma									
<65	3 (0.9)	3	0.7	2 (0.6)	3	0.7	2 (0.6)	2	0.5
>=65	0			3 (3.4)	3	2.7	1 (1.2)	1	0.9
Bronchospasm									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Chronic obstructive pulmonary disease									
<65	2 (0.6)	2	0.5	0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Childhood asthma									
<65	0			0			1 (0.3)	1	0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Lower respiratory tract disorders (excl obstruction and infection)									
<65	1 (0.3)	2	0.5	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Idiopathic interstitial pneumonia									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Atelectasis									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Emphysema									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Pleural disorders									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Pneumothorax									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Eye disorders									
<65	36 (11.3)	54	12.8	34 (10.8)	46	10.9	28 (8.8)	33	7.8
>=65	10 (12.0)	11	10.1	16 (18.2)	23	20.7	14 (16.5)	23	21.8
Retina, choroid and vitreous haemorrhages and vascular disorders									
<65	10 (3.1)	11	2.6	16 (5.1)	18	4.3	9 (2.8)	10	2.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	2 (2.4)	2	1.8	5 (5.7)	5	4.5	2 (2.4)	2	1.9
Diabetic retinopathy									
<65	9 (2.8)	10	2.4	11 (3.5)	12	2.8	9 (2.8)	10	2.4
>=65	2 (2.4)	2	1.8	4 (4.5)	4	3.6	2 (2.4)	2	1.9
Retinal haemorrhage									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			1 (1.1)	1	0.9	0		
Non-proliferative retinopathy									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			0			0		
Retinopathy hypertensive									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			0			0		
Retinal artery occlusion									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Retinopathy									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Anterior eye structural change, deposit and degeneration									
<65	6 (1.9)	6	1.4	3 (1.0)	3	0.7	5 (1.6)	6	1.4
>=65	2 (2.4)	2	1.8	6 (6.8)	8	7.2	7 (8.2)	9	8.5
Cataract									
<65	4 (1.3)	4	1.0	0			3 (0.9)	3	0.7
>=65	1 (1.2)	1	0.9	5 (5.7)	6	5.4	5 (5.9)	6	5.7
Narrow anterior chamber angle									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			0		
>=65	0			1 (1.1)	2	1.8	0		
Cataract cortical									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Cataract subcapsular									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Dermatochalasis									
<65	0			1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			2 (2.4)	2	1.9
Cataract nuclear									
<65	2 (0.6)	2	0.5	0			1 (0.3)	2	0.5
>=65	0			0			0		
Pinguecula									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Posterior capsule opacification									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Ocular structural change, deposit and degeneration NEC									
<65	9 (2.8)	11	2.6	3 (1.0)	3	0.7	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	3 (3.4)	3	2.7	2 (2.4)	3	2.8
Macular fibrosis									
<65	1 (0.3)	2	0.5	0			0		
>=65	0			1 (1.1)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Retinal depigmentation									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Vitreous detachment									
<65	1 (0.3)	2	0.5	0			0		
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Detachment of retinal pigment epithelium									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Optic disc disorder									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Retinal degeneration									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			1 (1.2)	1	0.9
Age-related macular degeneration									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			0			0		
Choroidal dystrophy									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Macular degeneration									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Optic atrophy									
<65	0			0			1 (0.3)	1	0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Retinal drusen									
<65	1 (0.3)	1	0.2	0			0		
>=65	1 (1.2)	1	0.9	0			0		
Vitreous floaters									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			0			1 (1.2)	1	0.9
Eye disorders NEC									
<65	7 (2.2)	7	1.7	6 (1.9)	6	1.4	3 (0.9)	3	0.7
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	4 (4.7)	4	3.8
Dry eye									
<65	3 (0.9)	3	0.7	4 (1.3)	4	0.9	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	3 (3.5)	3	2.8
Lacrimation increased									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Vitreous disorder									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Eyelid disorder									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Retinal disorder									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Ocular infections, irritations and inflammations									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	11 (3.4)	11	2.6	6 (1.9)	7	1.7	5 (1.6)	5	1.2
>=65	2 (2.4)	2	1.8	2 (2.3)	3	2.7	1 (1.2)	1	0.9
Blepharitis									
<65	3 (0.9)	3	0.7	1 (0.3)	2	0.5	1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Macular oedema									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			1 (1.1)	2	1.8	0		
Eyelid rash									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Keratitis									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Meibomian gland dysfunction									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Ocular hyperaemia									
<65	0			1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	0			0			0		
Conjunctivitis allergic									
<65	2 (0.6)	2	0.5	0			0		
>=65	1 (1.2)	1	0.9	0			0		
Episcleritis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Eye pruritus									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Punctate keratitis									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			0			0		
Swelling of eyelid									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Uveitis									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Vision disorders									
<65	7 (2.2)	7	1.7	5 (1.6)	5	1.2	6 (1.9)	6	1.4
>=65	1 (1.2)	1	0.9	0			2 (2.4)	2	1.9
Vision blurred									
<65	3 (0.9)	3	0.7	3 (1.0)	3	0.7	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Myopia									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Visual impairment									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			1 (1.2)	1	0.9
Astigmatism									
<65	0			0			3 (0.9)	3	0.7
>=65	0			0			0		
Hypermetropia									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Pathologic myopia									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Presbyopia									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			0			0		
Ocular haemorrhages and vascular disorders NEC									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	1 (1.2)	1	0.9
Eye haemorrhage									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Conjunctival haemorrhage									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			1 (1.2)	1	0.9
Optic disc haemorrhage									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Ocular neuromuscular disorders									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Eyelid ptosis									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Glaucoma and ocular hypertension									
<65	0			2 (0.6)	3	0.7	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Glaucoma									
<65	0			2 (0.6)	3	0.7	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Ocular sensory symptoms NEC									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Asthenopia									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Injury, poisoning and procedural complications									
<65	38 (11.9)	52	12.4	36 (11.4)	44	10.4	45 (14.2)	57	13.5
>=65	13 (15.7)	19	17.4	12 (13.6)	24	21.6	4 (4.7)	4	3.8
Injuries NEC									
<65	25 (7.8)	34	8.1	23 (7.3)	26	6.2	34 (10.7)	38	9.0
>=65	12 (14.5)	15	13.7	9 (10.2)	13	11.7	2 (2.4)	2	1.9
Muscle strain									
<65	3 (0.9)	3	0.7	6 (1.9)	6	1.4	1 (0.3)	1	0.2
>=65	2 (2.4)	2	1.8	2 (2.3)	2	1.8	0		
Fall									
<65	3 (0.9)	3	0.7	3 (1.0)	4	0.9	2 (0.6)	3	0.7
>=65	5 (6.0)	5	4.6	2 (2.3)	2	1.8	0		
Ligament sprain									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	5 (1.6)	7	1.7	2 (0.6)	2	0.5	6 (1.9)	6	1.4
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Skin laceration									
<65	2 (0.6)	2	0.5	2 (0.6)	2	0.5	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Contusion									
<65	0			1 (0.3)	1	0.2	8 (2.5)	9	2.1
>=65	0			1 (1.1)	2	1.8	0		
Arthropod sting									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Face injury									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Head injury									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Road traffic accident									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Traumatic haemothorax									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Limb injury									
<65	3 (0.9)	3	0.7	3 (1.0)	3	0.7	0		
>=65	0			0			0		
Bone contusion									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			2 (0.6)	2	0.5	1 (0.3)	1	0.2
>=65	0			0			0		
Animal bite									
<65	0			1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	0			0			0		
Epicondylitis									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Muscle injury									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Post-traumatic pain									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Skin abrasion									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Tooth fracture									
<65	3 (0.9)	3	0.7	1 (0.3)	1	0.2	3 (0.9)	3	0.7
>=65	1 (1.2)	1	0.9	0			0		
Abdominal injury									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Arthropod bite									
<65	0			0			1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			0		
Chest injury									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Craniocerebral injury									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Foreign body in eye									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Injury corneal									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Ligament rupture									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			0			0		
Muscle rupture									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Post-traumatic neck syndrome									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Soft tissue injury									
<65	4 (1.3)	4	1.0	0			0		
>=65	1 (1.2)	1	0.9	0			0		
Spinal column injury									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Subdural haematoma									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Tendon injury									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Tendon rupture									
<65	0			0			1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			0		
Wound									
<65	0			0			2 (0.6)	2	0.5
>=65	0			0			1 (1.2)	1	0.9
Bone and joint injuries									
<65	6 (1.9)	7	1.7	11 (3.5)	12	2.8	11 (3.5)	11	2.6
>=65	2 (2.4)	2	1.8	3 (3.4)	7	6.3	2 (2.4)	2	1.9
Rib fracture									
<65	0			3 (1.0)	3	0.7	0		
>=65	0			1 (1.1)	1	0.9	0		
Foot fracture									
<65	0			4 (1.3)	4	0.9	3 (0.9)	3	0.7
>=65	0			0			0		
Cervical vertebral fracture									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Joint injury									
<65	1 (0.3)	1	0.2	0			4 (1.3)	4	0.9
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Radius fracture									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
<65	0				0				0			
>=65	0				1	(1.1)	1	0.9	0			
Spinal compression fracture												
<65	0				0				0			
>=65	0				1	(1.1)	1	0.9	0			
Thoracic vertebral fracture												
<65	0				0				0			
>=65	0				1	(1.1)	1	0.9	0			
Upper limb fracture												
<65	0				0				0			
>=65	0				1	(1.1)	1	0.9	0			
Humerus fracture												
<65	0				2	(0.6)	2	0.5	0			
>=65	1	(1.2)	1	0.9	0				0			
Meniscus injury												
<65	0				1	(0.3)	1	0.2	0			
>=65	0				0				1	(1.2)	1	0.9
Stress fracture												
<65	1	(0.3)	1	0.2	1	(0.3)	1	0.2	0			
>=65	0				0				0			
Wrist fracture												
<65	0				1	(0.3)	1	0.2	0			
>=65	0				0				0			
Ankle fracture												
<65	1	(0.3)	1	0.2	0				0			
>=65	0				0				0			
Bone fissure												

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Cartilage injury									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Hand fracture									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Hip fracture									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Joint dislocation									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Lisfranc fracture									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Spinal fracture									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Sternal fracture									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Procedural related injuries and complications NEC									
<65	1 (0.3)	1	0.2	3 (1.0)	3	0.7	5 (1.6)	5	1.2
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Post procedural haemorrhage									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			1 (1.1)	1	0.9	0		
Graft complication									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Anaemia postoperative									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Procedural pain									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			0		
Dental restoration failure									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Incision site pain									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Post procedural complication									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Surgical skin tear									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Injuries by physical agents									
<65	2 (0.6)	2	0.5	2 (0.6)	2	0.5	0		
>=65	0			1 (1.1)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Sunburn									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Hypobarism									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Thermal burn									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Heat illness									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Medication errors and other product use errors and issues									
<65	4 (1.3)	7	1.7	1 (0.3)	1	0.2	2 (0.6)	3	0.7
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Extra dose administered									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Accidental overdose									
<65	2 (0.6)	4	1.0	1 (0.3)	1	0.2	2 (0.6)	3	0.7
>=65	1 (1.2)	1	0.9	0			0		
Dose calculation error									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Incorrect dose administered									
<65	1 (0.3)	2	0.5	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Overdoses and underdoses NEC									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Intentional overdose									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Investigations									
<65	13 (4.1)	15	3.6	28 (8.9)	34	8.1	29 (9.1)	38	9.0
>=65	5 (6.0)	8	7.3	12 (13.6)	14	12.6	4 (4.7)	4	3.8
Cardiac and vascular investigations (excl enzyme tests)									
<65	1 (0.3)	1	0.2	4 (1.3)	4	0.9	4 (1.3)	4	0.9
>=65	1 (1.2)	1	0.9	4 (4.5)	5	4.5	0		
Blood pressure decreased									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Cardiac murmur									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Cardiac stress test abnormal									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Carotid pulse decreased									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Electrocardiogram Q waves									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Heart rate increased									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	0		
>=65	1 (1.2)	1	0.9	0			0		
Blood pressure increased									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Electrocardiogram QT prolonged									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Electrocardiogram PR prolongation									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Electrocardiogram ST-T segment abnormal									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Gastrointestinal investigations									
<65	3 (0.9)	3	0.7	2 (0.6)	2	0.5	3 (0.9)	4	0.9
>=65	2 (2.4)	2	1.8	4 (4.5)	4	3.6	0		
Lipase increased									
<65	3 (0.9)	3	0.7	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	0		
Colonoscopy normal									
<65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			1 (1.1)	1	0.9	0		
Occult blood positive									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Occult blood									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Amylase increased									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Faecal volume increased									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Pancreatic enzymes increased									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Renal and urinary tract investigations and urinalyses									
<65	0			4 (1.3)	4	0.9	0		
>=65	0			2 (2.3)	2	1.8	0		
Urine albumin/creatinine ratio increased									
<65	0			0			0		
>=65	0			2 (2.3)	2	1.8	0		
Glomerular filtration rate decreased									
<65	0			3 (1.0)	3	0.7	0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Urine albumin/creatinine ratio abnormal									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Endocrine investigations (incl sex hormones)									
<65	2 (0.6)	2	0.5	4 (1.3)	4	0.9	2 (0.6)	2	0.5
>=65	0			0			0		
Blood thyroid stimulating hormone decreased									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			0			0		
Blood thyroid stimulating hormone increased									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	2 (0.6)	2	0.5
>=65	0			0			0		
Blood parathyroid hormone increased									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Haematology investigations (incl blood groups)									
<65	0			4 (1.3)	6	1.4	1 (0.3)	1	0.2
>=65	0			0			0		
Haemoglobin decreased									
<65	0			3 (1.0)	3	0.7	1 (0.3)	1	0.2
>=65	0			0			0		
Haematocrit decreased									

Adverse events with onset prior to randomisation are not included.
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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			2 (0.6)	2	0.5	0		
>=65	0			0			0		
Platelet count decreased									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Microbiology and serology investigations									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Helicobacter test positive									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Protein and chemistry analyses NEC									
<65	2 (0.6)	2	0.5	0			4 (1.3)	4	0.9
>=65	0			1 (1.1)	1	0.9	0		
C-reactive protein increased									
<65	2 (0.6)	2	0.5	0			4 (1.3)	4	0.9
>=65	0			1 (1.1)	1	0.9	0		
Reproductive organ and breast investigations (excl hormone analyses)									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Mammogram abnormal									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Enzyme investigations NEC									
<65	2 (0.6)	2	0.5	3 (1.0)	3	0.7	1 (0.3)	1	0.2

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Blood creatine phosphokinase increased									
<65	2 (0.6)	2	0.5	3 (1.0)	3	0.7	1 (0.3)	1	0.2
>=65	0			0			0		
Hepatobiliary investigations									
<65	2 (0.6)	2	0.5	3 (1.0)	3	0.7	6 (1.9)	9	2.1
>=65	1 (1.2)	2	1.8	0			1 (1.2)	1	0.9
Hepatic enzyme increased									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Liver function test abnormal									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Liver function test increased									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Alanine aminotransferase increased									
<65	0			0			3 (0.9)	3	0.7
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Aspartate aminotransferase increased									
<65	0			0			2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	0			0		
Blood bilirubin increased									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Transaminases increased									

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Lipid analyses									
<65	0			2 (0.6)	2	0.5	2 (0.6)	2	0.5
>=65	0			0			0		
Lipids abnormal									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Low density lipoprotein increased									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Blood cholesterol increased									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Blood triglycerides increased									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Investigations, imaging and histopathology procedures NEC									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Endoscopy abnormal									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Metabolic, nutritional and blood gas investigations									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	7 (2.2)	8	1.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Vitamin B12 decreased									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Blood glucose decreased									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Blood glucose increased									
<65	0			0			3 (0.9)	3	0.7
>=65	0			0			1 (1.2)	1	0.9
Blood uric acid increased									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Brain natriuretic peptide increased									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Glycosylated haemoglobin increased									
<65	1 (0.3)	1	0.2	0			3 (0.9)	3	0.7
>=65	0			0			0		
Neurological, special senses and psychiatric investigations									
<65	0			1 (0.3)	2	0.5	0		
>=65	0			0			0		
Intraocular pressure increased									
<65	0			1 (0.3)	2	0.5	0		
>=65	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Physical examination and organ system status topics									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			1 (1.2)	1	0.9
Weight decreased									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Weight increased									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Water, electrolyte and mineral investigations									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Blood potassium increased									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Blood potassium decreased									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Blood sodium increased									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Cytogenetic investigations									
<65	0			0			2 (0.6)	2	0.5
>=65	0			0			0		
Prostatic specific antigen increased									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			2 (0.6)	2	0.5
>=65	0			0			0		
Immunology and allergy investigations									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Antinuclear antibody increased									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Skin and subcutaneous tissue disorders									
<65	30 (9.4)	35	8.3	31 (9.8)	43	10.2	28 (8.8)	33	7.8
>=65	8 (9.6)	8	7.3	9 (10.2)	11	9.9	9 (10.6)	9	8.5
Epidermal and dermal conditions									
<65	19 (6.0)	21	5.0	21 (6.7)	27	6.4	18 (5.7)	19	4.5
>=65	4 (4.8)	4	3.7	6 (6.8)	8	7.2	4 (4.7)	4	3.8
Rash									
<65	5 (1.6)	5	1.2	6 (1.9)	9	2.1	3 (0.9)	3	0.7
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Eczema									
<65	3 (0.9)	3	0.7	3 (1.0)	3	0.7	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Dry skin									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	0		
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Blister									
<65	0			1 (0.3)	2	0.5	0		
>=65	0			1 (1.1)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Pruritus									
<65	2 (0.6)	2	0.5	0			3 (0.9)	3	0.7
>=65	0			1 (1.1)	1	0.9	0		
Psoriasis									
<65	0			0			1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Sensitive skin									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Skin burning sensation									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Rash pruritic									
<65	1 (0.3)	2	0.5	2 (0.6)	2	0.5	1 (0.3)	1	0.2
>=65	0			0			0		
Decubitus ulcer									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Dermatitis allergic									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Dermatitis contact									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Drug eruption									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	2 (0.6)	3	0.7
>=65	0			0			1 (1.2)	1	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Intertrigo									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Pain of skin									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Perioral dermatitis									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Skin exfoliation									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Skin lesion									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Dermatitis									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Erythema									
<65	1 (0.3)	2	0.5	0			0		
>=65	0			0			0		
Neurodermatitis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Parapsoriasis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Rash erythematous									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Stasis dermatitis									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Xanthelasma									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Skin appendage conditions									
<65	9 (2.8)	9	2.1	8 (2.5)	11	2.6	7 (2.2)	7	1.7
>=65	2 (2.4)	2	1.8	1 (1.1)	1	0.9	1 (1.2)	1	0.9
Alopecia									
<65	4 (1.3)	4	1.0	3 (1.0)	4	0.9	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Acne									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Alopecia areata									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Hyperhidrosis									
<65	1 (0.3)	1	0.2	1 (0.3)	2	0.5	3 (0.9)	3	0.7
>=65	1 (1.2)	1	0.9	0			0		
Ingrowing nail									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			1 (1.2)	1	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Onychomadesis									
<65	0			1 (0.3)	2	0.5	0		
>=65	0			0			0		
Miliaria									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Nail dystrophy									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Cornification and dystrophic skin disorders									
<65	1 (0.3)	1	0.2	0			2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Actinic keratosis									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Dermatitis papillaris capillitii									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Hyperkeratosis									
<65	0			0			1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			0		
Punctate keratosis									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Cutaneous neoplasms benign									
<65	0			0			1 (0.3)	2	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	2 (2.4)	2	1.9
Dermal cyst									
<65	0			0			1 (0.3)	2	0.5
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	2 (2.4)	2	1.9
Angioedema and urticaria									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	0			0			0		
Urticaria									
<65	0			1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	0			0			0		
Chronic spontaneous urticaria									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Skin and subcutaneous tissue disorders NEC									
<65	1 (0.3)	1	0.2	1 (0.3)	4	0.9	0		
>=65	0			0			2 (2.4)	2	1.9
Diabetic foot									
<65	0			1 (0.3)	3	0.7	0		
>=65	0			0			0		
Skin ulcer									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			2 (2.4)	2	1.9
Skin vascular abnormalities									
<65	2 (0.6)	2	0.5	0			1 (0.3)	1	0.2
>=65	0			0			0		
Ecchymosis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Haemorrhage subcutaneous									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Renal and urinary disorders									
<65	14 (4.4)	17	4.0	19 (6.0)	24	5.7	21 (6.6)	27	6.4
>=65	5 (6.0)	5	4.6	12 (13.6)	13	11.7	7 (8.2)	7	6.6
Urinary tract signs and symptoms									
<65	5 (1.6)	5	1.2	9 (2.9)	9	2.1	13 (4.1)	16	3.8
>=65	2 (2.4)	2	1.8	8 (9.1)	8	7.2	3 (3.5)	3	2.8
Dysuria									
<65	0			1 (0.3)	1	0.2	4 (1.3)	4	0.9
>=65	0			2 (2.3)	2	1.8	0		
Haematuria									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			2 (2.3)	2	1.8	0		
Nocturia									
<65	0			0			0		
>=65	0			2 (2.3)	2	1.8	0		
Microalbuminuria									
<65	2 (0.6)	2	0.5	3 (1.0)	3	0.7	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Proteinuria									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	0			1 (1.1)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Renal colic									
<65	0			2 (0.6)	2	0.5	1 (0.3)	1	0.2
>=65	0			0			0		
Pollakiuria									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Lower urinary tract symptoms									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Micturition disorder									
<65	0			0			1 (0.3)	2	0.5
>=65	0			0			0		
Polyuria									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			1 (1.2)	1	0.9
Urethral pain									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Urinary incontinence									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Nephropathies									
<65	3 (0.9)	3	0.7	5 (1.6)	5	1.2	1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Diabetic nephropathy									
<65	2 (0.6)	2	0.5	4 (1.3)	4	0.9	1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Nephropathy									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Renal disorders (excl nephropathies)									
<65	4 (1.3)	4	1.0	5 (1.6)	7	1.7	5 (1.6)	5	1.2
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	2 (2.4)	2	1.9
Acute kidney injury									
<65	1 (0.3)	1	0.2	2 (0.6)	3	0.7	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Renal cyst									
<65	2 (0.6)	2	0.5	2 (0.6)	2	0.5	1 (0.3)	1	0.2
>=65	0			0			2 (2.4)	2	1.9
Chronic kidney disease									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Renal impairment									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Hydronephrosis									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Kidney fibrosis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Bladder and bladder neck disorders (excl calculi)									
<65	0			0			1 (0.3)	1	0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			2 (2.3)	2	1.8	0		
Bladder outlet obstruction									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Hypertonic bladder									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Bladder hypertrophy									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Urolithiases									
<65	4 (1.3)	5	1.2	3 (1.0)	3	0.7	4 (1.3)	4	0.9
>=65	2 (2.4)	2	1.8	1 (1.1)	1	0.9	2 (2.4)	2	1.9
Stag horn calculus									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Nephrolithiasis									
<65	4 (1.3)	5	1.2	2 (0.6)	2	0.5	3 (0.9)	3	0.7
>=65	2 (2.4)	2	1.8	0			1 (1.2)	1	0.9
Calculus urinary									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Ureterolithiasis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			1 (1.2)	1	0.9
Ear and labyrinth disorders									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	8 (2.5)	11	2.6	10 (3.2)	10	2.4	8 (2.5)	10	2.4
>=65	3 (3.6)	3	2.7	10 (11.4)	10	9.0	4 (4.7)	4	3.8
Inner ear and VIIIth cranial nerve disorders									
<65	6 (1.9)	9	2.1	6 (1.9)	6	1.4	4 (1.3)	5	1.2
>=65	2 (2.4)	2	1.8	4 (4.5)	4	3.6	4 (4.7)	4	3.8
Vertigo									
<65	2 (0.6)	4	1.0	4 (1.3)	4	0.9	4 (1.3)	5	1.2
>=65	1 (1.2)	1	0.9	3 (3.4)	3	2.7	2 (2.4)	2	1.9
Vertigo positional									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			1 (1.1)	1	0.9	1 (1.2)	1	0.9
Motion sickness									
<65	2 (0.6)	3	0.7	0			0		
>=65	0			0			0		
Tinnitus									
<65	2 (0.6)	2	0.5	0			0		
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Aural disorders NEC									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	3 (0.9)	3	0.7
>=65	0			4 (4.5)	4	3.6	0		
Ear pain									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	2 (0.6)	2	0.5
>=65	0			3 (3.4)	3	2.7	0		
Ear pruritus									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Ear discomfort									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Hearing disorders									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Deafness bilateral									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Hypoacusis									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			0			0		
Deafness unilateral									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Mixed deafness									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
External ear disorders (excl congenital)									
<65	0			0			1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Cerumen impaction									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Excessive cerumen production									
<65	0			0			0		

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	1 (1.2)	1	0.9	0			0		
Psychiatric disorders									
<65	19 (6.0)	21	5.0	17 (5.4)	19	4.5	13 (4.1)	14	3.3
>=65	4 (4.8)	7	6.4	7 (8.0)	10	9.0	2 (2.4)	2	1.9
Sleep disorders and disturbances									
<65	5 (1.6)	5	1.2	8 (2.5)	8	1.9	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	2 (2.4)	2	1.9
Insomnia									
<65	5 (1.6)	5	1.2	7 (2.2)	7	1.7	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	0			2 (2.4)	2	1.9
Middle insomnia									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Sleep disorder									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Abnormal dreams									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Depressed mood disorders and disturbances									
<65	4 (1.3)	4	1.0	4 (1.3)	4	0.9	5 (1.6)	5	1.2
>=65	1 (1.2)	1	0.9	3 (3.4)	3	2.7	0		
Depressed mood									
<65	3 (0.9)	3	0.7	3 (1.0)	3	0.7	0		
>=65	0			1 (1.1)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Depression									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	5 (1.6)	5	1.2
>=65	0			1 (1.1)	1	0.9	0		
Anhedonia									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Major depression									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Anxiety disorders and symptoms									
<65	7 (2.2)	8	1.9	3 (1.0)	3	0.7	6 (1.9)	6	1.4
>=65	3 (3.6)	3	2.7	2 (2.3)	2	1.8	0		
Anxiety									
<65	7 (2.2)	8	1.9	1 (0.3)	1	0.2	4 (1.3)	4	0.9
>=65	0			2 (2.3)	2	1.8	0		
Anxiety disorder due to a general medical condition									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Stress									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Generalised anxiety disorder									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Nervousness									
<65	0			0			0		

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	2 (2.4)	2	1.8	0			0		
Post-traumatic stress disorder									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Adjustment disorders (incl subtypes)									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Grief reaction									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Adjustment disorder with depressed mood									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Mood disorders and disturbances NEC									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			1 (1.1)	2	1.8	0		
Mood altered									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	2	1.8	0		
Irritability									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Mood swings									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Changes in physical activity									

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Restlessness									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Suicidal and self-injurious behaviours NEC									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Suicidal ideation									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Psychiatric disorders NEC									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Mental status changes									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Sexual dysfunctions, disturbances and gender identity disorders									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Libido decreased									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Cardiac disorders									

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	10 (3.1)	11	2.6	16 (5.1)	22	5.2	8 (2.5)	8	1.9
>=65	10 (12.0)	13	11.9	6 (6.8)	6	5.4	5 (5.9)	9	8.5
Cardiac arrhythmias									
<65	5 (1.6)	5	1.2	9 (2.9)	12	2.8	2 (0.6)	2	0.5
>=65	5 (6.0)	7	6.4	4 (4.5)	4	3.6	2 (2.4)	3	2.8
Atrial fibrillation									
<65	0			3 (1.0)	3	0.7	1 (0.3)	1	0.2
>=65	2 (2.4)	2	1.8	2 (2.3)	2	1.8	1 (1.2)	1	0.9
Supraventricular extrasystoles									
<65	0			2 (0.6)	2	0.5	0		
>=65	0			2 (2.3)	2	1.8	0		
Tachycardia									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	0		
>=65	0			0			0		
Atrioventricular block first degree									
<65	0			1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			0		
Bundle branch block right									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Sinus tachycardia									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			0		
Supraventricular tachycardia									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Ventricular extrasystoles									

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Atrial flutter									
<65	0			0			0		
>=65	0			0			1 (1.2)	2	1.9
Bradycardia									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Bundle branch block left									
<65	1 (0.3)	1	0.2	0			0		
>=65	2 (2.4)	2	1.8	0			0		
Coronary artery disorders									
<65	4 (1.3)	4	1.0	6 (1.9)	6	1.4	3 (0.9)	3	0.7
>=65	3 (3.6)	3	2.7	1 (1.1)	1	0.9	1 (1.2)	1	0.9
Angina pectoris									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	0			1 (1.1)	1	0.9	0		
Acute myocardial infarction									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Angina unstable									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Coronary artery disease									
<65	0			1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			0		
Myocardial infarction									

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Myocardial ischaemia									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			0		
Arteriosclerosis coronary artery									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Cardiac disorders, signs and symptoms NEC									
<65	2 (0.6)	2	0.5	2 (0.6)	3	0.7	3 (0.9)	3	0.7
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	1 (1.2)	1	0.9
Palpitations									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	0		
Cardiovascular disorder									
<65	0			1 (0.3)	2	0.5	1 (0.3)	1	0.2
>=65	0			0			0		
Hypertensive heart disease									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Heart failures									
<65	0			1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			2 (2.4)	3	2.8
Cardiac failure congestive									
<65	0			1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Cardiac failure acute									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Left ventricular failure									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Myocardial disorders									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Cardiac hypertrophy									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Left ventricular hypertrophy									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Vascular disorders									
<65	18 (5.6)	18	4.3	20 (6.3)	22	5.2	25 (7.9)	26	6.2
>=65	4 (4.8)	5	4.6	4 (4.5)	4	3.6	5 (5.9)	6	5.7
Vascular hypertensive disorders									
<65	8 (2.5)	8	1.9	9 (2.9)	10	2.4	11 (3.5)	12	2.8
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	4 (4.7)	4	3.8
Hypertension									
<65	8 (2.5)	8	1.9	9 (2.9)	10	2.4	10 (3.2)	10	2.4
>=65	1 (1.2)	1	0.9	1 (1.1)	1	0.9	2 (2.4)	2	1.9
Hypertensive crisis									
<65	0			0			2 (0.6)	2	0.5

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			1 (1.2)	1	0.9
Hypertensive urgency									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Decreased and nonspecific blood pressure disorders and shock									
<65	3 (0.9)	3	0.7	3 (1.0)	4	0.9	4 (1.3)	4	0.9
>=65	2 (2.4)	3	2.7	1 (1.1)	1	0.9	0		
Hypotension									
<65	3 (0.9)	3	0.7	1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	1 (1.2)	2	1.8	1 (1.1)	1	0.9	0		
Blood pressure inadequately controlled									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Orthostatic hypotension									
<65	0			1 (0.3)	2	0.5	2 (0.6)	2	0.5
>=65	0			0			0		
Shock									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Vascular disorders NEC									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	2 (0.6)	2	0.5
>=65	0			1 (1.1)	1	0.9	0		
Aortic rupture									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Aortic dilatation									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Hot flush									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	2 (0.6)	2	0.5
>=65	0			0			0		
Aneurysms and artery dissections									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Aortic aneurysm									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Vascular haemorrhagic disorders									
<65	0			3 (1.0)	3	0.7	1 (0.3)	1	0.2
>=65	0			0			0		
Haematoma									
<65	0			3 (1.0)	3	0.7	1 (0.3)	1	0.2
>=65	0			0			0		
Arteriosclerosis, stenosis, vascular insufficiency and necrosis									
<65	5 (1.6)	5	1.2	1 (0.3)	1	0.2	4 (1.3)	4	0.9
>=65	1 (1.2)	1	0.9	0			1 (1.2)	2	1.9
Aortic arteriosclerosis									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			0		
Arteriosclerosis									
<65	1 (0.3)	1	0.2	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=65	0			0			0		
Peripheral arterial occlusive disease									
<65	0			0			2	(0.6)	2 0.5
>=65	0			0			0		
Peripheral artery stenosis									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Peripheral coldness									
<65	2	(0.6)	2 0.5	0			0		
>=65	0			0			0		
Peripheral venous disease									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			1	(1.2)	2 1.9
Embolism and thrombosis									
<65	0			1	(0.3)	1 0.2	1	(0.3)	1 0.2
>=65	0			0			0		
Post thrombotic syndrome									
<65	0			1	(0.3)	1 0.2	0		
>=65	0			0			0		
Deep vein thrombosis									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Vascular infections and inflammations									
<65	0			1	(0.3)	1 0.2	0		
>=65	0			0			0		
Temporal arteritis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Lymphatic vessel disorders									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Lymphoedema									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Venous varices									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Varicose vein									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Blood and lymphatic system disorders									
<65	8 (2.5)	8	1.9	10 (3.2)	10	2.4	5 (1.6)	6	1.4
>=65	1 (1.2)	1	0.9	2 (2.3)	3	2.7	5 (5.9)	5	4.7
Anaemias nonhaemolytic and marrow depression									
<65	7 (2.2)	7	1.7	8 (2.5)	8	1.9	4 (1.3)	4	0.9
>=65	1 (1.2)	1	0.9	2 (2.3)	3	2.7	2 (2.4)	2	1.9
Anaemia									
<65	3 (0.9)	3	0.7	7 (2.2)	7	1.7	3 (0.9)	3	0.7
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	1 (1.2)	1	0.9
Pancytopenia									
<65	0			0			0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			1 (1.1)	1	0.9	0		
Iron deficiency anaemia									
<65	2 (0.6)	2	0.5	1 (0.3)	1	0.2	0		
>=65	0			0			1 (1.2)	1	0.9
Hypochromic anaemia									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Microcytic anaemia									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Normocytic anaemia									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Platelet disorders									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Thrombocytosis									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Spleen, lymphatic and reticuloendothelial system disorders									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			2 (2.4)	2	1.9
Splenomegaly									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			1 (1.2)	1	0.9
Lymphadenopathy									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			1 (1.2)	1	0.9
White blood cell disorders									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			1 (1.2)	1	0.9
Leukocytosis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			1 (1.2)	1	0.9
Lymphopenia									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Reproductive system and breast disorders									
<65	11 (3.4)	16	3.8	10 (3.2)	10	2.4	8 (2.5)	10	2.4
>=65	4 (4.8)	4	3.7	2 (2.3)	2	1.8	1 (1.2)	1	0.9
Vulvovaginal disorders (excl infections and inflammations)									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	2 (0.6)	2	0.5
>=65	0			1 (1.1)	1	0.9	0		
Vulvovaginal pruritus									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Vulva cyst									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Vulval disorder									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Vaginal disorder									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Vaginal haemorrhage									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Vulvovaginal dryness									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Reproductive tract disorders NEC									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			1 (1.1)	1	0.9	0		
Pruritus genital									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			1 (1.1)	1	0.9	0		
Pelvic pain									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Menstrual cycle and uterine bleeding disorders									
<65	2 (0.6)	2	0.5	3 (1.0)	3	0.7	1 (0.3)	2	0.5
>=65	0			0			0		
Dysmenorrhoea									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Metrorrhagia									
<65	0			1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Oligomenorrhoea									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Menorrhagia									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Menstruation irregular									
<65	1 (0.3)	1	0.2	0			1 (0.3)	2	0.5
>=65	0			0			0		
Sexual function and fertility disorders									
<65	2 (0.6)	2	0.5	2 (0.6)	2	0.5	1 (0.3)	1	0.2
>=65	0			0			0		
Erectile dysfunction									
<65	2 (0.6)	2	0.5	2 (0.6)	2	0.5	1 (0.3)	1	0.2
>=65	0			0			0		
Breast disorders									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	2 (2.4)	2	1.8	0			0		
Breast mass									
<65	0			1 (0.3)	1	0.2	0		
>=65	1 (1.2)	1	0.9	0			0		
Breast cyst									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Breast pain									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Menopause related conditions									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Atrophic vulvovaginitis									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Uterine, pelvic and broad ligament disorders									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			1 (1.2)	1	0.9
Uterine polyp									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Adenomyosis									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Endometriosis									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Male reproductive tract infections and inflammations									
<65	4 (1.3)	4	1.0	0			1 (0.3)	1	0.2
>=65	0			0			0		
Balanoposthitis									
<65	3 (0.9)	3	0.7	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Prostatitis									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Ovarian and fallopian tube disorders									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			0			0		
Haemorrhagic ovarian cyst									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Ovarian cyst									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Penile and scrotal disorders (excl infections and inflammations)									
<65	1 (0.3)	2	0.5	0			0		
>=65	0			0			0		
Penile erosion									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Peyronie's disease									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Prostatic disorders (excl infections and inflammations)									
<65	0			0			1 (0.3)	1	0.2
>=65	2 (2.4)	2	1.8	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Benign prostatic hyperplasia									
<65	0			0			1 (0.3)	1	0.2
>=65	2 (2.4)	2	1.8	0			0		
Testicular and epididymal disorders									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Testicular disorder									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)									
<65	9 (2.8)	12	2.9	6 (1.9)	6	1.4	6 (1.9)	6	1.4
>=65	4 (4.8)	4	3.7	3 (3.4)	4	3.6	6 (7.1)	8	7.6
Leukaemias									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			1 (1.1)	1	0.9	0		
Myeloid leukaemia									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Chronic lymphocytic leukaemia									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Miscellaneous and site unspecified neoplasms malignant and unspecified									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Squamous cell carcinoma									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Respiratory and mediastinal neoplasms malignant and unspecified									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Nasal cavity cancer									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Keratinising squamous cell carcinoma of nasopharynx									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Skeletal neoplasms benign									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Osteochondroma									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Gastrointestinal neoplasms benign									
<65	2 (0.6)	3	0.7	2 (0.6)	2	0.5	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Benign duodenal neoplasm									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Gastrointestinal tract adenoma									

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Colon adenoma									
<65	2 (0.6)	3	0.7	0			1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			1 (1.2)	1	0.9
Cutaneous neoplasms benign									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			1 (1.2)	1	0.9
Anogenital warts									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Melanocytic naevus									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Lymphomas non-Hodgkin's unspecified histology									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Gastrointestinal lymphoma									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Soft tissue neoplasms benign									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			0		
Lipoma									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	1 (1.2)	1	0.9	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Breast neoplasms malignant and unspecified (incl nipple)									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Invasive ductal breast carcinoma									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Endocrine neoplasms benign									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Pituitary tumour benign									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Endocrine neoplasms malignant and unspecified									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Neuroendocrine tumour									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Gastrointestinal neoplasms malignant and unspecified									
<65	3 (0.9)	3	0.7	0			0		
>=65	2 (2.4)	2	1.8	0			2 (2.4)	2	1.9
Adenocarcinoma gastric									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Adenocarcinoma of colon									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Gastric cancer									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Gastric cancer stage IV									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Gastrointestinal stromal tumour									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Gastrointestinal submucosal tumour									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Oral neoplasm									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Hepatobiliary neoplasms malignant and unspecified									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Hepatocellular carcinoma									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Metastases									
<65	1 (0.3)	1	0.2	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=65	0			0			0		
Metastases to liver									
<65	1	(0.3)	1 0.2	0			0		
>=65	0			0			0		
Reproductive neoplasms female benign									
<65	1	(0.3)	1 0.2	0			0		
>=65	0			0			0		
Uterine leiomyoma									
<65	1	(0.3)	1 0.2	0			0		
>=65	0			0			0		
Reproductive neoplasms female malignant and unspecified									
<65	1	(0.3)	1 0.2	0			0		
>=65	0			0			0		
Uterine cancer									
<65	1	(0.3)	1 0.2	0			0		
>=65	0			0			0		
Reproductive neoplasms male malignant and unspecified									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			2	(2.4)	2 1.9
Prostate cancer									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			2	(2.4)	2 1.9
Skin neoplasms malignant and unspecified									
<65	0			0			1	(0.3)	1 0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			1 (1.2)	1	0.9
Basal cell carcinoma									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			1 (1.2)	1	0.9
Hepatobiliary disorders									
<65	10 (3.1)	11	2.6	9 (2.9)	12	2.8	6 (1.9)	10	2.4
>=65	0			1 (1.1)	1	0.9	3 (3.5)	4	3.8
Hepatic and hepatobiliary disorders									
<65	6 (1.9)	6	1.4	7 (2.2)	8	1.9	6 (1.9)	6	1.4
>=65	0			1 (1.1)	1	0.9	3 (3.5)	4	3.8
Hepatic steatosis									
<65	3 (0.9)	3	0.7	4 (1.3)	4	0.9	4 (1.3)	4	0.9
>=65	0			0			1 (1.2)	1	0.9
Hepatic cyst									
<65	0			0			1 (0.3)	1	0.2
>=65	0			1 (1.1)	1	0.9	0		
Hepatic lesion									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Non-alcoholic steatohepatitis									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Nonalcoholic fatty liver disease									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Portal vein thrombosis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			1 (1.2)	1	0.9
Drug-induced liver injury									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Hepatic cirrhosis									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Hepatomegaly									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Liver disorder									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Portal hypertension									
<65	0			0			0		
>=65	0			0			1 (1.2)	1	0.9
Gallbladder disorders									
<65	4 (1.3)	5	1.2	3 (1.0)	4	0.9	3 (0.9)	4	0.9
>=65	0			0			0		
Gallbladder polyp									
<65	2 (0.6)	2	0.5	2 (0.6)	2	0.5	0		
>=65	0			0			0		
Cholecystitis chronic									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Cholelithiasis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	3 (0.9)	3	0.7	1 (0.3)	1	0.2	3 (0.9)	3	0.7
>=65	0			0			0		
Cholecystitis acute									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Immune system disorders									
<65	5 (1.6)	5	1.2	4 (1.3)	4	0.9	5 (1.6)	6	1.4
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	1 (1.2)	1	0.9
Allergic conditions									
<65	4 (1.3)	4	1.0	4 (1.3)	4	0.9	5 (1.6)	6	1.4
>=65	1 (1.2)	1	0.9	2 (2.3)	2	1.8	1 (1.2)	1	0.9
Seasonal allergy									
<65	2 (0.6)	2	0.5	2 (0.6)	2	0.5	3 (0.9)	4	0.9
>=65	0			2 (2.3)	2	1.8	1 (1.2)	1	0.9
Allergy to arthropod sting									
<65	0			1 (0.3)	1	0.2	1 (0.3)	1	0.2
>=65	0			0			0		
Hypersensitivity									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	0		
>=65	0			0			0		
Allergy to chemicals									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Drug hypersensitivity									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Multiple allergies									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Immune disorders NEC									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Immunisation reaction									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Endocrine disorders									
<65	3 (0.9)	3	0.7	2 (0.6)	2	0.5	4 (1.3)	4	0.9
>=65	0			2 (2.3)	2	1.8	0		
Thyroid gland disorders									
<65	3 (0.9)	3	0.7	2 (0.6)	2	0.5	4 (1.3)	4	0.9
>=65	0			2 (2.3)	2	1.8	0		
Primary hyperthyroidism									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Thyroid cyst									
<65	0			0			0		
>=65	0			1 (1.1)	1	0.9	0		
Hypothyroidism									
<65	1 (0.3)	1	0.2	2 (0.6)	2	0.5	0		
>=65	0			0			0		
Autoimmune thyroiditis									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Goitre									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Silent thyroiditis									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Thyroid mass									
<65	0			0			2 (0.6)	2	0.5
>=65	0			0			0		
Surgical and medical procedures									
<65	1 (0.3)	1	0.2	1 (0.3)	1	0.2	3 (0.9)	4	0.9
>=65	2 (2.4)	2	1.8	0			2 (2.4)	2	1.9
Endocrine gland therapeutic procedures									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Thyroidectomy									
<65	0			1 (0.3)	1	0.2	0		
>=65	0			0			0		
Bone and joint therapeutic procedures									
<65	1 (0.3)	1	0.2	0			1 (0.3)	1	0.2
>=65	0			0			0		
Bone graft									
<65	1 (0.3)	1	0.2	0			0		
>=65	0			0			0		
Joint injection									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Cardiac therapeutic procedures									
<65	0			0			0		
>=65	1	(1.2)	1 0.9	0			0		
Cardiac pacemaker replacement									
<65	0			0			0		
>=65	1	(1.2)	1 0.9	0			0		
Eye therapeutic procedures									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Cataract operation									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Head and neck therapeutic procedures									
<65	0			0			0		
>=65	1	(1.2)	1 0.9	0			0		
Tooth extraction									
<65	0			0			0		
>=65	1	(1.2)	1 0.9	0			0		
Male genital tract therapeutic procedures									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Sperm aspiration									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Therapeutic procedures and supportive care NEC									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			2	(2.4)	2 1.9
Cyst removal									
<65	0			0			0		
>=65	0			0			1	(1.2)	1 0.9
Nerve block									
<65	0			0			1	(0.3)	1 0.2
>=65	0			0			0		
Stent placement									
<65	0			0			0		
>=65	0			0			1	(1.2)	1 0.9
Congenital, familial and genetic disorders									
<65	0			0			2	(0.6)	2 0.5
>=65	1	(1.2)	1 0.9	0			0		
Reproductive tract and breast disorders congenital									
<65	0			0			2	(0.6)	2 0.5
>=65	0			0			0		
Phimosis									
<65	0			0			2	(0.6)	2 0.5
>=65	0			0			0		
Respiratory disorders congenital									
<65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	1 (1.2)	1	0.9	0			0		
Laryngeal web									
<65	0			0			0		
>=65	1 (1.2)	1	0.9	0			0		
Pregnancy, puerperium and perinatal conditions									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Abortions and stillbirth									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Abortion spontaneous									
<65	0			0			1 (0.3)	1	0.2
>=65	0			0			0		
Social circumstances									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			0			0		
Economic and housing issues									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			0			0		
Stress at work									
<65	2 (0.6)	2	0.5	0			0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

11 Adverse events by age at baseline - overview - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
<65	90	122.4			166	229.0			95	133.3		
>=65	10	13.8			33	46.0			6	8.6		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Events												
<65	73	(81.1)	422	344.8	142	(85.5)	692	302.2	75	(78.9)	224	168.1
>=65	9	(90.0)	61	441.6	29	(87.9)	142	308.5	5	(83.3)	11	128.2
Serious												
Yes												
<65	6	(6.7)	9	7.4	8	(4.8)	10	4.4	5	(5.3)	5	3.8
>=65	1	(10.0)	1	7.2	2	(6.1)	2	4.3	2	(33.3)	2	23.3
No												
<65	73	(81.1)	413	337.4	141	(84.9)	682	297.8	74	(77.9)	219	164.3
>=65	9	(90.0)	60	434.4	29	(87.9)	140	304.2	4	(66.7)	9	104.9
Severity												
Severe												
<65	2	(2.2)	2	1.6	2	(1.2)	3	1.3	3	(3.2)	3	2.3
>=65	1	(10.0)	1	7.2	1	(3.0)	1	2.2	2	(33.3)	2	23.3
Moderate												
<65	12	(13.3)	51	41.7	23	(13.9)	39	17.0	11	(11.6)	13	9.8
>=65	2	(20.0)	12	86.9	2	(6.1)	3	6.5	0			
Mild												
<65	70	(77.8)	369	301.5	139	(83.7)	650	283.9	72	(75.8)	208	156.1
>=65	9	(90.0)	48	347.5	29	(87.9)	138	299.8	4	(66.7)	9	104.9

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by age at baseline - overview - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Relationship to trial product												
Missing												
<65	0				1	(0.6)	1	0.4	0			
>=65	0				0				0			
Probable												
<65	20	(22.2)	49	40.0	41	(24.7)	125	54.6	10	(10.5)	16	12.0
>=65	5	(50.0)	12	86.9	14	(42.4)	33	71.7	0			
Possible												
<65	49	(54.4)	176	143.8	67	(40.4)	165	72.1	9	(9.5)	15	11.3
>=65	6	(60.0)	14	101.4	17	(51.5)	41	89.1	1	(16.7)	2	23.3
Unlikely												
<65	64	(71.1)	197	161.0	126	(75.9)	401	175.1	69	(72.6)	193	144.8
>=65	9	(90.0)	35	253.4	26	(78.8)	68	147.7	5	(83.3)	9	104.9
Outcome												
Recovered												
<65	70	(77.8)	364	297.4	136	(81.9)	606	264.6	70	(73.7)	175	131.3
>=65	8	(80.0)	45	325.8	28	(84.8)	123	267.2	5	(83.3)	11	128.2
Recovering												
<65	9	(10.0)	16	13.1	13	(7.8)	18	7.9	5	(5.3)	5	3.8
>=65	0				3	(9.1)	3	6.5	0			
Not Recovered												
<65	29	(32.2)	42	34.3	42	(25.3)	68	29.7	26	(27.4)	44	33.0
>=65	6	(60.0)	16	115.8	12	(36.4)	16	34.8	0			
Leading to												
Permanent treatment discontinuation												
<65	2	(2.2)	5	4.1	3	(1.8)	5	2.2	1	(1.1)	1	0.8
>=65	1	(10.0)	1	7.2	2	(6.1)	4	8.7	0			

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by age at baseline - overview - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Leading to												
Temporary interruption of trial product												
<65	6	(6.7)	7	5.7	8	(4.8)	16	7.0	3	(3.2)	3	2.3
>=65	1	(10.0)	2	14.5	6	(18.2)	10	21.7	2	(33.3)	2	23.3
Dose reduction of trial product												
<65	3	(3.3)	3	2.5	10	(6.0)	15	6.6	0			
>=65	0				4	(12.1)	4	8.7	0			

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

12 Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N		PYE		N		PYE		N		PYE	
<65	90		122.4		166		229.0		95		133.3	
>=65	10		13.8		33		46.0		6		8.6	
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Adverse events												
<65	73	(81.1)	422	344.8	142	(85.5)	692	302.2	75	(78.9)	224	168.1
>=65	9	(90.0)	61	441.6	29	(87.9)	142	308.5	5	(83.3)	11	128.2
Gastrointestinal disorders												
<65	56	(62.2)	230	187.9	95	(57.2)	284	124.0	29	(30.5)	41	30.8
>=65	8	(80.0)	26	188.2	23	(69.7)	59	128.2	1	(16.7)	2	23.3
Gastrointestinal motility and defaecation conditions												
<65	34	(37.8)	72	58.8	59	(35.5)	89	38.9	8	(8.4)	8	6.0
>=65	7	(70.0)	12	86.9	19	(57.6)	30	65.2	1	(16.7)	1	11.7
Constipation												
<65	14	(15.6)	16	13.1	38	(22.9)	41	17.9	3	(3.2)	3	2.3
>=65	5	(50.0)	6	43.4	14	(42.4)	19	41.3	0			
Diarrhoea												
<65	19	(21.1)	53	43.3	25	(15.1)	43	18.8	5	(5.3)	5	3.8
>=65	3	(30.0)	6	43.4	7	(21.2)	9	19.6	1	(16.7)	1	11.7
Gastrooesophageal reflux disease												
<65	2	(2.2)	2	1.6	4	(2.4)	4	1.7	0			
>=65	0				2	(6.1)	2	4.3	0			
Gastrointestinal motility disorder												

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Irritable bowel syndrome									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Gastrointestinal signs and symptoms									
<65	33 (36.7)	141	115.2	60 (36.1)	146	63.8	10 (10.5)	16	12.0
>=65	6 (60.0)	10	72.4	11 (33.3)	23	50.0	1 (16.7)	1	11.7
Nausea									
<65	16 (17.8)	25	20.4	30 (18.1)	60	26.2	4 (4.2)	4	3.0
>=65	2 (20.0)	2	14.5	5 (15.2)	6	13.0	0		
Vomiting									
<65	7 (7.8)	31	25.3	15 (9.0)	27	11.8	2 (2.1)	2	1.5
>=65	3 (30.0)	3	21.7	2 (6.1)	2	4.3	0		
Abdominal discomfort									
<65	10 (11.1)	11	9.0	10 (6.0)	14	6.1	1 (1.1)	1	0.8
>=65	1 (10.0)	1	7.2	2 (6.1)	2	4.3	0		
Abdominal pain									
<65	2 (2.2)	2	1.6	10 (6.0)	14	6.1	0		
>=65	1 (10.0)	2	14.5	2 (6.1)	2	4.3	0		
Abdominal distension									
<65	7 (7.8)	8	6.5	4 (2.4)	4	1.7	1 (1.1)	2	1.5
>=65	0			3 (9.1)	4	8.7	1 (16.7)	1	11.7
Abdominal pain upper									
<65	3 (3.3)	5	4.1	8 (4.8)	11	4.8	1 (1.1)	1	0.8
>=65	0			2 (6.1)	2	4.3	0		
Dyspepsia									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	5 (5.6)	16	13.1	7 (4.2)	12	5.2	1 (1.1)	4	3.0
>=65	1 (10.0)	1	7.2	2 (6.1)	2	4.3	0		
Eructation									
<65	3 (3.3)	20	16.3	1 (0.6)	1	0.4	0		
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Faeces hard									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Flatulence									
<65	1 (1.1)	18	14.7	0			0		
>=65	0			1 (3.0)	1	2.2	0		
Faeces soft									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	0		
>=65	0			0			0		
Abdominal tenderness									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Abdominal pain lower									
<65	1 (1.1)	2	1.6	0			1 (1.1)	2	1.5
>=65	0			0			0		
Epigastric discomfort									
<65	2 (2.2)	2	1.6	0			0		
>=65	0			0			0		
Dental and gingival conditions									
<65	3 (3.3)	3	2.5	11 (6.6)	12	5.2	6 (6.3)	6	4.5
>=65	3 (30.0)	3	21.7	3 (9.1)	3	6.5	0		
Dental caries									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (1.1)	1	0.8	9 (5.4)	10	4.4	5 (5.3)	5	3.8
>=65	3 (30.0)	3	21.7	2 (6.1)	2	4.3	0		
Toothache									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			1 (3.0)	1	2.2	0		
Tooth impacted									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Dental cyst									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Gastrointestinal inflammatory conditions									
<65	1 (1.1)	1	0.8	8 (4.8)	9	3.9	5 (5.3)	5	3.8
>=65	0			2 (6.1)	2	4.3	0		
Gastritis									
<65	0			2 (1.2)	2	0.9	3 (3.2)	3	2.3
>=65	0			1 (3.0)	1	2.2	0		
Colitis ischaemic									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Enterocolitis									
<65	1 (1.1)	1	0.8	4 (2.4)	4	1.7	1 (1.1)	1	0.8
>=65	0			0			0		
Chronic gastritis									
<65	0			1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Colitis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Enteritis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Gastrointestinal conditions NEC									
<65	4 (4.4)	4	3.3	9 (5.4)	11	4.8	1 (1.1)	1	0.8
>=65	0			1 (3.0)	1	2.2	0		
Gastric disorder									
<65	2 (2.2)	2	1.6	2 (1.2)	2	0.9	0		
>=65	0			1 (3.0)	1	2.2	0		
Gastrointestinal disorder									
<65	2 (2.2)	2	1.6	4 (2.4)	6	2.6	0		
>=65	0			0			0		
Food poisoning									
<65	0			3 (1.8)	3	1.3	0		
>=65	0			0			0		
Barrett's oesophagus									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Benign neoplasms gastrointestinal									
<65	2 (2.2)	2	1.6	6 (3.6)	7	3.1	2 (2.1)	2	1.5
>=65	1 (10.0)	1	7.2	0			0		
Large intestine polyp									
<65	1 (1.1)	1	0.8	4 (2.4)	4	1.7	2 (2.1)	2	1.5
>=65	1 (10.0)	1	7.2	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gastric polyps									
<65	0			3 (1.8)	3	1.3	0		
>=65	0			0			0		
Rectal polyp									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Oral soft tissue conditions									
<65	0			3 (1.8)	3	1.3	0		
>=65	0			0			0		
Stomatitis									
<65	0			2 (1.2)	2	0.9	0		
>=65	0			0			0		
Angular cheilitis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Gastrointestinal haemorrhages NEC									
<65	0			2 (1.2)	2	0.9	0		
>=65	0			0			0		
Anal haemorrhage									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Mallory-Weiss syndrome									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Anal and rectal conditions NEC									
<65	2 (2.2)	2	1.6	1 (0.6)	1	0.4	0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Anal fissure									
<65	2 (2.2)	2	1.6	1 (0.6)	1	0.4	0		
>=65	0			0			0		
Diverticular disorders									
<65	2 (2.2)	2	1.6	1 (0.6)	1	0.4	0		
>=65	0			0			0		
Diverticulum intestinal									
<65	2 (2.2)	2	1.6	1 (0.6)	1	0.4	0		
>=65	0			0			0		
Gastrointestinal ulceration and perforation									
<65	0			1 (0.6)	2	0.9	1 (1.1)	1	0.8
>=65	0			0			0		
Erosive duodenitis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Gastritis erosive									
<65	0			1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Gastrointestinal vascular conditions									
<65	2 (2.2)	2	1.6	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Haemorrhoids									
<65	2 (2.2)	2	1.6	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Gastrointestinal stenosis and obstruction									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Intestinal obstruction									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Salivary gland conditions									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Parotid gland enlargement									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Infections and infestations									
<65	38 (42.2)	58	47.4	68 (41.0)	131	57.2	34 (35.8)	52	39.0
>=65	4 (40.0)	6	43.4	12 (36.4)	22	47.8	1 (16.7)	1	11.7
Infections - pathogen unspecified									
<65	35 (38.9)	52	42.5	60 (36.1)	113	49.3	33 (34.7)	50	37.5
>=65	4 (40.0)	6	43.4	11 (33.3)	19	41.3	1 (16.7)	1	11.7
Nasopharyngitis									
<65	21 (23.3)	33	27.0	45 (27.1)	69	30.1	17 (17.9)	23	17.3
>=65	3 (30.0)	3	21.7	8 (24.2)	12	26.1	1 (16.7)	1	11.7
Gastroenteritis									
<65	7 (7.8)	8	6.5	10 (6.0)	12	5.2	1 (1.1)	1	0.8
>=65	0			1 (3.0)	1	2.2	0		
Cystitis									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	1 (1.1)	2	1.5
>=65	0			1 (3.0)	1	2.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Conjunctivitis									
<65	0			1 (0.6)	2	0.9	2 (2.1)	2	1.5
>=65	0			1 (3.0)	1	2.2	0		
Bronchitis									
<65	2 (2.2)	2	1.6	6 (3.6)	9	3.9	0		
>=65	1 (10.0)	1	7.2	0			0		
Enteritis infectious									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Urinary tract infection									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			1 (3.0)	3	6.5	0		
Pharyngitis									
<65	3 (3.3)	3	2.5	3 (1.8)	4	1.7	4 (4.2)	5	3.8
>=65	0			0			0		
Rhinitis									
<65	0			2 (1.2)	2	0.9	2 (2.1)	2	1.5
>=65	1 (10.0)	1	7.2	0			0		
Tonsillitis									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	3 (3.2)	4	3.0
>=65	0			0			0		
Acute sinusitis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Diverticulitis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Folliculitis									
<65	0			1 (0.6)	2	0.9	0		
>=65	0			0			0		
Gingivitis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Hordeolum									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Pelvic inflammatory disease									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Pyelonephritis									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	0		
>=65	0			0			0		
Pyelonephritis acute									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Sinusitis									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	3 (3.2)	3	2.3
>=65	0			0			0		
Urethritis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Periodontitis									
<65	0			0			1 (1.1)	1	0.8
>=65	1 (10.0)	1	7.2	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Pyoderma									
<65	0			0			1 (1.1)	2	1.5
>=65	0			0			0		
Upper respiratory tract infection									
<65	0			0			2 (2.1)	3	2.3
>=65	0			0			0		
Vaginal infection									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Viral infectious disorders									
<65	5 (5.6)	5	4.1	12 (7.2)	12	5.2	1 (1.1)	1	0.8
>=65	0			1 (3.0)	2	4.3	0		
Influenza									
<65	2 (2.2)	2	1.6	7 (4.2)	7	3.1	1 (1.1)	1	0.8
>=65	0			1 (3.0)	1	2.2	0		
Herpes zoster									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	0		
>=65	0			1 (3.0)	1	2.2	0		
Gastroenteritis viral									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	0		
>=65	0			0			0		
Herpes simplex									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Infectious mononucleosis									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Bacterial infectious disorders									
<65	1 (1.1)	1	0.8	3 (1.8)	4	1.7	1 (1.1)	1	0.8
>=65	0			1 (3.0)	1	2.2	0		
Alpha haemolytic streptococcal infection									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Cellulitis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Erysipelas									
<65	0			1 (0.6)	2	0.9	0		
>=65	0			0			0		
Furuncle									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Helicobacter infection									
<65	1 (1.1)	1	0.8	0			1 (1.1)	1	0.8
>=65	0			0			0		
Fungal infectious disorders									
<65	0			2 (1.2)	2	0.9	0		
>=65	0			0			0		
Tinea pedis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Vulvovaginal candidiasis									
<65	0			1 (0.6)	1	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=65	0			0			0		
Nervous system disorders									
<65	6	(6.7)	9 7.4	27	(16.3)	41 17.9	5	(5.3)	5 3.8
>=65	2	(20.0)	2 14.5	8	(24.2)	11 23.9	1	(16.7)	1 11.7
Neurological disorders NEC									
<65	5	(5.6)	7 5.7	16	(9.6)	26 11.4	2	(2.1)	2 1.5
>=65	1	(10.0)	1 7.2	6	(18.2)	7 15.2	1	(16.7)	1 11.7
Dizziness									
<65	2	(2.2)	4 3.3	10	(6.0)	14 6.1	0		
>=65	1	(10.0)	1 7.2	4	(12.1)	5 10.9	0		
Hypoaesthesia									
<65	2	(2.2)	2 1.6	2	(1.2)	3 1.3	0		
>=65	0			1	(3.0)	1 2.2	0		
Neurological symptom									
<65	0			0			0		
>=65	0			1	(3.0)	1 2.2	0		
Dizziness postural									
<65	0			1	(0.6)	2 0.9	0		
>=65	0			0			0		
Dysaesthesia									
<65	0			1	(0.6)	2 0.9	0		
>=65	0			0			0		
Dysgeusia									
<65	0			1	(0.6)	1 0.4	0		
>=65	0			0			0		
Neuralgia									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	0		
>=65	0			0			0		
Paraesthesia									
<65	0			1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Somnolence									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Taste disorder									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Intercostal neuralgia									
<65	0			0			0		
>=65	0			0			1 (16.7)	1	11.7
Sensory loss									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Headaches									
<65	1 (1.1)	1	0.8	8 (4.8)	10	4.4	3 (3.2)	3	2.3
>=65	1 (10.0)	1	7.2	2 (6.1)	2	4.3	0		
Headache									
<65	1 (1.1)	1	0.8	8 (4.8)	10	4.4	3 (3.2)	3	2.3
>=65	1 (10.0)	1	7.2	2 (6.1)	2	4.3	0		
Spinal cord and nerve root disorders									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	0		
>=65	0			1 (3.0)	1	2.2	0		
Sciatica									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	0		
>=65	0			1 (3.0)	1	2.2	0		
Central nervous system vascular disorders									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Lacunar infarction									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Cranial nerve disorders (excl neoplasms)									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Parosmia									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Neuromuscular disorders									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Autonomic nervous system imbalance									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Peripheral neuropathies									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Carpal tunnel syndrome									
<65	0			1 (0.6)	1	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Musculoskeletal and connective tissue disorders									
<65	19 (21.1)	25	20.4	37 (22.3)	45	19.7	23 (24.2)	33	24.8
>=65	5 (50.0)	9	65.2	6 (18.2)	7	15.2	1 (16.7)	1	11.7
Musculoskeletal and connective tissue disorders NEC									
<65	7 (7.8)	9	7.4	18 (10.8)	19	8.3	12 (12.6)	14	10.5
>=65	3 (30.0)	5	36.2	4 (12.1)	4	8.7	1 (16.7)	1	11.7
Back pain									
<65	6 (6.7)	8	6.5	16 (9.6)	17	7.4	8 (8.4)	10	7.5
>=65	2 (20.0)	4	29.0	3 (9.1)	3	6.5	1 (16.7)	1	11.7
Pain in extremity									
<65	1 (1.1)	1	0.8	0			2 (2.1)	2	1.5
>=65	0			1 (3.0)	1	2.2	0		
Musculoskeletal discomfort									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Neck pain									
<65	0			1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Musculoskeletal pain									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Musculoskeletal stiffness									
<65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	1 (10.0)	1	7.2	0			0		
Muscle disorders									
<65	1 (1.1)	1	0.8	7 (4.2)	7	3.1	1 (1.1)	1	0.8
>=65	0			2 (6.1)	2	4.3	0		
Myalgia									
<65	1 (1.1)	1	0.8	3 (1.8)	3	1.3	1 (1.1)	1	0.8
>=65	0			1 (3.0)	1	2.2	0		
Fibromyalgia									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Muscle spasms									
<65	0			3 (1.8)	3	1.3	0		
>=65	0			0			0		
Rhabdomyolysis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Joint disorders									
<65	12 (13.3)	13	10.6	12 (7.2)	12	5.2	11 (11.6)	16	12.0
>=65	3 (30.0)	4	29.0	1 (3.0)	1	2.2	0		
Periarthritis									
<65	1 (1.1)	1	0.8	3 (1.8)	3	1.3	1 (1.1)	1	0.8
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Arthralgia									
<65	7 (7.8)	7	5.7	5 (3.0)	5	2.2	6 (6.3)	9	6.8
>=65	2 (20.0)	3	21.7	0			0		
Osteoarthritis									
<65	2 (2.2)	2	1.6	2 (1.2)	2	0.9	2 (2.1)	2	1.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Rotator cuff syndrome									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Spinal osteoarthritis									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Arthritis									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Articular calcification									
<65	0			0			1 (1.1)	2	1.5
>=65	0			0			0		
Tendon, ligament and cartilage disorders									
<65	1 (1.1)	1	0.8	3 (1.8)	4	1.7	0		
>=65	0			0			0		
Tendonitis									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	0		
>=65	0			0			0		
Trigger finger									
<65	0			1 (0.6)	2	0.9	0		
>=65	0			0			0		
Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Intervertebral disc protrusion									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Spinal stenosis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Synovial and bursal disorders									
<65	0			1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Bursitis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Synovitis									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Injury, poisoning and procedural complications									
<65	13 (14.4)	17	13.9	21 (12.7)	22	9.6	9 (9.5)	11	8.3
>=65	2 (20.0)	2	14.5	4 (12.1)	4	8.7	3 (50.0)	3	35.0
Injuries NEC									
<65	5 (5.6)	9	7.4	14 (8.4)	15	6.6	7 (7.4)	8	6.0
>=65	1 (10.0)	1	7.2	3 (9.1)	3	6.5	2 (33.3)	2	23.3
Arthropod bite									
<65	0			0			1 (1.1)	1	0.8
>=65	0			1 (3.0)	1	2.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Limb injury									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Tooth fracture									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Contusion									
<65	1 (1.1)	1	0.8	4 (2.4)	4	1.7	0		
>=65	1 (10.0)	1	7.2	0			0		
Arthropod sting									
<65	0			3 (1.8)	3	1.3	0		
>=65	0			0			0		
Ligament sprain									
<65	3 (3.3)	4	3.3	3 (1.8)	3	1.3	1 (1.1)	1	0.8
>=65	0			0			1 (16.7)	1	11.7
Tendon rupture									
<65	0			2 (1.2)	2	0.9	1 (1.1)	1	0.8
>=65	0			0			0		
Epicondylitis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Post-traumatic neck syndrome									
<65	0			1 (0.6)	1	0.4	2 (2.1)	2	1.5
>=65	0			0			0		
Subcutaneous haematoma									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Limb crushing injury									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Muscle contusion									
<65	0			0			2 (2.1)	2	1.5
>=65	0			0			0		
Muscle strain									
<65	1 (1.1)	2	1.6	0			0		
>=65	0			0			0		
Road traffic accident									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Skin laceration									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Subdural haematoma									
<65	0			0			0		
>=65	0			0			1 (16.7)	1	11.7
Medication errors and other product use errors and issues									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	0		
>=65	0			1 (3.0)	1	2.2	0		
Product administration error									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			1 (3.0)	1	2.2	0		
Accidental overdose									
<65	0			1 (0.6)	1	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Bone and joint injuries									
<65	4 (4.4)	4	3.3	4 (2.4)	4	1.7	1 (1.1)	1	0.8
>=65	1 (10.0)	1	7.2	0			0		
Ankle fracture									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Meniscus injury									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	0		
>=65	0			0			0		
Radius fracture									
<65	0			1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Rib fracture									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	0		
>=65	1 (10.0)	1	7.2	0			0		
Fracture									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Joint injury									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Injuries by physical agents									
<65	3 (3.3)	3	2.5	2 (1.2)	2	0.9	2 (2.1)	2	1.5
>=65	0			0			1 (16.7)	1	11.7
Heat stroke									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Thermal burn									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Heat illness									
<65	1 (1.1)	1	0.8	0			1 (1.1)	1	0.8
>=65	0			0			1 (16.7)	1	11.7
Respiratory, thoracic and mediastinal disorders									
<65	10 (11.1)	13	10.6	20 (12.0)	21	9.2	13 (13.7)	19	14.3
>=65	0			4 (12.1)	6	13.0	0		
Respiratory tract signs and symptoms									
<65	6 (6.7)	7	5.7	11 (6.6)	11	4.8	11 (11.6)	15	11.3
>=65	0			4 (12.1)	6	13.0	0		
Upper respiratory tract inflammation									
<65	5 (5.6)	6	4.9	8 (4.8)	8	3.5	9 (9.5)	13	9.8
>=65	0			3 (9.1)	5	10.9	0		
Hiccups									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Oropharyngeal pain									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	2 (2.1)	2	1.5
>=65	0			0			0		
Rhinorrhoea									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Upper respiratory tract disorders (excl infections)									
<65	2 (2.2)	2	1.6	7 (4.2)	7	3.1	1 (1.1)	2	1.5
>=65	0			0			0		
Rhinitis allergic									
<65	1 (1.1)	1	0.8	6 (3.6)	6	2.6	1 (1.1)	2	1.5
>=65	0			0			0		
Epistaxis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Vasomotor rhinitis									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Respiratory disorders NEC									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	1 (1.1)	1	0.8
>=65	0			0			0		
Cough									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Dyspnoea									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Bronchial disorders (excl neoplasms)									
<65	3 (3.3)	3	2.5	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Asthma									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Cough variant asthma									
<65	2 (2.2)	2	1.6	0			1 (1.1)	1	0.8
>=65	0			0			0		
Metabolism and nutrition disorders									
<65	5 (5.6)	5	4.1	19 (11.4)	20	8.7	7 (7.4)	9	6.8
>=65	1 (10.0)	1	7.2	4 (12.1)	4	8.7	1 (16.7)	2	23.3
Appetite and general nutritional disorders									
<65	4 (4.4)	4	3.3	9 (5.4)	9	3.9	0		
>=65	1 (10.0)	1	7.2	4 (12.1)	4	8.7	0		
Decreased appetite									
<65	4 (4.4)	4	3.3	9 (5.4)	9	3.9	0		
>=65	1 (10.0)	1	7.2	4 (12.1)	4	8.7	0		
Purine and pyrimidine metabolism disorders									
<65	1 (1.1)	1	0.8	4 (2.4)	4	1.7	3 (3.2)	3	2.3
>=65	0			0			1 (16.7)	2	23.3
Gout									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	0		
>=65	0			0			1 (16.7)	2	23.3
Hyperuricaemia									
<65	0			2 (1.2)	2	0.9	3 (3.2)	3	2.3
>=65	0			0			0		
Glucose metabolism disorders (incl diabetes mellitus)									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			2 (1.2)	3	1.3	3 (3.2)	4	3.0
>=65	0			0			0		
Diabetes mellitus									
<65	0			1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Type 2 diabetes mellitus									
<65	0			1 (0.6)	2	0.9	1 (1.1)	1	0.8
>=65	0			0			0		
Glucose tolerance impaired									
<65	0			0			1 (1.1)	2	1.5
>=65	0			0			0		
Lipid metabolism disorders									
<65	0			2 (1.2)	2	0.9	2 (2.1)	2	1.5
>=65	0			0			0		
Dyslipidaemia									
<65	0			2 (1.2)	2	0.9	2 (2.1)	2	1.5
>=65	0			0			0		
Electrolyte and fluid balance conditions									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Dehydration									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Metabolism disorders NEC									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Hypercreatininaemia									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Investigations									
<65	11 (12.2)	14	11.4	11 (6.6)	14	6.1	9 (9.5)	11	8.3
>=65	2 (20.0)	2	14.5	5 (15.2)	6	13.0	0		
Cardiac and vascular investigations (excl enzyme tests)									
<65	2 (2.2)	2	1.6	1 (0.6)	1	0.4	0		
>=65	0			2 (6.1)	2	4.3	0		
Blood pressure decreased									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			2 (6.1)	2	4.3	0		
Electrocardiogram QRS complex prolonged									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Electrocardiogram QT prolonged									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Enzyme investigations NEC									
<65	4 (4.4)	4	3.3	5 (3.0)	6	2.6	2 (2.1)	2	1.5
>=65	0			1 (3.0)	1	2.2	0		
Blood creatine phosphokinase increased									
<65	4 (4.4)	4	3.3	5 (3.0)	6	2.6	2 (2.1)	2	1.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			1 (3.0)	1	2.2	0		
Hepatobiliary investigations									
<65	0			1 (0.6)	1	0.4	5 (5.3)	5	3.8
>=65	0			1 (3.0)	1	2.2	0		
Liver function test increased									
<65	0			0			2 (2.1)	2	1.5
>=65	0			1 (3.0)	1	2.2	0		
Aspartate aminotransferase increased									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Alanine aminotransferase increased									
<65	0			0			2 (2.1)	2	1.5
>=65	0			0			0		
Blood bilirubin increased									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Haematology investigations (incl blood groups)									
<65	1 (1.1)	2	1.6	0			0		
>=65	0			1 (3.0)	1	2.2	0		
Haemoglobin decreased									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Lymphocyte count decreased									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
White blood cell count increased									

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Physical examination and organ system status topics									
<65	0			0			0		
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Weight decreased									
<65	0			0			0		
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Gastrointestinal investigations									
<65	4 (4.4)	4	3.3	4 (2.4)	5	2.2	0		
>=65	1 (10.0)	1	7.2	0			0		
Lipase increased									
<65	2 (2.2)	2	1.6	4 (2.4)	4	1.7	0		
>=65	1 (10.0)	1	7.2	0			0		
Amylase increased									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	0		
>=65	0			0			0		
Occult blood positive									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Endocrine investigations (incl sex hormones)									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Blood thyroid stimulating hormone decreased									

Adverse events with onset prior to randomisation are not included.
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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<65	0			1	(0.6)	1 0.4	0		
>=65	0			0			0		
Lipid analyses									
<65	0			0			1	(1.1)	1 0.8
>=65	0			0			0		
Blood triglycerides increased									
<65	0			0			1	(1.1)	1 0.8
>=65	0			0			0		
Metabolic, nutritional and blood gas investigations									
<65	0			0			2	(2.1)	2 1.5
>=65	0			0			0		
Blood uric acid increased									
<65	0			0			1	(1.1)	1 0.8
>=65	0			0			0		
Glycosylated haemoglobin increased									
<65	0			0			1	(1.1)	1 0.8
>=65	0			0			0		
Protein and chemistry analyses NEC									
<65	1	(1.1)	1 0.8	0			1	(1.1)	1 0.8
>=65	0			0			0		
C-reactive protein increased									
<65	1	(1.1)	1 0.8	0			1	(1.1)	1 0.8
>=65	0			0			0		
Water, electrolyte and mineral investigations									
<65	1	(1.1)	1 0.8	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Blood potassium increased									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Skin and subcutaneous tissue disorders									
<65	10 (11.1)	18	14.7	21 (12.7)	26	11.4	11 (11.6)	14	10.5
>=65	3 (30.0)	4	29.0	3 (9.1)	4	8.7	0		
Epidermal and dermal conditions									
<65	8 (8.9)	11	9.0	14 (8.4)	16	7.0	8 (8.4)	10	7.5
>=65	2 (20.0)	2	14.5	3 (9.1)	3	6.5	0		
Eczema									
<65	3 (3.3)	3	2.5	3 (1.8)	3	1.3	2 (2.1)	2	1.5
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Pruritus									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	2 (2.1)	3	2.3
>=65	0			1 (3.0)	1	2.2	0		
Dermatitis contact									
<65	0			0			3 (3.2)	3	2.3
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Dermatitis									
<65	0			2 (1.2)	3	1.3	0		
>=65	0			0			0		
Eczema asteatotic									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	0		
>=65	0			0			0		
Dermatitis atopic									

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			1 (0.6)	2	0.9	0		
>=65	0			0			0		
Dyshidrotic eczema									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Erythema									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Rash									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Stasis dermatitis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Drug eruption									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Dry skin									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Pain of skin									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Rash pruritic									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Seborrhoeic dermatitis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Xanthelasma									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Skin appendage conditions									
<65	4 (4.4)	4	3.3	7 (4.2)	7	3.1	2 (2.1)	2	1.5
>=65	0			0			0		
Alopecia									
<65	2 (2.2)	2	1.6	2 (1.2)	2	0.9	0		
>=65	0			0			0		
Alopecia areata									
<65	0			2 (1.2)	2	0.9	0		
>=65	0			0			0		
Acne									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	0		
>=65	0			0			0		
Ingrowing nail									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Miliaria									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	2 (2.1)	2	1.5
>=65	0			0			0		
Angioedema and urticaria									
<65	2 (2.2)	2	1.6	1 (0.6)	1	0.4	2 (2.1)	2	1.5
>=65	1 (10.0)	2	14.5	1 (3.0)	1	2.2	0		
Urticaria									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	2 (2.2)	2	1.6	1 (0.6)	1	0.4	2 (2.1)	2	1.5
>=65	1 (10.0)	2	14.5	1 (3.0)	1	2.2	0		
Cornification and dystrophic skin disorders									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	0		
>=65	0			0			0		
Hyperkeratosis									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	0		
>=65	0			0			0		
Xeroderma									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Eye disorders									
<65	4 (4.4)	5	4.1	13 (7.8)	15	6.6	7 (7.4)	8	6.0
>=65	2 (20.0)	2	14.5	4 (12.1)	4	8.7	0		
Anterior eye structural change, deposit and degeneration									
<65	0			1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			2 (6.1)	2	4.3	0		
Cataract									
<65	0			1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			2 (6.1)	2	4.3	0		
Ocular haemorrhages and vascular disorders NEC									
<65	0			0			1 (1.1)	1	0.8
>=65	0			1 (3.0)	1	2.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Optic disc haemorrhage									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Conjunctival haemorrhage									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Ocular structural change, deposit and degeneration NEC									
<65	1 (1.1)	1	0.8	0			1 (1.1)	1	0.8
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Retinal tear									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			1 (3.0)	1	2.2	0		
Macular fibrosis									
<65	0			0			0		
>=65	1 (10.0)	1	7.2	0			0		
Rhegmatogenous retinal detachment									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Retina, choroid and vitreous haemorrhages and vascular disorders									
<65	2 (2.2)	3	2.5	5 (3.0)	5	2.2	2 (2.1)	2	1.5
>=65	0			0			0		
Diabetic retinopathy									
<65	1 (1.1)	2	1.6	3 (1.8)	3	1.3	2 (2.1)	2	1.5
>=65	0			0			0		
Retinal exudates									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Retinal haemorrhage									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Retinopathy									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Vision disorders									
<65	0			4 (2.4)	4	1.7	0		
>=65	0			0			0		
Amblyopia									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Optic nerve disorder									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Presbyopia									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Visual acuity reduced									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Ocular infections, irritations and inflammations									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	1 (1.1)	1	0.8
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Conjunctivitis allergic									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Ocular hyperaemia									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Eye disorders NEC									
<65	0			1 (0.6)	2	0.9	1 (1.1)	1	0.8
>=65	1 (10.0)	1	7.2	0			0		
Lacrimal disorder									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Lacrimation increased									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Dry eye									
<65	0			0			1 (1.1)	1	0.8
>=65	1 (10.0)	1	7.2	0			0		
Glaucoma and ocular hypertension									
<65	0			1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Glaucoma									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Open angle glaucoma									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
General disorders and administration site conditions									
<65	3 (3.3)	5	4.1	12 (7.2)	30	13.1	2 (2.1)	2	1.5
>=65	0			4 (12.1)	5	10.9	0		
General system disorders NEC									
<65	2 (2.2)	4	3.3	9 (5.4)	15	6.6	1 (1.1)	1	0.8
>=65	0			2 (6.1)	3	6.5	0		
Malaise									
<65	1 (1.1)	1	0.8	3 (1.8)	5	2.2	0		
>=65	0			2 (6.1)	3	6.5	0		
Fatigue									
<65	0			3 (1.8)	3	1.3	0		
>=65	0			0			0		
Feeling abnormal									
<65	0			2 (1.2)	2	0.9	0		
>=65	0			0			0		
Influenza like illness									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Non-cardiac chest pain									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Oedema peripheral									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Pain									
<65	0			1 (0.6)	1	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Thirst									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Hangover									
<65	1 (1.1)	3	2.5	0			0		
>=65	0			0			0		
Hunger									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Administration site reactions									
<65	0			2 (1.2)	13	5.7	0		
>=65	0			2 (6.1)	2	4.3	0		
Injection site dermatitis									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Injection site discomfort									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Injection site erythema									
<65	0			2 (1.2)	13	5.7	0		
>=65	0			0			0		
Body temperature conditions									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	1 (1.1)	1	0.8
>=65	0			0			0		
Pyrexia									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Vascular disorders									
<65	1 (1.1)	1	0.8	9 (5.4)	9	3.9	4 (4.2)	4	3.0
>=65	1 (10.0)	1	7.2	2 (6.1)	2	4.3	0		
Decreased and nonspecific blood pressure disorders and shock									
<65	0			3 (1.8)	3	1.3	0		
>=65	0			2 (6.1)	2	4.3	0		
Hypotension									
<65	0			0			0		
>=65	0			2 (6.1)	2	4.3	0		
Orthostatic hypotension									
<65	0			3 (1.8)	3	1.3	0		
>=65	0			0			0		
Vascular hypertensive disorders									
<65	1 (1.1)	1	0.8	4 (2.4)	4	1.7	3 (3.2)	3	2.3
>=65	0			0			0		
Hypertension									
<65	1 (1.1)	1	0.8	4 (2.4)	4	1.7	3 (3.2)	3	2.3
>=65	0			0			0		
Arteriosclerosis, stenosis, vascular insufficiency and necrosis									
<65	0			2 (1.2)	2	0.9	1 (1.1)	1	0.8
>=65	0			0			0		
Arteriosclerosis									
<65	0			2 (1.2)	2	0.9	1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Embolism and thrombosis									
<65	0			0			0		
>=65	1 (10.0)	1	7.2	0			0		
Venous thrombosis limb									
<65	0			0			0		
>=65	1 (10.0)	1	7.2	0			0		
Hepatobiliary disorders									
<65	2 (2.2)	2	1.6	3 (1.8)	3	1.3	1 (1.1)	1	0.8
>=65	0			2 (6.1)	2	4.3	0		
Gallbladder disorders									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	0		
>=65	0			1 (3.0)	1	2.2	0		
Cholelithiasis									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			1 (3.0)	1	2.2	0		
Gallbladder polyp									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Hyperplastic cholecystopathy									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Hepatic and hepatobiliary disorders									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			1 (3.0)	1	2.2	0		
Hepatic function abnormal									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Hepatic cyst									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Alcoholic liver disease									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Hepatic steatosis									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Reproductive system and breast disorders									
<65	2 (2.2)	3	2.5	8 (4.8)	9	3.9	0		
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Prostatic disorders (excl infections and inflammations)									
<65	0			1 (0.6)	1	0.4	0		
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Benign prostatic hyperplasia									
<65	0			1 (0.6)	1	0.4	0		
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Menstrual cycle and uterine bleeding disorders									
<65	0			4 (2.4)	4	1.7	0		
>=65	0			0			0		
Dysmenorrhoea									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
<65	0				2	(1.2)	2	0.9	0			
>=65	0				0				0			
Menstrual disorder												
<65	0				1	(0.6)	1	0.4	0			
>=65	0				0				0			
Menstruation irregular												
<65	0				1	(0.6)	1	0.4	0			
>=65	0				0				0			
Breast disorders												
<65	0				1	(0.6)	1	0.4	0			
>=65	0				0				0			
Breast calcifications												
<65	0				1	(0.6)	1	0.4	0			
>=65	0				0				0			
Male reproductive tract infections and inflammations												
<65	0				1	(0.6)	2	0.9	0			
>=65	0				0				0			
Prostatitis												
<65	0				1	(0.6)	2	0.9	0			
>=65	0				0				0			
Menopause related conditions												
<65	0				1	(0.6)	1	0.4	0			
>=65	0				0				0			
Menopausal symptoms												
<65	0				1	(0.6)	1	0.4	0			
>=65	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Uterine, pelvic and broad ligament disorders									
<65	2 (2.2)	3	2.5	0			0		
>=65	0			0			0		
Endometrial hyperplasia									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Endometriosis									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Uterine haemorrhage									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Psychiatric disorders									
<65	4 (4.4)	4	3.3	5 (3.0)	5	2.2	1 (1.1)	1	0.8
>=65	0			1 (3.0)	1	2.2	0		
Sleep disorders and disturbances									
<65	3 (3.3)	3	2.5	3 (1.8)	3	1.3	0		
>=65	0			1 (3.0)	1	2.2	0		
Insomnia									
<65	3 (3.3)	3	2.5	3 (1.8)	3	1.3	0		
>=65	0			1 (3.0)	1	2.2	0		
Depressed mood disorders and disturbances									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Depression									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Mood disorders and disturbances NEC									
<65	0			1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Emotional disorder									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Listless									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Adjustment disorders (incl subtypes)									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Adjustment disorder									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Renal and urinary disorders									
<65	4 (4.4)	4	3.3	4 (2.4)	4	1.7	5 (5.3)	7	5.3
>=65	1 (10.0)	2	14.5	1 (3.0)	1	2.2	0		
Renal disorders (excl nephropathies)									
<65	0			1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			1 (3.0)	1	2.2	0		
Renal cyst									
<65	0			0			1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			1 (3.0)	1	2.2	0		
Azotaemia									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Urolithiases									
<65	3 (3.3)	3	2.5	2 (1.2)	2	0.9	3 (3.2)	5	3.8
>=65	0			0			0		
Ureterolithiasis									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	2 (2.1)	4	3.0
>=65	0			0			0		
Calculus urinary									
<65	2 (2.2)	2	1.6	0			1 (1.1)	1	0.8
>=65	0			0			0		
Urinary tract signs and symptoms									
<65	0			1 (0.6)	1	0.4	0		
>=65	1 (10.0)	2	14.5	0			0		
Hyperuricosuria									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Nocturia									
<65	0			0			0		
>=65	1 (10.0)	1	7.2	0			0		
Proteinuria									
<65	0			0			0		
>=65	1 (10.0)	1	7.2	0			0		
Nephropathies									
<65	1 (1.1)	1	0.8	0			1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=65	0			0			0		
Diabetic nephropathy									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Nephropathy toxic									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Cardiac disorders									
<65	1 (1.1)	1	0.8	3 (1.8)	3	1.3	3 (3.2)	3	2.3
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Cardiac arrhythmias									
<65	0			1 (0.6)	1	0.4	2 (2.1)	2	1.5
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Tachycardia									
<65	0			0			0		
>=65	0			1 (3.0)	1	2.2	0		
Ventricular extrasystoles									
<65	0			1 (0.6)	1	0.4	0		
>=65	1 (10.0)	1	7.2	0			0		
Arrhythmia									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Atrial fibrillation									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Cardiac disorders, signs and symptoms NEC									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Palpitations									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Coronary artery disorders									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Acute myocardial infarction									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Ear and labyrinth disorders									
<65	3 (3.3)	3	2.5	2 (1.2)	2	0.9	1 (1.1)	1	0.8
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Inner ear and VIIIth cranial nerve disorders									
<65	3 (3.3)	3	2.5	0			1 (1.1)	1	0.8
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Vertigo									
<65	2 (2.2)	2	1.6	0			1 (1.1)	1	0.8
>=65	1 (10.0)	1	7.2	1 (3.0)	1	2.2	0		
Tinnitus									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Hearing disorders												
<65	0				2	(1.2)	2	0.9	0			
>=65	0				0				0			
Deafness												
<65	0				1	(0.6)	1	0.4	0			
>=65	0				0				0			
Deafness neurosensory												
<65	0				1	(0.6)	1	0.4	0			
>=65	0				0				0			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)												
<65	1	(1.1)	1	0.8	1	(0.6)	1	0.4	0			
>=65	1	(10.0)	1	7.2	1	(3.0)	1	2.2	1	(16.7)	1	11.7
Gastrointestinal neoplasms benign												
<65	0				0				0			
>=65	0				1	(3.0)	1	2.2	0			
Intraductal papillary mucinous neoplasm												
<65	0				0				0			
>=65	0				1	(3.0)	1	2.2	0			
Reproductive neoplasms female benign												
<65	0				1	(0.6)	1	0.4	0			
>=65	0				0				0			
Uterine leiomyoma												
<65	0				1	(0.6)	1	0.4	0			
>=65	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Hepatobiliary neoplasms malignant and unspecified									
<65	0			0			0		
>=65	1	(10.0)	1 7.2	0			0		
Bile duct adenocarcinoma									
<65	0			0			0		
>=65	1	(10.0)	1 7.2	0			0		
Renal and urinary tract neoplasms malignant and unspecified									
<65	1	(1.1)	1 0.8	0			0		
>=65	0			0			0		
Clear cell renal cell carcinoma									
<65	1	(1.1)	1 0.8	0			0		
>=65	0			0			0		
Respiratory and mediastinal neoplasms malignant and unspecified									
<65	0			0			0		
>=65	0			0			1	(16.7)	1 11.7
Lung neoplasm malignant									
<65	0			0			0		
>=65	0			0			1	(16.7)	1 11.7
Blood and lymphatic system disorders									
<65	2	(2.2)	2 1.6	2	(1.2)	2 0.9	1	(1.1)	1 0.8
>=65	0			0			0		
Anaemias nonhaemolytic and marrow depression									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	1 (1.1)	1	0.8
>=65	0			0			0		
Iron deficiency anaemia									
<65	1 (1.1)	1	0.8	2 (1.2)	2	0.9	0		
>=65	0			0			0		
Anaemia									
<65	0			0			1 (1.1)	1	0.8
>=65	0			0			0		
Spleen, lymphatic and reticuloendothelial system disorders									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Lymphadenitis									
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Congenital, familial and genetic disorders									
<65	0			2 (1.2)	2	0.9	0		
>=65	0			0			0		
Gastrointestinal tract disorders congenital									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Diverticulitis Meckel's									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Skin and subcutaneous tissue disorders congenital									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Birth mark									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Endocrine disorders									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Thyroid gland disorders									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Hyperthyroidism									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Immune system disorders									
<65	2 (2.2)	2	1.6	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Allergic conditions									
<65	2 (2.2)	2	1.6	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Seasonal allergy									
<65	1 (1.1)	1	0.8	1 (0.6)	1	0.4	1 (1.1)	1	0.8
>=65	0			0			0		
Food allergy									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by age at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<65	1 (1.1)	1	0.8	0			0		
>=65	0			0			0		
Surgical and medical procedures									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Gastrointestinal therapeutic procedures									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		
Large intestinal polypectomy									
<65	0			1 (0.6)	1	0.4	0		
>=65	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

13 Adverse events by body weight at baseline - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
<90	339	440.9			162	208.3		
90-<100	267	352.7			151	190.2		
100-<115	331	429.8			163	211.0		
>=115	369	482.7			179	220.1		
Subjects with events	N	(%)	E	R	N	(%)	E	R
Events								
<90	311	(91.7)	2600	589.7	129	(79.6)	783	375.9
90-<100	232	(86.9)	1871	530.4	130	(86.1)	689	362.3
100-<115	299	(90.3)	2379	553.5	149	(91.4)	908	430.3
>=115	329	(89.2)	2808	581.8	158	(88.3)	922	419.0
Serious								
Yes								
<90	30	(8.8)	39	8.8	10	(6.2)	13	6.2
90-<100	29	(10.9)	35	9.9	9	(6.0)	9	4.7
100-<115	28	(8.5)	35	8.1	11	(6.7)	13	6.2
>=115	41	(11.1)	55	11.4	12	(6.7)	18	8.2
No								
<90	311	(91.7)	2561	580.9	128	(79.0)	770	369.6
90-<100	231	(86.5)	1836	520.5	128	(84.8)	680	357.6
100-<115	298	(90.0)	2344	545.4	148	(90.8)	895	424.2
>=115	329	(89.2)	2753	570.4	156	(87.2)	904	410.8
Severity								
Severe								
<90	36	(10.6)	67	15.2	12	(7.4)	13	6.2

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by body weight at baseline - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Severity								
Severe								
90-<100	30	(11.2)	49	13.9	9	(6.0)	9	4.7
100-<115	36	(10.9)	54	12.6	13	(8.0)	25	11.8
>=115	41	(11.1)	72	14.9	10	(5.6)	21	9.5
Moderate								
<90	180	(53.1)	650	147.4	70	(43.2)	190	91.2
90-<100	145	(54.3)	503	142.6	65	(43.0)	152	79.9
100-<115	189	(57.1)	667	155.2	87	(53.4)	296	140.3
>=115	209	(56.6)	792	164.1	89	(49.7)	225	102.2
Mild								
<90	286	(84.4)	1883	427.1	117	(72.2)	580	278.4
90-<100	206	(77.2)	1319	373.9	122	(80.8)	528	277.6
100-<115	277	(83.7)	1658	385.8	125	(76.7)	587	278.2
>=115	310	(84.0)	1944	402.8	143	(79.9)	676	307.2
Relationship to trial product								
Missing								
<90	3	(0.9)	3	0.7	2	(1.2)	2	1.0
90-<100	4	(1.5)	9	2.6	1	(0.7)	2	1.1
100-<115	4	(1.2)	5	1.2	0			
>=115	13	(3.5)	13	2.7	4	(2.2)	4	1.8
Probable								
<90	146	(43.1)	505	114.5	38	(23.5)	108	51.8
90-<100	107	(40.1)	441	125.0	34	(22.5)	71	37.3
100-<115	163	(49.2)	606	141.0	38	(23.3)	72	34.1
>=115	155	(42.0)	596	123.5	37	(20.7)	79	35.9
Possible								
<90	192	(56.6)	838	190.1	51	(31.5)	110	52.8
90-<100	145	(54.3)	552	156.5	53	(35.1)	119	62.6

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by body weight at baseline - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Relationship to trial product								
Possible								
100-<115	182	(55.0)	533	124.0	60	(36.8)	181	85.8
>=115	207	(56.1)	777	161.0	59	(33.0)	145	65.9
Unlikely								
<90	269	(79.4)	1254	284.4	117	(72.2)	563	270.3
90-<100	207	(77.5)	869	246.4	125	(82.8)	497	261.3
100-<115	256	(77.3)	1235	287.3	143	(87.7)	655	310.4
>=115	300	(81.3)	1422	294.6	151	(84.4)	694	315.4
Outcome								
Fatal								
<90	0				1	(0.6)	1	0.5
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Recovered								
<90	304	(89.7)	2305	522.8	124	(76.5)	657	315.4
90-<100	225	(84.3)	1599	453.3	123	(81.5)	555	291.8
100-<115	295	(89.1)	2091	486.5	144	(88.3)	751	355.9
>=115	316	(85.6)	2444	506.3	154	(86.0)	747	339.4
Recovering								
<90	15	(4.4)	22	5.0	8	(4.9)	9	4.3
90-<100	17	(6.4)	26	7.4	7	(4.6)	15	7.9
100-<115	7	(2.1)	17	4.0	6	(3.7)	9	4.3
>=115	20	(5.4)	26	5.4	4	(2.2)	4	1.8
Recovered With Sequelae								
<90	2	(0.6)	2	0.5	2	(1.2)	2	1.0
90-<100	3	(1.1)	6	1.7	0			
100-<115	3	(0.9)	7	1.6	1	(0.6)	2	0.9

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by body weight at baseline - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Outcome								
Recovered With Sequelae								
>=115	3	(0.8)	4	0.8	1	(0.6)	1	0.5
Not Recovered								
<90	121	(35.7)	271	61.5	59	(36.4)	114	54.7
90-<100	117	(43.8)	238	67.5	62	(41.1)	118	62.0
100-<115	113	(34.1)	263	61.2	67	(41.1)	146	69.2
>=115	162	(43.9)	334	69.2	77	(43.0)	170	77.2
Unknown								
<90	0				0			
90-<100	1	(0.4)	2	0.6	1	(0.7)	1	0.5
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Leading to								
Permanent treatment discontinuation								
<90	31	(9.1)	40	9.1	6	(3.7)	7	3.4
90-<100	18	(6.7)	22	6.2	3	(2.0)	5	2.6
100-<115	23	(6.9)	32	7.4	6	(3.7)	6	2.8
>=115	20	(5.4)	29	6.0	5	(2.8)	5	2.3
Temporary interruption of trial product								
<90	37	(10.9)	65	14.7	5	(3.1)	7	3.4
90-<100	27	(10.1)	57	16.2	6	(4.0)	7	3.7
100-<115	28	(8.5)	65	15.1	6	(3.7)	16	7.6
>=115	34	(9.2)	78	16.2	9	(5.0)	14	6.4
Dose reduction of trial product								
<90	43	(12.7)	83	18.8	2	(1.2)	3	1.4
90-<100	24	(9.0)	41	11.6	0			
100-<115	31	(9.4)	59	13.7	1	(0.6)	4	1.9
>=115	26	(7.0)	42	8.7	1	(0.6)	2	0.9

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

14 Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects and exposure	N		PYE		N		PYE	
<90	339		440.9		162		208.3	
90-<100	267		352.7		151		190.2	
100-<115	331		429.8		163		211.0	
>=115	369		482.7		179		220.1	
Subjects with events	N	(%)	E	R	N	(%)	E	R
Adverse events								
<90	311	(91.7)	2600	589.7	129	(79.6)	783	375.9
90-<100	232	(86.9)	1871	530.4	130	(86.1)	689	362.3
100-<115	299	(90.3)	2379	553.5	149	(91.4)	908	430.3
>=115	329	(89.2)	2808	581.8	158	(88.3)	922	419.0
Gastrointestinal disorders								
<90	249	(73.5)	1163	263.8	77	(47.5)	173	83.0
90-<100	187	(70.0)	830	235.3	67	(44.4)	149	78.3
100-<115	251	(75.8)	1069	248.7	84	(51.5)	218	103.3
>=115	282	(76.4)	1247	258.4	86	(48.0)	199	90.4
Gastrointestinal signs and symptoms								
<90	209	(61.7)	729	165.4	48	(29.6)	97	46.6
90-<100	166	(62.2)	516	146.3	44	(29.1)	82	43.1
100-<115	210	(63.4)	684	159.1	49	(30.1)	105	49.8
>=115	239	(64.8)	785	162.6	60	(33.5)	111	50.4
Nausea								
<90	153	(45.1)	286	64.9	26	(16.0)	32	15.4
90-<100	122	(45.7)	236	66.9	22	(14.6)	31	16.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	150 (45.3)	283	65.8	30 (18.4)	36	17.1
>=115	152 (41.2)	263	54.5	36 (20.1)	47	21.4
Vomiting						
<90	85 (25.1)	185	42.0	8 (4.9)	10	4.8
90-<100	62 (23.2)	111	31.5	12 (7.9)	14	7.4
100-<115	82 (24.8)	155	36.1	12 (7.4)	13	6.2
>=115	95 (25.7)	185	38.3	11 (6.1)	15	6.8
Dyspepsia						
<90	31 (9.1)	40	9.1	5 (3.1)	6	2.9
90-<100	23 (8.6)	29	8.2	6 (4.0)	8	4.2
100-<115	36 (10.9)	51	11.9	8 (4.9)	10	4.7
>=115	45 (12.2)	59	12.2	4 (2.2)	6	2.7
Abdominal pain						
<90	34 (10.0)	52	11.8	12 (7.4)	14	6.7
90-<100	24 (9.0)	28	7.9	7 (4.6)	8	4.2
100-<115	35 (10.6)	45	10.5	7 (4.3)	8	3.8
>=115	37 (10.0)	50	10.4	10 (5.6)	11	5.0
Abdominal pain upper						
<90	38 (11.2)	56	12.7	10 (6.2)	10	4.8
90-<100	21 (7.9)	33	9.4	7 (4.6)	9	4.7
100-<115	26 (7.9)	30	7.0	9 (5.5)	9	4.3
>=115	40 (10.8)	57	11.8	9 (5.0)	9	4.1
Eructation						
<90	28 (8.3)	39	8.8	1 (0.6)	1	0.5
90-<100	20 (7.5)	20	5.7	1 (0.7)	1	0.5
100-<115	33 (10.0)	39	9.1	1 (0.6)	1	0.5
>=115	31 (8.4)	41	8.5	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Abdominal distension						
<90	24 (7.1)	25	5.7	11 (6.8)	15	7.2
90-<100	19 (7.1)	27	7.7	4 (2.6)	4	2.1
100-<115	25 (7.6)	29	6.7	9 (5.5)	12	5.7
>=115	28 (7.6)	54	11.2	7 (3.9)	11	5.0
Flatulence						
<90	6 (1.8)	7	1.6	3 (1.9)	3	1.4
90-<100	11 (4.1)	12	3.4	5 (3.3)	5	2.6
100-<115	25 (7.6)	30	7.0	8 (4.9)	8	3.8
>=115	23 (6.2)	35	7.3	5 (2.8)	6	2.7
Abdominal discomfort						
<90	17 (5.0)	26	5.9	3 (1.9)	3	1.4
90-<100	11 (4.1)	12	3.4	1 (0.7)	1	0.5
100-<115	11 (3.3)	11	2.6	2 (1.2)	2	0.9
>=115	17 (4.6)	30	6.2	3 (1.7)	3	1.4
Abdominal pain lower						
<90	4 (1.2)	4	0.9	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	0		
100-<115	3 (0.9)	3	0.7	1 (0.6)	1	0.5
>=115	3 (0.8)	3	0.6	2 (1.1)	2	0.9
Gastrointestinal pain						
<90	1 (0.3)	1	0.2	0		
90-<100	2 (0.7)	3	0.9	0		
100-<115	0			0		
>=115	0			0		
Regurgitation						
<90	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	2	0.5	0		
>=115	0			0		
Epigastric discomfort						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Faeces soft						
<90	1 (0.3)	2	0.5	2 (1.2)	2	1.0
90-<100	0			1 (0.7)	1	0.5
100-<115	0			2 (1.2)	2	0.9
>=115	2 (0.5)	2	0.4	0		
Retching						
<90	0			0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Dysphagia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Faeces discoloured						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			1 (0.6)	1	0.5
Breath odour						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	2	0.5	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Gastrointestinal sounds abnormal						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Faeces hard						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Oesophageal pain						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Abnormal faeces						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Abdominal tenderness						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Aerophagia								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Gastrointestinal motility and defaecation conditions								
<90	155	(45.7)	336	76.2	36	(22.2)	48	23.0
90-<100	114	(42.7)	230	65.2	37	(24.5)	52	27.3
100-<115	170	(51.4)	320	74.5	51	(31.3)	83	39.3
>=115	187	(50.7)	385	79.8	42	(23.5)	56	25.4
Diarrhoea								
<90	98	(28.9)	198	44.9	22	(13.6)	26	12.5
90-<100	76	(28.5)	139	39.4	18	(11.9)	25	13.1
100-<115	108	(32.6)	181	42.1	39	(23.9)	56	26.5
>=115	130	(35.2)	248	51.4	25	(14.0)	31	14.1
Constipation								
<90	82	(24.2)	110	25.0	13	(8.0)	17	8.2
90-<100	51	(19.1)	65	18.4	18	(11.9)	20	10.5
100-<115	86	(26.0)	107	24.9	14	(8.6)	18	8.5
>=115	87	(23.6)	108	22.4	17	(9.5)	18	8.2
Gastrooesophageal reflux disease								
<90	23	(6.8)	25	5.7	3	(1.9)	3	1.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	15 (5.6)	19	5.4	6 (4.0)	6	3.2
100-<115	26 (7.9)	28	6.5	6 (3.7)	7	3.3
>=115	18 (4.9)	20	4.1	5 (2.8)	5	2.3
Irritable bowel syndrome						
<90	0			1 (0.6)	2	1.0
90-<100	1 (0.4)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	4 (1.1)	4	0.8	0		
Frequent bowel movements						
<90	1 (0.3)	1	0.2	0		
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	0		
Dyschezia						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Impaired gastric emptying						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Gastrointestinal hypermotility						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Bowel movement irregularity						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Gastrointestinal motility disorder						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Change of bowel habit						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Defaecation urgency						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Infrequent bowel movements						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Oesophageal achalasia						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Gastrointestinal inflammatory conditions						
<90	19 (5.6)	28	6.4	4 (2.5)	4	1.9
90-<100	26 (9.7)	38	10.8	1 (0.7)	1	0.5
100-<115	14 (4.2)	16	3.7	4 (2.5)	4	1.9
>=115	12 (3.3)	12	2.5	3 (1.7)	4	1.8
Gastritis						
<90	14 (4.1)	22	5.0	3 (1.9)	3	1.4
90-<100	19 (7.1)	27	7.7	0		
100-<115	10 (3.0)	11	2.6	1 (0.6)	1	0.5
>=115	7 (1.9)	7	1.5	2 (1.1)	3	1.4
Colitis						
<90	1 (0.3)	2	0.5	0		
90-<100	3 (1.1)	4	1.1	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Reflux gastritis						
<90	0			0		
90-<100	3 (1.1)	3	0.9	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Oesophagitis						
<90	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Duodenitis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Chronic gastritis						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Gastrointestinal inflammation						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Enteritis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Crohn's disease						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Eosinophilic oesophagitis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Gastroenteritis eosinophilic						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Colitis ischaemic						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Epiploic appendagitis						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Inflammatory bowel disease						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Gastrointestinal conditions NEC						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	13 (3.8)	23	5.2	4 (2.5)	5	2.4
90-<100	16 (6.0)	17	4.8	2 (1.3)	3	1.6
100-<115	9 (2.7)	10	2.3	5 (3.1)	7	3.3
>=115	10 (2.7)	17	3.5	1 (0.6)	1	0.5
Hyperchlorhydria						
<90	9 (2.7)	18	4.1	1 (0.6)	2	1.0
90-<100	5 (1.9)	6	1.7	1 (0.7)	2	1.1
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	4 (1.1)	11	2.3	0		
Food poisoning						
<90	3 (0.9)	3	0.7	1 (0.6)	1	0.5
90-<100	7 (2.6)	7	2.0	0		
100-<115	4 (1.2)	4	0.9	3 (1.8)	5	2.4
>=115	4 (1.1)	4	0.8	0		
Gastrointestinal disorder						
<90	1 (0.3)	2	0.5	2 (1.2)	2	1.0
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	2 (0.6)	3	0.7	0		
>=115	0			1 (0.6)	1	0.5
Anal fistula						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Gastric mucosal hypertrophy						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Functional gastrointestinal disorder						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Barrett's oesophagus						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Gastrointestinal vascular conditions						
<90	8 (2.4)	8	1.8	3 (1.9)	3	1.4
90-<100	8 (3.0)	9	2.6	1 (0.7)	1	0.5
100-<115	7 (2.1)	8	1.9	0		
>=115	5 (1.4)	5	1.0	1 (0.6)	1	0.5
Haemorrhoids						
<90	8 (2.4)	8	1.8	1 (0.6)	1	0.5
90-<100	7 (2.6)	7	2.0	1 (0.7)	1	0.5
100-<115	7 (2.1)	8	1.9	0		
>=115	4 (1.1)	4	0.8	1 (0.6)	1	0.5
Haemorrhoidal haemorrhage						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	2	0.6	0		
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Haemorrhoids thrombosed						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Salivary gland conditions						
<90	10 (2.9)	10	2.3	0		
90-<100	4 (1.5)	4	1.1	1 (0.7)	1	0.5
100-<115	4 (1.2)	4	0.9	2 (1.2)	2	0.9
>=115	9 (2.4)	9	1.9	5 (2.8)	6	2.7
Dry mouth						
<90	10 (2.9)	10	2.3	0		
90-<100	4 (1.5)	4	1.1	1 (0.7)	1	0.5
100-<115	3 (0.9)	3	0.7	2 (1.2)	2	0.9
>=115	8 (2.2)	8	1.7	4 (2.2)	5	2.3
Salivary gland calculus						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Salivary gland cyst						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Salivary gland enlargement						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Dental and gingival conditions						
<90	5 (1.5)	6	1.4	6 (3.7)	8	3.8
90-<100	2 (0.7)	3	0.9	6 (4.0)	6	3.2
100-<115	9 (2.7)	9	2.1	9 (5.5)	9	4.3
>=115	11 (3.0)	14	2.9	8 (4.5)	9	4.1
Toothache						
<90	2 (0.6)	2	0.5	4 (2.5)	5	2.4
90-<100	2 (0.7)	3	0.9	2 (1.3)	2	1.1
100-<115	4 (1.2)	4	0.9	4 (2.5)	4	1.9
>=115	9 (2.4)	11	2.3	7 (3.9)	7	3.2
Dental caries						
<90	2 (0.6)	3	0.7	2 (1.2)	2	1.0
90-<100	0			3 (2.0)	3	1.6
100-<115	1 (0.3)	1	0.2	4 (2.5)	4	1.9
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Gingival bleeding						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Gingival disorder						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Periodontal disease						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Tooth loss						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Gingival pain						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Noninfective gingivitis						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Tooth impacted						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Dental necrosis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Dental pulp disorder						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Tooth disorder						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Gastrointestinal haemorrhages NEC						
<90	7 (2.1)	7	1.6	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	4 (1.2)	4	0.9	2 (1.2)	3	1.4
>=115	3 (0.8)	4	0.8	3 (1.7)	3	1.4
Rectal haemorrhage						
<90	2 (0.6)	2	0.5	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	3 (0.9)	3	0.7	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Haematochezia						
<90	4 (1.2)	4	0.9	0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	1 (0.3)	1	0.2	1 (0.6)	2	0.9
>=115	2 (0.5)	2	0.4	2 (1.1)	2	0.9
Lower gastrointestinal haemorrhage						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Haematemesis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Melaena						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Upper gastrointestinal haemorrhage						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Benign neoplasms gastrointestinal						
<90	3 (0.9)	3	0.7	1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	2 (1.1)	2	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Large intestine polyp						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Gastric polyps						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Abdominal hernias and other abdominal wall conditions						
<90	2 (0.6)	2	0.5	0		
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	2 (1.2)	2	0.9
>=115	4 (1.1)	5	1.0	1 (0.6)	1	0.5
Hiatus hernia						
<90	2 (0.6)	2	0.5	0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	2 (0.5)	3	0.6	0		
Abdominal hernia						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Umbilical hernia						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Oral soft tissue conditions						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	1 (0.4)	2	0.6	1 (0.7)	1	0.5
100-<115	4 (1.2)	4	0.9	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	3 (1.7)	3	1.4
Lip swelling						
<90	0			0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Cheilitis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Stomatitis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Lip disorder						
<90	0			0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Paraesthesia oral						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Mouth ulceration						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			2 (1.1)	2	0.9
Aphthous ulcer						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Odynophagia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Oral mucosal eruption						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Diverticular disorders						
<90	2 (0.6)	2	0.5	2 (1.2)	2	1.0
90-<100	1 (0.4)	1	0.3	0		
100-<115	3 (0.9)	3	0.7	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9
Diverticulum						
<90	2 (0.6)	2	0.5	2 (1.2)	2	1.0
90-<100	1 (0.4)	1	0.3	0		
100-<115	3 (0.9)	3	0.7	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9
Anal and rectal conditions NEC						
<90	2 (0.6)	2	0.5	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	2 (0.6)	3	0.7	0		
>=115	2 (0.5)	3	0.6	0		
Anal fissure						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Proctalgia						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	2	0.4	0		
Anal pruritus						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Anorectal discomfort						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Rectal fissure						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Gastrointestinal ulceration and perforation						
<90	3 (0.9)	3	0.7	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Large intestine perforation						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Oesophageal ulcer						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Peptic ulcer						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Duodenal ulcer						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Gastric ulcer						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Gastrointestinal stenosis and obstruction						
<90	1 (0.3)	1	0.2	2 (1.2)	2	1.0
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Oesophageal stenosis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Volvulus						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Ileus						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Intestinal obstruction						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Exocrine pancreas conditions						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Pancreatitis acute						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Malabsorption conditions						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Coeliac disease								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Peritoneal and retroperitoneal conditions								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Pneumoperitoneum								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Tongue conditions								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Glossodynia								
<90	1	(0.3)	1	0.2	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Infections and infestations						
<90	179 (52.8)	399	90.5	84 (51.9)	194	93.1
90-<100	140 (52.4)	297	84.2	81 (53.6)	157	82.6
100-<115	185 (55.9)	409	95.2	99 (60.7)	230	109.0
>=115	210 (56.9)	510	105.7	108 (60.3)	221	100.4
Infections - pathogen unspecified						
<90	159 (46.9)	314	71.2	70 (43.2)	148	71.0
90-<100	116 (43.4)	235	66.6	70 (46.4)	125	65.7
100-<115	170 (51.4)	311	72.4	83 (50.9)	170	80.6
>=115	181 (49.1)	387	80.2	91 (50.8)	167	75.9
Nasopharyngitis						
<90	67 (19.8)	121	27.4	29 (17.9)	49	23.5
90-<100	50 (18.7)	88	24.9	34 (22.5)	52	27.3
100-<115	74 (22.4)	117	27.2	36 (22.1)	66	31.3
>=115	90 (24.4)	154	31.9	34 (19.0)	49	22.3
Upper respiratory tract infection						
<90	25 (7.4)	34	7.7	20 (12.3)	27	13.0
90-<100	19 (7.1)	25	7.1	11 (7.3)	19	10.0
100-<115	37 (11.2)	53	12.3	17 (10.4)	18	8.5
>=115	33 (8.9)	46	9.5	32 (17.9)	52	23.6
Gastroenteritis						
<90	25 (7.4)	29	6.6	11 (6.8)	12	5.8
90-<100	15 (5.6)	18	5.1	4 (2.6)	6	3.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	21 (6.3)	23	5.4	6 (3.7)	10	4.7
>=115	24 (6.5)	34	7.0	9 (5.0)	10	4.5
Urinary tract infection						
<90	16 (4.7)	18	4.1	11 (6.8)	14	6.7
90-<100	17 (6.4)	21	6.0	1 (0.7)	1	0.5
100-<115	17 (5.1)	23	5.4	8 (4.9)	11	5.2
>=115	18 (4.9)	21	4.4	8 (4.5)	8	3.6
Sinusitis						
<90	18 (5.3)	22	5.0	6 (3.7)	7	3.4
90-<100	9 (3.4)	12	3.4	10 (6.6)	10	5.3
100-<115	13 (3.9)	16	3.7	14 (8.6)	16	7.6
>=115	31 (8.4)	34	7.0	6 (3.4)	7	3.2
Bronchitis						
<90	16 (4.7)	17	3.9	8 (4.9)	10	4.8
90-<100	6 (2.2)	6	1.7	5 (3.3)	5	2.6
100-<115	11 (3.3)	13	3.0	8 (4.9)	9	4.3
>=115	14 (3.8)	16	3.3	4 (2.2)	4	1.8
Rhinitis						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	4 (1.5)	7	2.0	4 (2.6)	7	3.7
100-<115	8 (2.4)	10	2.3	2 (1.2)	3	1.4
>=115	6 (1.6)	7	1.5	2 (1.1)	3	1.4
Cystitis						
<90	6 (1.8)	7	1.6	2 (1.2)	2	1.0
90-<100	4 (1.5)	4	1.1	0		
100-<115	4 (1.2)	5	1.2	0		
>=115	5 (1.4)	5	1.0	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Laryngitis						
<90	4 (1.2)	4	0.9	1 (0.6)	2	1.0
90-<100	2 (0.7)	2	0.6	2 (1.3)	2	1.1
100-<115	2 (0.6)	2	0.5	0		
>=115	6 (1.6)	6	1.2	1 (0.6)	1	0.5
Pharyngitis						
<90	4 (1.2)	4	0.9	2 (1.2)	2	1.0
90-<100	3 (1.1)	3	0.9	3 (2.0)	3	1.6
100-<115	2 (0.6)	2	0.5	2 (1.2)	2	0.9
>=115	4 (1.1)	4	0.8	2 (1.1)	2	0.9
Tonsillitis						
<90	2 (0.6)	4	0.9	1 (0.6)	2	1.0
90-<100	4 (1.5)	5	1.4	3 (2.0)	4	2.1
100-<115	3 (0.9)	3	0.7	3 (1.8)	3	1.4
>=115	3 (0.8)	3	0.6	3 (1.7)	3	1.4
Acute sinusitis						
<90	4 (1.2)	4	0.9	1 (0.6)	1	0.5
90-<100	4 (1.5)	5	1.4	2 (1.3)	2	1.1
100-<115	1 (0.3)	1	0.2	3 (1.8)	4	1.9
>=115	2 (0.5)	2	0.4	2 (1.1)	2	0.9
Pneumonia						
<90	3 (0.9)	3	0.7	0		
90-<100	4 (1.5)	6	1.7	2 (1.3)	2	1.1
100-<115	0			2 (1.2)	2	0.9
>=115	4 (1.1)	5	1.0	4 (2.2)	4	1.8
Tooth infection						
<90	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	2 (0.7)	3	0.9	0		
100-<115	3 (0.9)	3	0.7	3 (1.8)	3	1.4
>=115	6 (1.6)	6	1.2	1 (0.6)	1	0.5
Vaginal infection						
<90	4 (1.2)	5	1.1	0		
90-<100	1 (0.4)	2	0.6	0		
100-<115	3 (0.9)	3	0.7	0		
>=115	3 (0.8)	3	0.6	0		
Ear infection						
<90	3 (0.9)	3	0.7	0		
90-<100	0			2 (1.3)	2	1.1
100-<115	4 (1.2)	6	1.4	0		
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Lower respiratory tract infection						
<90	1 (0.3)	1	0.2	2 (1.2)	3	1.4
90-<100	1 (0.4)	2	0.6	2 (1.3)	2	1.1
100-<115	2 (0.6)	2	0.5	5 (3.1)	8	3.8
>=115	5 (1.4)	5	1.0	3 (1.7)	3	1.4
Tooth abscess						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	2 (1.3)	2	1.1
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	3 (0.8)	3	0.6	4 (2.2)	5	2.3
Conjunctivitis						
<90	4 (1.2)	4	0.9	0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	1 (0.3)	1	0.2	3 (1.7)	3	1.4
Otitis media						
<90	3 (0.9)	3	0.7	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Folliculitis						
<90	1 (0.3)	1	0.2	0		
90-<100	3 (1.1)	3	0.9	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Pulpitis dental						
<90	1 (0.3)	1	0.2	0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Gastrointestinal infection						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	2 (0.7)	3	0.9	1 (0.7)	1	0.5
100-<115	0			1 (0.6)	1	0.5
>=115	2 (0.5)	3	0.6	0		
Eye infection						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	4 (1.2)	4	0.9	0		
>=115	0			0		
Appendicitis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Kidney infection						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Chronic sinusitis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Hordeolum						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Gingivitis						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Subcutaneous abscess						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Breast abscess						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Infected bite						
<90	2 (0.6)	2	0.5	0		
90-<100	0			2 (1.3)	2	1.1
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Pharyngotonsillitis						
<90	2 (0.6)	2	0.5	1 (0.6)	2	1.0
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Pyelonephritis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	3 (0.8)	3	0.6	0		
Localised infection						
<90	0			0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Infection						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Abscess						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Atypical pneumonia						
<90	0			0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Omphalitis						
<90	0			0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Diarrhoea infectious						
<90	1 (0.3)	1	0.2	1 (0.6)	2	1.0
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Postoperative wound infection						
<90	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Periodontitis								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	1	(0.3)	1	0.2	0			
Abdominal wall abscess								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	2	(0.5)	2	0.4	0			
Otitis externa								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	2	(0.5)	2	0.4	0			
Fracture infection								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Mastitis								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Nail infection						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Paronychia						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Prostate infection						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Diverticulitis						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Endometritis						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Skin infection						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Abdominal abscess						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Abscess limb						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Appendicitis perforated						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Carbuncle						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Eyelid infection						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Haematoma infection						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Large intestine infection						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Oophoritis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Parasitic gastroenteritis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Parotitis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Peritonitis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Salpingitis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Sepsis syndrome						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Bartholinitis						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Device related infection						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Epididymitis						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Groin abscess								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Oral infection								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Osteomyelitis								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Perirectal abscess								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	2	0.4	0			
Purulence								
<90	0				0			
90-<100	0				0			
100-<115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	1 (0.3)	1	0.2	0		
Respiratory tract infection						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Arthritis infective						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Cervicitis						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Empyema						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Gastric infection						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Infected dermal cyst						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Lymphangitis						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Neutropenic sepsis						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Otitis media acute						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Peritonsillar abscess						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Peritonsillitis						
<90	0			0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
100-<115	0				1	(0.6)	1	0.5
>=115	0				0			
Root canal infection								
<90	0				1	(0.6)	1	0.5
90-<100	0				0			
100-<115	0				1	(0.6)	1	0.5
>=115	0				0			
Septic shock								
<90	0				0			
90-<100	0				0			
100-<115	0				1	(0.6)	1	0.5
>=115	0				0			
Tracheitis								
<90	0				1	(0.6)	1	0.5
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Wound infection								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	0				1	(0.6)	1	0.5
Viral infectious disorders								
<90	46	(13.6)	59	13.4	24	(14.8)	31	14.9
90-<100	34	(12.7)	36	10.2	19	(12.6)	26	13.7
100-<115	53	(16.0)	73	17.0	32	(19.6)	43	20.4
>=115	61	(16.5)	80	16.6	28	(15.6)	36	16.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Influenza						
<90	23 (6.8)	28	6.4	15 (9.3)	17	8.2
90-<100	18 (6.7)	20	5.7	13 (8.6)	17	8.9
100-<115	25 (7.6)	32	7.4	20 (12.3)	25	11.8
>=115	23 (6.2)	32	6.6	15 (8.4)	20	9.1
Gastroenteritis viral						
<90	7 (2.1)	8	1.8	2 (1.2)	2	1.0
90-<100	6 (2.2)	6	1.7	3 (2.0)	3	1.6
100-<115	12 (3.6)	12	2.8	6 (3.7)	7	3.3
>=115	17 (4.6)	18	3.7	3 (1.7)	3	1.4
Viral infection						
<90	3 (0.9)	7	1.6	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	7 (2.1)	7	1.6	3 (1.8)	3	1.4
>=115	4 (1.1)	6	1.2	4 (2.2)	4	1.8
Herpes zoster						
<90	2 (0.6)	2	0.5	3 (1.9)	3	1.4
90-<100	0			3 (2.0)	3	1.6
100-<115	7 (2.1)	8	1.9	3 (1.8)	3	1.4
>=115	3 (0.8)	3	0.6	2 (1.1)	2	0.9
Gastrointestinal viral infection						
<90	1 (0.3)	1	0.2	0		
90-<100	3 (1.1)	3	0.9	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	3 (0.8)	4	0.8	1 (0.6)	1	0.5
Viral upper respiratory tract infection						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	2 (0.6)	2	0.5	2 (1.2)	3	1.4
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	4 (1.1)	4	0.8	2 (1.1)	2	0.9
Gastroenteritis norovirus						
<90	0			0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	2 (0.6)	3	0.7	0		
>=115	1 (0.3)	1	0.2	0		
Ear infection viral						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	1 (0.3)	1	0.2	0		
Herpes simplex						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Oral herpes						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	2 (0.5)	3	0.6	1 (0.6)	1	0.5
Dengue fever						
<90	2 (0.6)	2	0.5	2 (1.2)	2	1.0
90-<100	1 (0.4)	1	0.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Viral pharyngitis						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Herpes virus infection						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Respiratory tract infection viral						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Gastroenteritis astroviral						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Hepatitis E						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Infectious mononucleosis						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Oral viral infection						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Parainfluenzae virus infection						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Chronic hepatitis B						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Genital herpes zoster						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Respiratory syncytial virus infection						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Viral sinusitis								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				1	(0.6)	1	0.5
>=115	0				0			
Cytomegalovirus infection								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Papilloma viral infection								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Varicella								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Vestibular neuronitis								
<90	0				0			
90-<100	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
100-<115	0			0		
>=115	1	(0.3)	1 0.2	0		
Bronchitis viral						
<90	0			0		
90-<100	0			1	(0.7)	1 0.5
100-<115	0			0		
>=115	0			1	(0.6)	1 0.5
Conjunctivitis viral						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1	(0.6)	1 0.5
Hand-foot-and-mouth disease						
<90	0			0		
90-<100	0			1	(0.7)	1 0.5
100-<115	0			0		
>=115	0			0		
Meningitis viral						
<90	0			0		
90-<100	0			0		
100-<115	0			1	(0.6)	1 0.5
>=115	0			0		
Viral rhinitis						
<90	0			0		
90-<100	0			0		
100-<115	0			1	(0.6)	1 0.5
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Bacterial infectious disorders						
<90	9 (2.7)	9	2.0	8 (4.9)	9	4.3
90-<100	15 (5.6)	18	5.1	3 (2.0)	3	1.6
100-<115	17 (5.1)	18	4.2	7 (4.3)	9	4.3
>=115	16 (4.3)	18	3.7	9 (5.0)	10	4.5
Pharyngitis streptococcal						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	4 (1.5)	4	1.1	1 (0.7)	1	0.5
100-<115	4 (1.2)	4	0.9	2 (1.2)	2	0.9
>=115	2 (0.5)	2	0.4	2 (1.1)	2	0.9
Cellulitis						
<90	2 (0.6)	2	0.5	2 (1.2)	3	1.4
90-<100	2 (0.7)	2	0.6	0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	3 (0.8)	3	0.6	4 (2.2)	4	1.8
Helicobacter infection						
<90	0			0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	4 (1.2)	4	0.9	1 (0.6)	1	0.5
>=115	0			1 (0.6)	1	0.5
Ear infection bacterial						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Bacterial vaginosis						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	2 (0.7)	4	1.1	0		
100-<115	1 (0.3)	2	0.5	2 (1.2)	2	0.9
>=115	2 (0.5)	2	0.4	0		
Erysipelas						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Furuncle						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	1 (0.4)	2	0.6	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Staphylococcal infection						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Helicobacter gastritis						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Syphilis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=115	0				0			
Lyme disease								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Sinusitis bacterial								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Pharyngitis bacterial								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Salmonellosis								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Typhoid fever								
<90	1	(0.3)	1	0.2	0			
90-<100	0				1	(0.7)	1	0.5
100-<115	0				0			
>=115	0				0			
Bacterial colitis								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Bacterial vulvovaginitis								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Genital infection bacterial								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Skin bacterial infection								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Tonsillitis bacterial								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Bacteriuria								
<90	0				0			
90-<100	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Gastric ulcer helicobacter						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Listeriosis						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Staphylococcal sepsis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Streptococcal urinary tract infection						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Upper respiratory tract infection bacterial						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Fungal infectious disorders						
<90	13 (3.8)	17	3.9	5 (3.1)	5	2.4
90-<100	6 (2.2)	7	2.0	2 (1.3)	3	1.6
100-<115	5 (1.5)	6	1.4	8 (4.9)	8	3.8
>=115	21 (5.7)	23	4.8	7 (3.9)	8	3.6
Vulvovaginal mycotic infection						
<90	4 (1.2)	5	1.1	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	0		
100-<115	0			1 (0.6)	1	0.5
>=115	5 (1.4)	6	1.2	0		
Fungal infection						
<90	4 (1.2)	4	0.9	2 (1.2)	2	1.0
90-<100	1 (0.4)	2	0.6	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	4 (1.1)	4	0.8	1 (0.6)	1	0.5
Tinea pedis						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	3 (0.8)	3	0.6	1 (0.6)	1	0.5
Vulvovaginal candidiasis						
<90	2 (0.6)	4	0.9	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	2	0.5	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Body tinea						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Dermatophytosis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Fungal skin infection						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Onychomycosis						
<90	0			0		
90-<100	0			1 (0.7)	2	1.1
100-<115	0			2 (1.2)	2	0.9
>=115	2 (0.5)	2	0.4	2 (1.1)	2	0.9
Skin candida						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Dermatophytosis of nail						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Tinea infection								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Candida infection								
<90	0				0			
90-<100	0				0			
100-<115	0				1	(0.6)	1	0.5
>=115	1	(0.3)	1	0.2	1	(0.6)	1	0.5
Tinea capitis								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Tinea cruris								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Oral candidiasis								
<90	0				0			
90-<100	0				0			
100-<115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			1 (0.6)	1	0.5
Otitis externa fungal						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Protozoal infectious disorders						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Trichomoniasis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Toxoplasmosis						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Ectoparasitic disorders						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Acarodermatitis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Chlamydial infectious disorders								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Chlamydial infection								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Nervous system disorders								
<90	101	(29.8)	236	53.5	33	(20.4)	57	27.4
90-<100	76	(28.5)	154	43.7	26	(17.2)	37	19.5
100-<115	103	(31.1)	171	39.8	42	(25.8)	71	33.6
>=115	111	(30.1)	197	40.8	40	(22.3)	57	25.9
Headaches								
<90	62	(18.3)	159	36.1	22	(13.6)	26	12.5
90-<100	46	(17.2)	96	27.2	17	(11.3)	23	12.1
100-<115	53	(16.0)	78	18.1	26	(16.0)	41	19.4
>=115	68	(18.4)	118	24.4	24	(13.4)	28	12.7
Headache								
<90	54	(15.9)	139	31.5	20	(12.3)	24	11.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	43 (16.1)	85	24.1	15 (9.9)	19	10.0
100-<115	47 (14.2)	65	15.1	24 (14.7)	36	17.1
>=115	54 (14.6)	98	20.3	21 (11.7)	25	11.4
Migraine						
<90	4 (1.2)	13	2.9	2 (1.2)	2	1.0
90-<100	4 (1.5)	9	2.6	3 (2.0)	3	1.6
100-<115	9 (2.7)	12	2.8	2 (1.2)	4	1.9
>=115	15 (4.1)	18	3.7	2 (1.1)	2	0.9
Sinus headache						
<90	3 (0.9)	3	0.7	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Tension headache						
<90	3 (0.9)	3	0.7	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Migraine with aura						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Occipital neuralgia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Neurological disorders NEC						
<90	45 (13.3)	66	15.0	13 (8.0)	23	11.0
90-<100	38 (14.2)	46	13.0	8 (5.3)	9	4.7
100-<115	50 (15.1)	72	16.8	11 (6.7)	17	8.1
>=115	48 (13.0)	64	13.3	15 (8.4)	19	8.6
Dizziness						
<90	18 (5.3)	28	6.4	6 (3.7)	9	4.3
90-<100	20 (7.5)	23	6.5	5 (3.3)	6	3.2
100-<115	30 (9.1)	42	9.8	4 (2.5)	10	4.7
>=115	30 (8.1)	37	7.7	8 (4.5)	10	4.5
Dysgeusia						
<90	5 (1.5)	7	1.6	1 (0.6)	8	3.8
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	5 (1.5)	6	1.4	0		
>=115	7 (1.9)	10	2.1	2 (1.1)	2	0.9
Paraesthesia						
<90	6 (1.8)	8	1.8	3 (1.9)	3	1.4
90-<100	2 (0.7)	2	0.6	0		
100-<115	1 (0.3)	2	0.5	1 (0.6)	1	0.5
>=115	4 (1.1)	5	1.0	1 (0.6)	1	0.5
Syncope						
<90	2 (0.6)	2	0.5	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	7 (2.1)	7	1.6	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Taste disorder						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	3 (0.9)	4	0.9	0		
90-<100	2 (0.7)	3	0.9	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	0		
>=115	2 (0.5)	2	0.4	0		
Somnolence						
<90	1 (0.3)	1	0.2	0		
90-<100	3 (1.1)	4	1.1	1 (0.7)	1	0.5
100-<115	2 (0.6)	3	0.7	0		
>=115	1 (0.3)	1	0.2	0		
Hypoaesthesia						
<90	2 (0.6)	2	0.5	0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	0			1 (0.6)	1	0.5
>=115	3 (0.8)	3	0.6	1 (0.6)	1	0.5
Lethargy						
<90	3 (0.9)	3	0.7	2 (1.2)	2	1.0
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	3 (0.8)	3	0.6	0		
Neuralgia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	3 (0.9)	3	0.7	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Hyperaesthesia						
<90	1 (0.3)	1	0.2	0		
90-<100	2 (0.7)	4	1.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Dizziness postural						
<90	1 (0.3)	1	0.2	0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	0			0		
>=115	0			0		
Presyncope						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Balance disorder						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Allodynia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Burning sensation						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Ageusia								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Vertigo CNS origin								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Aphasia								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Dysaesthesia								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Loss of consciousness								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Hyporeflexia								
<90	1	(0.3)	1	0.2	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			1 (0.6)	1	0.5
Restless legs syndrome						
<90	1 (0.3)	2	0.5	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Sensory disturbance						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Dysarthria						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Sensory loss						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Spinal cord and nerve root disorders						
<90	5 (1.5)	5	1.1	3 (1.9)	3	1.4
90-<100	5 (1.9)	5	1.4	3 (2.0)	3	1.6
100-<115	6 (1.8)	7	1.6	5 (3.1)	5	2.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	4 (1.1)	5	1.0	3 (1.7)	3	1.4
Sciatica						
<90	4 (1.2)	4	0.9	1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	0		
100-<115	4 (1.2)	5	1.2	4 (2.5)	4	1.9
>=115	3 (0.8)	4	0.8	3 (1.7)	3	1.4
Cervicobrachial syndrome						
<90	0			2 (1.2)	2	1.0
90-<100	1 (0.4)	1	0.3	2 (1.3)	2	1.1
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Cervical radiculopathy						
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Lumbosacral radiculopathy						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Spinal cord compression						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Lumbar radiculopathy						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Peripheral neuropathies						
<90	3 (0.9)	3	0.7	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	5 (1.5)	6	1.4	4 (2.5)	4	1.9
>=115	3 (0.8)	3	0.6	3 (1.7)	4	1.8
Neuropathy peripheral						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	2 (0.6)	2	0.5	2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	0		
Carpal tunnel syndrome						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	2 (0.6)	3	0.7	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Nerve compression						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Peripheral sensory neuropathy						
<90	0			0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Peroneal nerve palsy						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Radial nerve compression						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Movement disorders (incl parkinsonism)						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	3 (0.9)	3	0.7	1 (0.6)	2	0.9
>=115	1 (0.3)	1	0.2	0		
Tremor						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	1 (0.6)	2	0.9
>=115	1 (0.3)	1	0.2	0		
Essential tremor						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Mental impairment disorders						
<90	0			1 (0.6)	2	1.0
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Memory impairment						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Dementia Alzheimer's type						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Disturbance in attention						
<90	0			1 (0.6)	2	1.0
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Amnesia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Sleep disturbances (incl subtypes)						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	3 (1.1)	3	0.9	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Poor quality sleep						
<90	0			0		
90-<100	3 (1.1)	3	0.9	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Cranial nerve disorders (excl neoplasms)						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Anosmia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Cranial nerve disorder						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Parosmia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
100-<115	0				0			
>=115	0				0			
Neurological disorders of the eye								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	1	(0.6)	1	0.5
>=115	0				0			
Visual field defect								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	1	(0.6)	1	0.5
>=115	0				0			
Neuromuscular disorders								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Autonomic nervous system imbalance								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Central nervous system vascular disorders								
<90	0				1	(0.6)	1	0.5
90-<100	0				0			
100-<115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	1 (0.3)	1	0.2	0		
Cerebral infarction						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Ischaemic stroke						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Increased intracranial pressure and hydrocephalus						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	2	0.4	0		
Idiopathic intracranial hypertension						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	2	0.4	0		
Demyelinating disorders						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Multiple sclerosis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Seizures (incl subtypes)						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Partial seizures						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Psychogenic seizure						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Musculoskeletal and connective tissue disorders						
<90	82 (24.2)	153	34.7	45 (27.8)	73	35.0
90-<100	66 (24.7)	90	25.5	48 (31.8)	72	37.9
100-<115	82 (24.8)	131	30.5	42 (25.8)	67	31.8
>=115	108 (29.3)	184	38.1	51 (28.5)	92	41.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Musculoskeletal and connective tissue disorders NEC						
<90	48 (14.2)	67	15.2	22 (13.6)	30	14.4
90-<100	30 (11.2)	33	9.4	28 (18.5)	31	16.3
100-<115	50 (15.1)	65	15.1	20 (12.3)	31	14.7
>=115	59 (16.0)	79	16.4	29 (16.2)	40	18.2
Back pain						
<90	28 (8.3)	33	7.5	12 (7.4)	12	5.8
90-<100	15 (5.6)	15	4.3	11 (7.3)	12	6.3
100-<115	31 (9.4)	35	8.1	14 (8.6)	14	6.6
>=115	33 (8.9)	38	7.9	17 (9.5)	18	8.2
Pain in extremity						
<90	11 (3.2)	13	2.9	3 (1.9)	4	1.9
90-<100	5 (1.9)	5	1.4	8 (5.3)	8	4.2
100-<115	9 (2.7)	10	2.3	5 (3.1)	7	3.3
>=115	19 (5.1)	20	4.1	8 (4.5)	9	4.1
Musculoskeletal pain						
<90	7 (2.1)	7	1.6	4 (2.5)	4	1.9
90-<100	6 (2.2)	6	1.7	2 (1.3)	2	1.1
100-<115	9 (2.7)	9	2.1	4 (2.5)	6	2.8
>=115	9 (2.4)	9	1.9	6 (3.4)	6	2.7
Neck pain						
<90	6 (1.8)	7	1.6	2 (1.2)	2	1.0
90-<100	2 (0.7)	2	0.6	3 (2.0)	3	1.6
100-<115	6 (1.8)	6	1.4	1 (0.6)	1	0.5
>=115	5 (1.4)	6	1.2	3 (1.7)	3	1.4
Musculoskeletal chest pain						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	2 (1.3)	2	1.1
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Musculoskeletal stiffness						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Flank pain						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Plantar fasciitis						
<90	1 (0.3)	1	0.2	2 (1.2)	3	1.4
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9
Axillary mass						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Musculoskeletal discomfort						
<90	0			0		
90-<100	1 (0.4)	2	0.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Dupuytren's contracture						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Groin pain						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Limb mass						
<90	0			1 (0.6)	2	1.0
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Muscle contracture						
<90	0			1 (0.6)	1	0.5
90-<100	0			2 (1.3)	2	1.1
100-<115	0			0		
>=115	0			0		
Neck mass						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Joint disorders						
<90	32 (9.4)	47	10.7	15 (9.3)	20	9.6
90-<100	30 (11.2)	34	9.6	20 (13.2)	28	14.7
100-<115	26 (7.9)	33	7.7	15 (9.2)	17	8.1
>=115	45 (12.2)	55	11.4	25 (14.0)	29	13.2
Arthralgia						
<90	19 (5.6)	21	4.8	9 (5.6)	10	4.8
90-<100	17 (6.4)	18	5.1	10 (6.6)	12	6.3
100-<115	15 (4.5)	17	4.0	11 (6.7)	11	5.2
>=115	30 (8.1)	36	7.5	13 (7.3)	14	6.4
Osteoarthritis						
<90	4 (1.2)	6	1.4	4 (2.5)	6	2.9
90-<100	7 (2.6)	7	2.0	4 (2.6)	4	2.1
100-<115	5 (1.5)	6	1.4	2 (1.2)	2	0.9
>=115	7 (1.9)	9	1.9	8 (4.5)	8	3.6
Spinal osteoarthritis						
<90	5 (1.5)	6	1.4	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	4 (1.2)	4	0.9	0		
>=115	2 (0.5)	2	0.4	0		
Arthritis						
<90	3 (0.9)	3	0.7	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	4 (2.6)	4	2.1
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Joint swelling						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	4 (1.1)	4	0.8	2 (1.1)	2	0.9
Rotator cuff syndrome						
<90	2 (0.6)	2	0.5	0		
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9
Joint stiffness						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Vertebral foraminal stenosis						
<90	3 (0.9)	4	0.9	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Facet joint syndrome						
<90	2 (0.6)	3	0.7	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Periarthritis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	2	1.1
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Spondylitis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Arthropathy						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	2	0.5	0		
>=115	0			1 (0.6)	1	0.5
Vertebral osteophyte						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Chondromalacia						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Haemarthrosis						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Joint noise						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Joint range of motion decreased						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Joint space narrowing						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Polyarthritis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Rheumatoid arthritis						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Spondyloarthropathy						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Muscle disorders						
<90	14 (4.1)	15	3.4	7 (4.3)	7	3.4
90-<100	10 (3.7)	11	3.1	4 (2.6)	5	2.6
100-<115	15 (4.5)	16	3.7	7 (4.3)	8	3.8
>=115	19 (5.1)	22	4.6	5 (2.8)	9	4.1
Myalgia						
<90	6 (1.8)	7	1.6	3 (1.9)	3	1.4
90-<100	3 (1.1)	3	0.9	3 (2.0)	4	2.1
100-<115	7 (2.1)	8	1.9	0		
>=115	7 (1.9)	8	1.7	2 (1.1)	6	2.7
Muscle spasms						
<90	3 (0.9)	3	0.7	4 (2.5)	4	1.9
90-<100	5 (1.9)	5	1.4	1 (0.7)	1	0.5
100-<115	4 (1.2)	4	0.9	3 (1.8)	4	1.9
>=115	7 (1.9)	7	1.5	2 (1.1)	2	0.9
Muscular weakness						
<90	0			0		
90-<100	1 (0.4)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	3 (0.8)	3	0.6	0		
Fibromyalgia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Myofascial pain syndrome						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Muscle fatigue						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Torticollis						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Muscle disorder						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Muscle tightness						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Muscle twitching						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Myalgia intercostal						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Myosclerosis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Tendon, ligament and cartilage disorders						
<90	7 (2.1)	7	1.6	3 (1.9)	4	1.9
90-<100	3 (1.1)	4	1.1	1 (0.7)	1	0.5
100-<115	3 (0.9)	4	0.9	7 (4.3)	8	3.8
>=115	12 (3.3)	12	2.5	2 (1.1)	2	0.9
Tendonitis						
<90	3 (0.9)	3	0.7	2 (1.2)	3	1.4
90-<100	3 (1.1)	3	0.9	1 (0.7)	1	0.5
100-<115	3 (0.9)	4	0.9	5 (3.1)	6	2.8
>=115	4 (1.1)	4	0.8	1 (0.6)	1	0.5
Tenosynovitis						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Costochondritis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	3 (0.8)	3	0.6	0		
Tendon disorder						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Tendon pain						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Trigger finger						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Osteochondrosis						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Posterior tibial tendon dysfunction						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Tendon discomfort						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)						
<90	5 (1.5)	9	2.0	2 (1.2)	2	1.0
90-<100	2 (0.7)	3	0.9	1 (0.7)	1	0.5
100-<115	6 (1.8)	6	1.4	1 (0.6)	1	0.5
>=115	6 (1.6)	6	1.2	7 (3.9)	9	4.1
Intervertebral disc protrusion						
<90	0			1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	4 (1.1)	4	0.8	3 (1.7)	4	1.8
Intervertebral disc degeneration						
<90	2 (0.6)	4	0.9	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			2 (1.1)	2	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Scoliosis						
<90	3 (0.9)	3	0.7	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Finger deformity						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Spinal stenosis						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Intervertebral disc displacement						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Kyphoscoliosis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Cervical spinal stenosis						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Spondylolisthesis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Foot deformity						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			1 (0.6)	1	0.5
>=115	0			1 (0.6)	1	0.5
Intervertebral disc annular tear						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Kyphosis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Synovial and bursal disorders						
<90	3 (0.9)	3	0.7	2 (1.2)	2	1.0
90-<100	2 (0.7)	2	0.6	2 (1.3)	2	1.1
100-<115	5 (1.5)	5	1.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	6 (1.6)	6	1.2	1 (0.6)	1	0.5
Bursitis						
<90	1 (0.3)	1	0.2	2 (1.2)	2	1.0
90-<100	0			1 (0.7)	1	0.5
100-<115	5 (1.5)	5	1.2	0		
>=115	4 (1.1)	4	0.8	0		
Synovial cyst						
<90	2 (0.6)	2	0.5	0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Synovitis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Bursal fluid accumulation						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Bone disorders (excl congenital and fractures)						
<90	4 (1.2)	4	0.9	7 (4.3)	7	3.4
90-<100	2 (0.7)	2	0.6	4 (2.6)	4	2.1
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	3 (0.8)	4	0.8	2 (1.1)	2	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Osteopenia						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Pain in jaw						
<90	0			1 (0.6)	1	0.5
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Coccydynia						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Metatarsalgia						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Exostosis						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			2 (1.3)	2	1.1
100-<115	0			0		
>=115	0			0		
Osteoporosis						
<90	1 (0.3)	1	0.2	2 (1.2)	2	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Bone cyst						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	2	0.4	0		
Osteonecrosis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Pubic pain						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Connective tissue disorders (excl congenital)						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Sjogren's syndrome						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Myofascitis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Systemic lupus erythematosus						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Systemic scleroderma						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
General disorders and administration site conditions						
<90	77 (22.7)	130	29.5	28 (17.3)	60	28.8
90-<100	57 (21.3)	100	28.3	31 (20.5)	50	26.3
100-<115	75 (22.7)	108	25.1	32 (19.6)	50	23.7
>=115	82 (22.2)	127	26.3	40 (22.3)	62	28.2
General system disorders NEC						
<90	57 (16.8)	89	20.2	20 (12.3)	30	14.4
90-<100	45 (16.9)	68	19.3	18 (11.9)	19	10.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	60 (18.1)	78	18.1	22 (13.5)	26	12.3
>=115	63 (17.1)	89	18.4	26 (14.5)	38	17.3
Fatigue						
<90	25 (7.4)	31	7.0	5 (3.1)	5	2.4
90-<100	24 (9.0)	29	8.2	9 (6.0)	9	4.7
100-<115	27 (8.2)	29	6.7	7 (4.3)	7	3.3
>=115	28 (7.6)	31	6.4	7 (3.9)	8	3.6
Asthenia						
<90	15 (4.4)	19	4.3	8 (4.9)	9	4.3
90-<100	8 (3.0)	11	3.1	0		
100-<115	4 (1.2)	7	1.6	2 (1.2)	2	0.9
>=115	8 (2.2)	16	3.3	1 (0.6)	1	0.5
Early satiety						
<90	7 (2.1)	7	1.6	1 (0.6)	1	0.5
90-<100	8 (3.0)	8	2.3	0		
100-<115	5 (1.5)	5	1.2	1 (0.6)	1	0.5
>=115	6 (1.6)	6	1.2	0		
Pain						
<90	9 (2.7)	10	2.3	3 (1.9)	3	1.4
90-<100	1 (0.4)	1	0.3	0		
100-<115	6 (1.8)	6	1.4	1 (0.6)	1	0.5
>=115	5 (1.4)	6	1.2	3 (1.7)	3	1.4
Malaise						
<90	5 (1.5)	7	1.6	0		
90-<100	5 (1.9)	6	1.7	0		
100-<115	5 (1.5)	5	1.2	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	3 (1.7)	4	1.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Influenza like illness						
<90	2 (0.6)	2	0.5	3 (1.9)	3	1.4
90-<100	2 (0.7)	3	0.9	1 (0.7)	1	0.5
100-<115	7 (2.1)	7	1.6	2 (1.2)	2	0.9
>=115	6 (1.6)	6	1.2	7 (3.9)	7	3.2
Chest discomfort						
<90	2 (0.6)	2	0.5	0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	3 (0.9)	3	0.7	2 (1.2)	3	1.4
>=115	2 (0.5)	2	0.4	0		
Chills						
<90	2 (0.6)	2	0.5	0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	2 (0.6)	2	0.5	2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	0		
Non-cardiac chest pain						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	4 (1.1)	4	0.8	2 (1.1)	2	0.9
Hunger						
<90	0			0		
90-<100	2 (0.7)	2	0.6	2 (1.3)	2	1.1
100-<115	3 (0.9)	3	0.7	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Oedema peripheral						
<90	0			2 (1.2)	2	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	1 (0.4)	1	0.3	2 (1.3)	2	1.1
100-<115	0			2 (1.2)	2	0.9
>=115	3 (0.8)	3	0.6	2 (1.1)	2	0.9
Thirst						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			1 (0.6)	1	0.5
Chest pain						
<90	2 (0.6)	2	0.5	3 (1.9)	3	1.4
90-<100	0			0		
100-<115	0			2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9
Swelling face						
<90	0			0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Peripheral swelling						
<90	1 (0.3)	1	0.2	2 (1.2)	2	1.0
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			2 (1.1)	2	0.9
Swelling						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			2 (1.1)	2	0.9
Feeling cold						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Feeling hot						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Ill-defined disorder						
<90	1 (0.3)	1	0.2	0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Sensation of foreign body						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Hernia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Axillary pain						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Pseudocyst						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Fat tissue increased						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Inflammation						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	2	0.5	1 (0.6)	1	0.5
>=115	0			0		
Crying						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Hangover						
<90	0			0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Sense of oppression						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	2	0.4	0		
Sluggishness						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Discomfort						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Facial pain						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Granuloma						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Gravitational oedema						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Temperature intolerance						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Administration site reactions						
<90	15 (4.4)	26	5.9	9 (5.6)	27	13.0
90-<100	17 (6.4)	24	6.8	14 (9.3)	25	13.1
100-<115	14 (4.2)	22	5.1	12 (7.4)	18	8.5
>=115	19 (5.1)	27	5.6	9 (5.0)	12	5.5
Injection site bruising						
<90	9 (2.7)	10	2.3	4 (2.5)	6	2.9
90-<100	4 (1.5)	4	1.1	10 (6.6)	15	7.9
100-<115	6 (1.8)	7	1.6	6 (3.7)	6	2.8
>=115	9 (2.4)	10	2.1	6 (3.4)	7	3.2
Injection site pain						
<90	1 (0.3)	2	0.5	3 (1.9)	6	2.9
90-<100	7 (2.6)	8	2.3	5 (3.3)	7	3.7
100-<115	4 (1.2)	4	0.9	4 (2.5)	4	1.9
>=115	7 (1.9)	10	2.1	4 (2.2)	4	1.8
Injection site pruritus						
<90	2 (0.6)	2	0.5	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	4 (1.5)	4	1.1	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	0		
>=115	1 (0.3)	1	0.2	0		
Injection site mass						
<90	0			0		
90-<100	3 (1.1)	3	0.9	2 (1.3)	2	1.1
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Injection site erythema						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	0		
Injection site haematoma						
<90	2 (0.6)	7	1.6	2 (1.2)	10	4.8
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Injection site reaction						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Injection site inflammation						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	3	0.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Injection site haemorrhage						
<90	0			0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	0			0		
Application site haematoma						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Injection site paraesthesia						
<90	0			2 (1.2)	2	1.0
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Injection site induration						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Injection site urticaria						
<90	0			0		
90-<100	1 (0.4)	2	0.6	0		
100-<115	0			0		
>=115	0			0		
Vessel puncture site rash						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Infusion site extravasation								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Vessel puncture site bruise								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Injection site swelling								
<90	0				0			
90-<100	0				0			
100-<115	0				1	(0.6)	2	0.9
>=115	1	(0.3)	1	0.2	0			
Application site bruise								
<90	0				0			
90-<100	0				0			
100-<115	0				1	(0.6)	1	0.5
>=115	0				0			
Puncture site pain								
<90	0				1	(0.6)	2	1.0
90-<100	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Body temperature conditions						
<90	10 (2.9)	14	3.2	1 (0.6)	1	0.5
90-<100	4 (1.5)	6	1.7	4 (2.6)	5	2.6
100-<115	7 (2.1)	7	1.6	6 (3.7)	6	2.8
>=115	6 (1.6)	6	1.2	6 (3.4)	9	4.1
Pyrexia						
<90	10 (2.9)	14	3.2	1 (0.6)	1	0.5
90-<100	4 (1.5)	6	1.7	4 (2.6)	5	2.6
100-<115	7 (2.1)	7	1.6	6 (3.7)	6	2.8
>=115	6 (1.6)	6	1.2	6 (3.4)	9	4.1
Tissue disorders NEC						
<90	1 (0.3)	1	0.2	2 (1.2)	2	1.0
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			0		
>=115	3 (0.8)	3	0.6	2 (1.1)	2	0.9
Cyst						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Nodule						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Dysplasia								
<90	0				0			
90-<100	0				1	(0.7)	1	0.5
100-<115	0				0			
>=115	0				0			
Fat necrosis								
<90	0				1	(0.6)	1	0.5
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Hyperplasia								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	0				1	(0.6)	1	0.5
Complications associated with device								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	1	(0.6)	1	0.5
Vascular stent occlusion								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Injury associated with device								
<90	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Therapeutic and nontherapeutic effects (excl toxicity)						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Withdrawal syndrome						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Metabolism and nutrition disorders						
<90	67 (19.8)	91	20.6	22 (13.6)	29	13.9
90-<100	40 (15.0)	55	15.6	20 (13.2)	24	12.6
100-<115	46 (13.9)	64	14.9	20 (12.3)	28	13.3
>=115	46 (12.5)	57	11.8	21 (11.7)	27	12.3
Appetite and general nutritional disorders						
<90	54 (15.9)	63	14.3	9 (5.6)	12	5.8
90-<100	30 (11.2)	43	12.2	7 (4.6)	8	4.2
100-<115	32 (9.7)	37	8.6	8 (4.9)	11	5.2
>=115	25 (6.8)	29	6.0	4 (2.2)	5	2.3
Decreased appetite						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	49 (14.5)	56	12.7	7 (4.3)	9	4.3
90-<100	28 (10.5)	31	8.8	7 (4.6)	8	4.2
100-<115	24 (7.3)	26	6.0	5 (3.1)	5	2.4
>=115	23 (6.2)	26	5.4	3 (1.7)	4	1.8
Food craving						
<90	2 (0.6)	2	0.5	0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	4 (1.2)	4	0.9	2 (1.2)	2	0.9
>=115	0			0		
Hyperphagia						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	3 (0.9)	4	0.9	1 (0.6)	3	1.4
>=115	1 (0.3)	1	0.2	0		
Increased appetite						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	3 (1.1)	4	1.1	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Food aversion						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	3	0.9	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Lack of satiety						
<90	0			1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Malnutrition						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Vitamin related disorders						
<90	3 (0.9)	3	0.7	1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	5 (3.3)	6	3.2
100-<115	7 (2.1)	12	2.8	2 (1.2)	2	0.9
>=115	9 (2.4)	10	2.1	2 (1.1)	3	1.4
Vitamin D deficiency						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	5 (3.3)	5	2.6
100-<115	5 (1.5)	5	1.2	1 (0.6)	1	0.5
>=115	8 (2.2)	8	1.7	1 (0.6)	1	0.5
Vitamin B12 deficiency						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	4 (1.2)	4	0.9	0		
>=115	0			0		
Folate deficiency						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Vitamin A deficiency						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Vitamin B2 deficiency						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Vitamin B complex deficiency						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Lipid metabolism disorders						
<90	6 (1.8)	7	1.6	8 (4.9)	8	3.8
90-<100	1 (0.4)	1	0.3	3 (2.0)	3	1.6
100-<115	7 (2.1)	7	1.6	5 (3.1)	6	2.8
>=115	6 (1.6)	6	1.2	4 (2.2)	4	1.8
Dyslipidaemia						
<90	3 (0.9)	3	0.7	4 (2.5)	4	1.9
90-<100	1 (0.4)	1	0.3	2 (1.3)	2	1.1
100-<115	3 (0.9)	3	0.7	2 (1.2)	3	1.4
>=115	3 (0.8)	3	0.6	1 (0.6)	1	0.5
Hypercholesterolaemia						
<90	1 (0.3)	1	0.2	3 (1.9)	3	1.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Hypertriglyceridaemia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Hyperlipidaemia						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			2 (1.1)	2	0.9
Cholesterosis						
<90	1 (0.3)	2	0.5	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Glucose metabolism disorders (incl diabetes mellitus)						
<90	3 (0.9)	8	1.8	4 (2.5)	5	2.4
90-<100	3 (1.1)	3	0.9	4 (2.6)	4	2.1
100-<115	1 (0.3)	2	0.5	7 (4.3)	8	3.8
>=115	3 (0.8)	4	0.8	6 (3.4)	8	3.6
Hypoglycaemia						
<90	3 (0.9)	8	1.8	1 (0.6)	2	1.0
90-<100	1 (0.4)	1	0.3	2 (1.3)	2	1.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	1 (0.3)	2	0.5	1 (0.6)	2	0.9
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Glucose tolerance impaired						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			1 (0.6)	1	0.5
>=115	0			1 (0.6)	1	0.5
Type 2 diabetes mellitus						
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			1 (0.6)	1	0.5
>=115	0			4 (2.2)	5	2.3
Postprandial hypoglycaemia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	2	0.4	0		
Diabetes mellitus						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Hyperglycaemia						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Impaired fasting glucose						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			1 (0.6)	1	0.5
Insulin resistance						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Electrolyte and fluid balance conditions						
<90	3 (0.9)	4	0.9	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	2 (0.6)	4	0.9	1 (0.6)	1	0.5
>=115	3 (0.8)	3	0.6	3 (1.7)	3	1.4
Hypokalaemia						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	2 (0.6)	4	0.9	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Hyperkalaemia						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Hyponatraemia						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Dehydration						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Electrolyte imbalance						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Polydipsia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Fluid retention						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Iron and trace metal metabolism disorders						
<90	2 (0.6)	2	0.5	2 (1.2)	2	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			2 (1.3)	2	1.1
100-<115	0			0		
>=115	3 (0.8)	3	0.6	0		
Iron deficiency						
<90	2 (0.6)	2	0.5	2 (1.2)	2	1.0
90-<100	0			2 (1.3)	2	1.1
100-<115	0			0		
>=115	3 (0.8)	3	0.6	0		
Purine and pyrimidine metabolism disorders						
<90	1 (0.3)	2	0.5	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	4 (2.2)	4	1.8
Gout						
<90	1 (0.3)	2	0.5	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	3 (1.7)	3	1.4
Hyperuricaemia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Food intolerance syndromes						
<90	0			0		
90-<100	3 (1.1)	3	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
100-<115	0				0			
>=115	0				0			
Dairy intolerance								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Food intolerance								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Lactose intolerance								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Metabolism disorders NEC								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Hyperlipasaemia								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Bone, calcium, magnesium and phosphorus metabolism disorders								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Hypomagnesaemia								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Protein and amino acid metabolism disorders NEC								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Hypoalbuminaemia								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Skin and subcutaneous tissue disorders								
<90	56	(16.5)	84	19.1	14	(8.6)	20	9.6
90-<100	40	(15.0)	50	14.2	21	(13.9)	24	12.6
100-<115	38	(11.5)	51	11.9	18	(11.0)	21	10.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=115	54	(14.6)	64	13.3	22	(12.3)	31	14.1
Epidermal and dermal conditions								
<90	30	(8.8)	44	10.0	7	(4.3)	10	4.8
90-<100	23	(8.6)	25	7.1	16	(10.6)	19	10.0
100-<115	23	(6.9)	26	6.0	11	(6.7)	12	5.7
>=115	29	(7.9)	34	7.0	18	(10.1)	24	10.9
Rash								
<90	9	(2.7)	12	2.7	2	(1.2)	4	1.9
90-<100	9	(3.4)	9	2.6	4	(2.6)	4	2.1
100-<115	5	(1.5)	5	1.2	5	(3.1)	5	2.4
>=115	3	(0.8)	4	0.8	6	(3.4)	10	4.5
Pruritus								
<90	4	(1.2)	5	1.1	1	(0.6)	1	0.5
90-<100	4	(1.5)	4	1.1	2	(1.3)	2	1.1
100-<115	3	(0.9)	3	0.7	1	(0.6)	1	0.5
>=115	6	(1.6)	6	1.2	2	(1.1)	2	0.9
Eczema								
<90	6	(1.8)	6	1.4	1	(0.6)	1	0.5
90-<100	2	(0.7)	2	0.6	1	(0.7)	1	0.5
100-<115	2	(0.6)	2	0.5	1	(0.6)	1	0.5
>=115	3	(0.8)	3	0.6	1	(0.6)	1	0.5
Dry skin								
<90	2	(0.6)	2	0.5	1	(0.6)	1	0.5
90-<100	1	(0.4)	1	0.3	0			
100-<115	2	(0.6)	2	0.5	1	(0.6)	1	0.5
>=115	3	(0.8)	3	0.6	1	(0.6)	1	0.5
Skin burning sensation								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	3 (0.9)	9	2.0	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	3 (0.8)	3	0.6	1 (0.6)	1	0.5
Dermatitis contact						
<90	1 (0.3)	2	0.5	0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	2 (0.6)	3	0.7	2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Skin lesion						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Pain of skin						
<90	1 (0.3)	1	0.2	0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Psoriasis						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Rash pruritic						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Erythema						
<90	0			0		
90-<100	0			3 (2.0)	3	1.6
100-<115	3 (0.9)	3	0.7	1 (0.6)	1	0.5
>=115	0			0		
Skin irritation						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Dermatitis						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Decubitus ulcer						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Skin disorder						
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	1 (0.3)	2	0.5	0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Dermatitis allergic								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	1	(0.3)	1	0.2	0			
Blister								
<90	0				0			
90-<100	0				2	(1.3)	2	1.1
100-<115	0				0			
>=115	2	(0.5)	2	0.4	3	(1.7)	3	1.4
Papule								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Perioral dermatitis								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Prurigo								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Skin discolouration								
<90	1	(0.3)	1	0.2	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			2 (1.3)	2	1.1
100-<115	0			0		
>=115	0			0		
Dermatitis atopic						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Macule						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Pityriasis rosea						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Rash maculo-papular						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Skin odour abnormal						
<90	0			0		
90-<100	0			0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	1 (0.3)	1	0.2	0		
Xanthelasma						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Drug eruption						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Photosensitivity reaction						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Rash erythematous						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Rash macular						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Skin reaction						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Skin appendage conditions						
<90	29 (8.6)	32	7.3	3 (1.9)	4	1.9
90-<100	17 (6.4)	22	6.2	4 (2.6)	4	2.1
100-<115	15 (4.5)	17	4.0	6 (3.7)	7	3.3
>=115	21 (5.7)	21	4.4	6 (3.4)	6	2.7
Alopecia						
<90	22 (6.5)	23	5.2	3 (1.9)	3	1.4
90-<100	12 (4.5)	12	3.4	1 (0.7)	1	0.5
100-<115	11 (3.3)	12	2.8	1 (0.6)	1	0.5
>=115	8 (2.2)	8	1.7	0		
Hyperhidrosis						
<90	0			0		
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	3 (1.8)	3	1.4
>=115	4 (1.1)	4	0.8	4 (2.2)	4	1.8
Acne						
<90	1 (0.3)	1	0.2	0		
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Hirsutism						
<90	0			1 (0.6)	1	0.5
90-<100	2 (0.7)	3	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Cold sweat						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Ingrowing nail						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	2	0.9
>=115	2 (0.5)	2	0.4	0		
Hair growth abnormal						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Miliaria						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Rosacea						
<90	1 (0.3)	2	0.5	0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Hidradenitis								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	2	(0.5)	2	0.4	0			
Hypertrichosis								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Diffuse alopecia								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Nail discolouration								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Night sweats								
<90	1	(0.3)	1	0.2	0			
90-<100	0				1	(0.7)	1	0.5
100-<115	0				0			
>=115	0				0			
Nail bed inflammation								
<90	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Onychoclasis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Angioedema and urticaria						
<90	3 (0.9)	3	0.7	4 (2.5)	4	1.9
90-<100	2 (0.7)	2	0.6	0		
100-<115	4 (1.2)	4	0.9	2 (1.2)	2	0.9
>=115	4 (1.1)	4	0.8	0		
Urticaria						
<90	3 (0.9)	3	0.7	3 (1.9)	3	1.4
90-<100	1 (0.4)	1	0.3	0		
100-<115	4 (1.2)	4	0.9	2 (1.2)	2	0.9
>=115	4 (1.1)	4	0.8	0		
Cold urticaria						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Angioedema						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Cornification and dystrophic skin disorders						
<90	3 (0.9)	4	0.9	0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	2 (0.5)	3	0.6	0		
Actinic keratosis						
<90	2 (0.6)	3	0.7	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Hyperkeratosis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Skin striae						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Lichenoid keratosis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	2	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Pigmentation disorders						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Ephelides						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Skin hyperpigmentation						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Cutaneous neoplasms benign						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Dermal cyst						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Skin vascular abnormalities						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Ecchymosis						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Skin and subcutaneous tissue disorders NEC						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Erythema nodosum						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Skin ulcer						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Injury, poisoning and procedural complications						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	43 (12.7)	55	12.5	31 (19.1)	56	26.9
90-<100	32 (12.0)	42	11.9	24 (15.9)	32	16.8
100-<115	51 (15.4)	72	16.8	30 (18.4)	41	19.4
>=115	62 (16.8)	95	19.7	36 (20.1)	47	21.4
Injuries NEC						
<90	25 (7.4)	29	6.6	24 (14.8)	38	18.2
90-<100	23 (8.6)	31	8.8	17 (11.3)	20	10.5
100-<115	37 (11.2)	46	10.7	24 (14.7)	32	15.2
>=115	41 (11.1)	62	12.8	31 (17.3)	40	18.2
Ligament sprain						
<90	3 (0.9)	5	1.1	6 (3.7)	7	3.4
90-<100	4 (1.5)	4	1.1	3 (2.0)	3	1.6
100-<115	5 (1.5)	5	1.2	4 (2.5)	4	1.9
>=115	9 (2.4)	10	2.1	6 (3.4)	6	2.7
Fall						
<90	3 (0.9)	3	0.7	4 (2.5)	6	2.9
90-<100	3 (1.1)	3	0.9	1 (0.7)	3	1.6
100-<115	8 (2.4)	8	1.9	5 (3.1)	7	3.3
>=115	5 (1.4)	5	1.0	2 (1.1)	3	1.4
Muscle strain						
<90	2 (0.6)	2	0.5	5 (3.1)	5	2.4
90-<100	3 (1.1)	3	0.9	2 (1.3)	2	1.1
100-<115	4 (1.2)	5	1.2	3 (1.8)	3	1.4
>=115	8 (2.2)	8	1.7	5 (2.8)	5	2.3
Contusion						
<90	0			3 (1.9)	4	1.9
90-<100	3 (1.1)	3	0.9	4 (2.6)	4	2.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	7 (2.1)	8	1.9	3 (1.8)	4	1.9
>=115	5 (1.4)	8	1.7	5 (2.8)	7	3.2
Arthropod bite						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	3 (0.8)	3	0.6	4 (2.2)	4	1.8
Skin laceration						
<90	1 (0.3)	1	0.2	3 (1.9)	4	1.9
90-<100	2 (0.7)	2	0.6	0		
100-<115	3 (0.9)	3	0.7	4 (2.5)	4	1.9
>=115	3 (0.8)	3	0.6	1 (0.6)	1	0.5
Arthropod sting						
<90	3 (0.9)	3	0.7	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Limb injury						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	2 (1.2)	2	0.9
>=115	4 (1.1)	4	0.8	1 (0.6)	1	0.5
Skin abrasion						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	2 (0.5)	5	1.0	2 (1.1)	2	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Tooth fracture						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	3 (0.9)	3	0.7	0		
>=115	1 (0.3)	1	0.2	3 (1.7)	3	1.4
Concussion						
<90	0			0		
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Epicondylitis						
<90	1 (0.3)	1	0.2	2 (1.2)	2	1.0
90-<100	2 (0.7)	2	0.6	3 (2.0)	3	1.6
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Ligament rupture						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Muscle rupture						
<90	0			1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Animal bite						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Back injury						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Road traffic accident						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Wound						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Injury						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Eyelid injury						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Post-traumatic pain						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Bone contusion						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			1 (0.6)	1	0.5
Eye burns						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Foreign body in eye						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Head injury						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Ligament injury						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Face injury						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Nerve injury						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Skeletal injury						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Tendon injury						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Eyelid contusion						
<90	0			0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Muscle injury								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Musculoskeletal injury								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Post-traumatic neck syndrome								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	1	(0.6)	1	0.5
Soft tissue foreign body								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Subdural haematoma								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Chest injury						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Corneal abrasion						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Eye injury						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Gun shot wound						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Post concussion syndrome						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Scar						
<90	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Tendon rupture						
<90	0			0		
90-<100	0			0		
100-<115	0			2 (1.2)	3	1.4
>=115	0			0		
Bone and joint injuries						
<90	8 (2.4)	9	2.0	6 (3.7)	7	3.4
90-<100	3 (1.1)	3	0.9	4 (2.6)	4	2.1
100-<115	9 (2.7)	10	2.3	8 (4.9)	8	3.8
>=115	15 (4.1)	17	3.5	4 (2.2)	4	1.8
Foot fracture						
<90	3 (0.9)	4	0.9	1 (0.6)	1	0.5
90-<100	0			3 (2.0)	3	1.6
100-<115	1 (0.3)	2	0.5	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Joint injury						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	3 (0.8)	3	0.6	0		
Meniscus injury						
<90	0			1 (0.6)	2	1.0
90-<100	0			0		
100-<115	0			2 (1.2)	2	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	4 (1.1)	4	0.8	1 (0.6)	1	0.5
Joint dislocation						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Hand fracture						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Radius fracture						
<90	0			0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Rib fracture						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Ankle fracture						
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Facial bones fracture						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Spinal compression fracture						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Upper limb fracture						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Wrist fracture						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Tibia fracture						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Femur fracture						
<90	0			0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	1 (0.3)	2	0.4	0		
Fractured coccyx						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Stress fracture						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Thoracic vertebral fracture						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Fibula fracture						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Torus fracture						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Procedural related injuries and complications NEC						
<90	9 (2.7)	10	2.3	4 (2.5)	5	2.4
90-<100	3 (1.1)	3	0.9	5 (3.3)	6	3.2
100-<115	7 (2.1)	12	2.8	1 (0.6)	1	0.5
>=115	8 (2.2)	10	2.1	1 (0.6)	1	0.5
Procedural pain						
<90	4 (1.2)	4	0.9	4 (2.5)	5	2.4
90-<100	1 (0.4)	1	0.3	2 (1.3)	3	1.6
100-<115	3 (0.9)	4	0.9	0		
>=115	4 (1.1)	4	0.8	1 (0.6)	1	0.5
Injection related reaction						
<90	2 (0.6)	2	0.5	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Post procedural complication						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	2	0.4	0		
Administration related reaction						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Procedural nausea						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Anaemia postoperative						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Anaphylactic transfusion reaction						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Post procedural constipation						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Suture related complication						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Urinary retention postoperative						
<90	0			0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Vaccination complication								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	1	(0.6)	1	0.5
>=115	0				0			
Post procedural haemorrhage								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Procedural haemorrhage								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Procedural vomiting								
<90	0				0			
90-<100	0				1	(0.7)	1	0.5
100-<115	0				0			
>=115	0				0			
Seroma								
<90	0				0			
90-<100	0				1	(0.7)	1	0.5
100-<115	0				0			
>=115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Medication errors and other product use errors and issues						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	1 (0.7)	2	1.1
100-<115	4 (1.2)	4	0.9	0		
>=115	2 (0.5)	2	0.4	0		
Accidental overdose						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	1 (0.7)	2	1.1
100-<115	2 (0.6)	2	0.5	0		
>=115	2 (0.5)	2	0.4	0		
Incorrect dose administered						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Medication error						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Injuries by physical agents						
<90	4 (1.2)	4	0.9	3 (1.9)	3	1.4
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9
Sunburn						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Heat exhaustion						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Heat illness						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Hypobarism						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Thermal burn						
<90	0			2 (1.2)	2	1.0
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Burns second degree						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			2 (1.1)	2	0.9
Overdoses and underdoses NEC						
<90	1 (0.3)	1	0.2	2 (1.2)	2	1.0
90-<100	0			0		
100-<115	0			0		
>=115	3 (0.8)	3	0.6	0		
Overdose						
<90	1 (0.3)	1	0.2	2 (1.2)	2	1.0
90-<100	0			0		
100-<115	0			0		
>=115	3 (0.8)	3	0.6	0		
Exposures, chemical injuries and poisoning						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Reactive gastropathy						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Exposure to toxic agent						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Respiratory, thoracic and mediastinal disorders						
<90	41 (12.1)	49	11.1	17 (10.5)	21	10.1
90-<100	30 (11.2)	39	11.1	20 (13.2)	22	11.6
100-<115	49 (14.8)	64	14.9	30 (18.4)	42	19.9
>=115	53 (14.4)	73	15.1	37 (20.7)	49	22.3
Respiratory tract signs and symptoms						
<90	16 (4.7)	18	4.1	6 (3.7)	8	3.8
90-<100	14 (5.2)	16	4.5	12 (7.9)	12	6.3
100-<115	24 (7.3)	25	5.8	9 (5.5)	10	4.7
>=115	21 (5.7)	22	4.6	6 (3.4)	7	3.2
Oropharyngeal pain						
<90	9 (2.7)	11	2.5	6 (3.7)	7	3.4
90-<100	7 (2.6)	8	2.3	6 (4.0)	6	3.2
100-<115	15 (4.5)	16	3.7	8 (4.9)	9	4.3
>=115	17 (4.6)	18	3.7	3 (1.7)	4	1.8
Rhinorrhoea						
<90	0			0		
90-<100	3 (1.1)	3	0.9	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	0		
>=115	1 (0.3)	1	0.2	0		
Upper respiratory tract inflammation						
<90	3 (0.9)	3	0.7	0		
90-<100	2 (0.7)	3	0.9	4 (2.6)	4	2.1
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Hiccups						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Upper-airway cough syndrome						
<90	3 (0.9)	3	0.7	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Catarrh						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Dysphonia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Diaphragmalgia						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Paranasal sinus discomfort						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			1 (0.6)	1	0.5
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Pleuritic pain						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Yawning						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Oropharyngeal discomfort						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Sinus pain						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Upper respiratory tract congestion						
<90	0			0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Respiratory disorders NEC						
<90	13 (3.8)	14	3.2	10 (6.2)	10	4.8
90-<100	13 (4.9)	14	4.0	6 (4.0)	7	3.7
100-<115	14 (4.2)	16	3.7	13 (8.0)	14	6.6
>=115	21 (5.7)	26	5.4	22 (12.3)	25	11.4
Cough						
<90	7 (2.1)	7	1.6	4 (2.5)	4	1.9
90-<100	9 (3.4)	10	2.8	6 (4.0)	7	3.7
100-<115	9 (2.7)	10	2.3	10 (6.1)	10	4.7
>=115	15 (4.1)	18	3.7	13 (7.3)	14	6.4
Dyspnoea						
<90	5 (1.5)	5	1.1	3 (1.9)	3	1.4
90-<100	0			0		
100-<115	0			2 (1.2)	2	0.9
>=115	3 (0.8)	3	0.6	3 (1.7)	3	1.4
Sleep apnoea syndrome						
<90	1 (0.3)	1	0.2	2 (1.2)	2	1.0
90-<100	2 (0.7)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	2 (0.5)	2	0.4	2 (1.1)	2	0.9
Productive cough						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Haemoptysis						
<90	0			0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	0			0		
>=115	0			0		
Respiratory disorder						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	0			2 (1.1)	2	0.9
Dyspnoea exertional						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Hyperventilation						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Respiratory tract congestion						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Acute respiratory failure						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Pulmonary mass						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Upper respiratory tract disorders (excl infections)						
<90	15 (4.4)	15	3.4	1 (0.6)	1	0.5
90-<100	7 (2.6)	7	2.0	2 (1.3)	2	1.1
100-<115	14 (4.2)	16	3.7	7 (4.3)	10	4.7
>=115	15 (4.1)	15	3.1	8 (4.5)	8	3.6
Sinus congestion						
<90	2 (0.6)	2	0.5	0		
90-<100	2 (0.7)	2	0.6	2 (1.3)	2	1.1
100-<115	5 (1.5)	5	1.2	2 (1.2)	4	1.9
>=115	4 (1.1)	4	0.8	1 (0.6)	1	0.5
Nasal congestion						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	4 (1.2)	4	0.9	1 (0.6)	1	0.5
>=115	4 (1.1)	4	0.8	4 (2.2)	4	1.8
Rhinitis allergic						
<90	5 (1.5)	5	1.1	0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	2 (0.6)	2	0.5	3 (1.8)	4	1.9
>=115	4 (1.1)	4	0.8	3 (1.7)	3	1.4
Epistaxis						
<90	2 (0.6)	2	0.5	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	2 (0.5)	2	0.4	0		
Tonsillar hypertrophy						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Paranasal sinus hypersecretion						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Nasal septum deviation						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Nasal polyps						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Vocal cord polyp						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Nasal dryness						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Paranasal cyst						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Nasal adhesions						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Bronchial disorders (excl neoplasms)						
<90	0			0		
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	6 (1.8)	6	1.4	5 (3.1)	6	2.8
>=115	6 (1.6)	6	1.2	7 (3.9)	9	4.1
Asthma						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	5 (1.5)	5	1.2	4 (2.5)	4	1.9
>=115	4 (1.1)	4	0.8	4 (2.2)	6	2.7
Chronic obstructive pulmonary disease						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	2 (1.1)	2	0.9
Wheezing						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Allergic bronchitis						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	2	0.9
>=115	0			0		
Lower respiratory tract disorders (excl obstruction and infection)						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Atelectasis						
<90	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	1	(0.6)	1	0.5
>=115	0				0			
Pulmonary fibrosis								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Pulmonary vascular disorders								
<90	1	(0.3)	1	0.2	1	(0.6)	1	0.5
90-<100	0				0			
100-<115	0				1	(0.6)	1	0.5
>=115	1	(0.3)	1	0.2	0			
Pulmonary embolism								
<90	1	(0.3)	1	0.2	1	(0.6)	1	0.5
90-<100	0				0			
100-<115	0				1	(0.6)	1	0.5
>=115	1	(0.3)	1	0.2	0			
Pleural disorders								
<90	0				1	(0.6)	1	0.5
90-<100	0				0			
100-<115	0				0			
>=115	2	(0.5)	2	0.4	0			
Pleural effusion								
<90	0				0			
90-<100	0				0			
100-<115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	2 (0.5)	2	0.4	0		
Pleurisy						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Psychiatric disorders						
<90	22 (6.5)	27	6.1	19 (11.7)	22	10.6
90-<100	29 (10.9)	38	10.8	15 (9.9)	22	11.6
100-<115	36 (10.9)	44	10.2	27 (16.6)	39	18.5
>=115	37 (10.0)	51	10.6	22 (12.3)	30	13.6
Anxiety disorders and symptoms						
<90	9 (2.7)	10	2.3	7 (4.3)	7	3.4
90-<100	9 (3.4)	9	2.6	5 (3.3)	5	2.6
100-<115	13 (3.9)	13	3.0	9 (5.5)	9	4.3
>=115	15 (4.1)	16	3.3	10 (5.6)	11	5.0
Anxiety						
<90	7 (2.1)	7	1.6	6 (3.7)	6	2.9
90-<100	7 (2.6)	7	2.0	4 (2.6)	4	2.1
100-<115	8 (2.4)	8	1.9	3 (1.8)	3	1.4
>=115	10 (2.7)	11	2.3	7 (3.9)	7	3.2
Stress						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	3 (0.9)	3	0.7	4 (2.5)	4	1.9
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Panic attack						
<90	1 (0.3)	1	0.2	0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Acute stress disorder						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Burnout syndrome						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Nervousness						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Post-traumatic stress disorder						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Agitation						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			2 (1.2)	2	0.9
>=115	0			0		
Generalised anxiety disorder						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Sleep disorders and disturbances						
<90	5 (1.5)	5	1.1	3 (1.9)	3	1.4
90-<100	11 (4.1)	11	3.1	10 (6.6)	12	6.3
100-<115	13 (3.9)	14	3.3	9 (5.5)	11	5.2
>=115	11 (3.0)	12	2.5	7 (3.9)	7	3.2
Insomnia						
<90	5 (1.5)	5	1.1	2 (1.2)	2	1.0
90-<100	7 (2.6)	7	2.0	9 (6.0)	10	5.3
100-<115	9 (2.7)	9	2.1	3 (1.8)	3	1.4
>=115	7 (1.9)	8	1.7	4 (2.2)	4	1.8
Sleep disorder						
<90	0			1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	0		
100-<115	3 (0.9)	3	0.7	5 (3.1)	6	2.8
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Initial insomnia						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	2	0.5	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	2 (0.5)	2	0.4	0		
Abnormal dreams						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Nightmare						
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	2	1.1
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Middle insomnia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Sleep terror						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Depressed mood disorders and disturbances						
<90	6 (1.8)	6	1.4	4 (2.5)	4	1.9
90-<100	8 (3.0)	9	2.6	3 (2.0)	3	1.6
100-<115	7 (2.1)	9	2.1	13 (8.0)	15	7.1
>=115	12 (3.3)	15	3.1	7 (3.9)	7	3.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Depression						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	5 (1.9)	5	1.4	2 (1.3)	2	1.1
100-<115	1 (0.3)	2	0.5	7 (4.3)	8	3.8
>=115	8 (2.2)	9	1.9	4 (2.2)	4	1.8
Depressed mood						
<90	4 (1.2)	4	0.9	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	4 (1.2)	5	1.2	4 (2.5)	4	1.9
>=115	4 (1.1)	4	0.8	3 (1.7)	3	1.4
Major depression						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	2 (0.5)	2	0.4	0		
Anhedonia						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Negative thoughts						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Tearfulness						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	1	(0.6)	1	0.5
>=115	0				0			
Depressive symptom								
<90	0				0			
90-<100	0				0			
100-<115	0				1	(0.6)	1	0.5
>=115	0				0			
Persistent depressive disorder								
<90	0				2	(1.2)	2	1.0
90-<100	0				0			
100-<115	0				1	(0.6)	1	0.5
>=115	0				0			
Mood disorders and disturbances NEC								
<90	3	(0.9)	3	0.7	1	(0.6)	1	0.5
90-<100	3	(1.1)	3	0.9	0			
100-<115	2	(0.6)	2	0.5	1	(0.6)	1	0.5
>=115	1	(0.3)	1	0.2	1	(0.6)	1	0.5
Irritability								
<90	2	(0.6)	2	0.5	1	(0.6)	1	0.5
90-<100	2	(0.7)	2	0.6	0			
100-<115	0				0			
>=115	0				1	(0.6)	1	0.5
Apathy								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	1 (0.3)	1	0.2	0		
Affective disorder						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Mood swings						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Changes in physical activity						
<90	2 (0.6)	2	0.5	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Restlessness						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Tic						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Suicidal and self-injurious behaviours NEC						
<90	0			1 (0.6)	2	1.0
90-<100	1 (0.4)	1	0.3	1 (0.7)	2	1.1
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Suicidal ideation						
<90	0			1 (0.6)	2	1.0
90-<100	1 (0.4)	1	0.3	1 (0.7)	2	1.1
100-<115	1 (0.3)	1	0.2	0		
>=115	2 (0.5)	2	0.4	0		
Suicide attempt						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Sexual dysfunctions, disturbances and gender identity disorders						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Libido decreased						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Libido increased						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Adjustment disorders (incl subtypes)						
<90	0			2 (1.2)	2	1.0
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9
Adjustment disorder with depressed mood						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			2 (1.1)	2	0.9
Adjustment disorder						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Grief reaction						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Cognitive and attention disorders and disturbances						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	2	0.5	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Mental fatigue						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	2	0.5	0		
>=115	0			0		
Attention deficit/hyperactivity disorder						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Deliria (incl confusion)						
<90	0			0		
90-<100	1 (0.4)	2	0.6	0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Disorientation						
<90	0			0		
90-<100	1 (0.4)	2	0.6	0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Psychiatric and behavioural symptoms NEC						
<90	0			2 (1.2)	2	1.0
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Abulia						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Psychiatric symptom						
<90	0			2 (1.2)	2	1.0
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Manic and bipolar mood disorders and disturbances						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Bipolar disorder						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Psychiatric disorders NEC						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Alcoholic hangover						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Somatic symptom and related disorders						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Conversion disorder						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Reproductive system and breast disorders						
<90	29 (8.6)	38	8.6	5 (3.1)	9	4.3
90-<100	17 (6.4)	22	6.2	8 (5.3)	9	4.7
100-<115	26 (7.9)	31	7.2	10 (6.1)	11	5.2
>=115	24 (6.5)	31	6.4	9 (5.0)	10	4.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Menstrual cycle and uterine bleeding disorders						
<90	14 (4.1)	17	3.9	1 (0.6)	4	1.9
90-<100	7 (2.6)	8	2.3	0		
100-<115	14 (4.2)	16	3.7	3 (1.8)	3	1.4
>=115	10 (2.7)	12	2.5	3 (1.7)	3	1.4
Menstruation irregular						
<90	1 (0.3)	1	0.2	0		
90-<100	5 (1.9)	5	1.4	0		
100-<115	5 (1.5)	5	1.2	0		
>=115	3 (0.8)	3	0.6	0		
Menorrhagia						
<90	3 (0.9)	4	0.9	0		
90-<100	1 (0.4)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	2 (1.2)	2	0.9
>=115	5 (1.4)	5	1.0	1 (0.6)	1	0.5
Dysmenorrhoea						
<90	3 (0.9)	4	0.9	1 (0.6)	3	1.4
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	2 (0.5)	2	0.4	0		
Metrorrhagia						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	5 (1.5)	5	1.2	1 (0.6)	1	0.5
>=115	0			0		
Menstrual disorder						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	2 (0.5)	2	0.4	0		
Dysfunctional uterine bleeding						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Oligomenorrhoea						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Amenorrhoea						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Menstruation delayed						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Premenstrual syndrome						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Premenstrual pain						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Breast disorders						
<90	7 (2.1)	8	1.8	2 (1.2)	2	1.0
90-<100	4 (1.5)	5	1.4	1 (0.7)	1	0.5
100-<115	4 (1.2)	4	0.9	2 (1.2)	3	1.4
>=115	2 (0.5)	3	0.6	2 (1.1)	2	0.9
Breast mass						
<90	3 (0.9)	3	0.7	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	3 (0.9)	3	0.7	1 (0.6)	2	0.9
>=115	1 (0.3)	1	0.2	0		
Breast cyst						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Breast pain						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Breast disorder						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Fibrocystic breast disease						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Breast inflammation						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Nipple pain						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Breast fibrosis						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Breast haematoma						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Uterine, pelvic and broad ligament disorders						
<90	4 (1.2)	4	0.9	0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	3 (0.9)	3	0.7	1 (0.6)	1	0.5
>=115	3 (0.8)	3	0.6	0		
Uterine haemorrhage						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Endometriosis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Uterine polyp						
<90	0			0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Adenomyosis						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Uterine enlargement						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Vaginal prolapse						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Menopause related conditions						
<90	3 (0.9)	3	0.7	2 (1.2)	3	1.4
90-<100	4 (1.5)	4	1.1	0		
100-<115	1 (0.3)	1	0.2	2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	0		
Menopausal symptoms						
<90	2 (0.6)	2	0.5	0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Atrophic vulvovaginitis						
<90	0			1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Postmenopausal haemorrhage						
<90	1 (0.3)	1	0.2	1 (0.6)	2	1.0
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Vulvovaginal disorders (excl infections and inflammations)						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	2 (1.3)	2	1.1
100-<115	4 (1.2)	4	0.9	0		
>=115	3 (0.8)	3	0.6	3 (1.7)	3	1.4
Vaginal haemorrhage						
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	3 (0.9)	3	0.7	0		
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Vulvovaginal dryness						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Vulvovaginal discomfort						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Vulvovaginal pain						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Vaginal polyp						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Vulvovaginal pruritus						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Ovarian and fallopian tube disorders						
<90	4 (1.2)	4	0.9	0		
90-<100	1 (0.4)	1	0.3	2 (1.3)	2	1.1
100-<115	1 (0.3)	1	0.2	0		
>=115	3 (0.8)	3	0.6	1 (0.6)	1	0.5
Ovarian cyst						
<90	3 (0.9)	3	0.7	0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Polycystic ovaries						
<90	1 (0.3)	1	0.2	0		
90-<100	0			1 (0.7)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
100-<115	0				0			
>=115	0				0			
Hydrosalpinx								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Reproductive tract disorders NEC								
<90	1	(0.3)	1	0.2	0			
90-<100	0				1	(0.7)	1	0.5
100-<115	0				0			
>=115	2	(0.5)	2	0.4	0			
Pelvic pain								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Genital rash								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Genital pain								
<90	0				0			
90-<100	0				1	(0.7)	1	0.5
100-<115	0				0			
>=115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Cervix disorders (excl infections and inflammations)						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Cervical leukoplakia						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Cervical dysplasia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Uterine cervical erosion						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Testicular and epididymal disorders						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Testicular pain						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Testicular mass						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Testicular disorder						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Sexual function and fertility disorders						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Dyspareunia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Erectile dysfunction						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
90-<100	0			1	(0.7)	1 0.5
100-<115	0			0		
>=115	1	(0.3)	1 0.2	0		
Prostatic disorders (excl infections and inflammations)						
<90	0			0		
90-<100	1	(0.4)	1 0.3	0		
100-<115	0			1	(0.6)	1 0.5
>=115	0			0		
Benign prostatic hyperplasia						
<90	0			0		
90-<100	1	(0.4)	1 0.3	0		
100-<115	0			1	(0.6)	1 0.5
>=115	0			0		
Female reproductive tract infections and inflammations						
<90	0			0		
90-<100	0			0		
100-<115	1	(0.3)	1 0.2	0		
>=115	0			0		
Uterine inflammation						
<90	0			0		
90-<100	0			0		
100-<115	1	(0.3)	1 0.2	0		
>=115	0			0		
Penile and scrotal disorders (excl infections and inflammations)						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Scrotal pain						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Investigations						
<90	24 (7.1)	27	6.1	6 (3.7)	6	2.9
90-<100	25 (9.4)	37	10.5	9 (6.0)	17	8.9
100-<115	17 (5.1)	21	4.9	15 (9.2)	19	9.0
>=115	27 (7.3)	33	6.8	19 (10.6)	25	11.4
Hepatobiliary investigations						
<90	2 (0.6)	3	0.7	0		
90-<100	5 (1.9)	5	1.4	3 (2.0)	5	2.6
100-<115	2 (0.6)	2	0.5	3 (1.8)	4	1.9
>=115	7 (1.9)	7	1.5	5 (2.8)	6	2.7
Gamma-glutamyltransferase increased						
<90	1 (0.3)	1	0.2	0		
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	2 (1.2)	2	0.9
>=115	3 (0.8)	3	0.6	0		
Hepatic enzyme increased						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	3 (0.8)	3	0.6	1 (0.6)	1	0.5
Aspartate aminotransferase increased						
<90	0			0		
90-<100	1 (0.4)	1	0.3	2 (1.3)	2	1.1
100-<115	0			0		
>=115	0			2 (1.1)	2	0.9
Alanine aminotransferase increased						
<90	1 (0.3)	1	0.2	0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			2 (1.1)	2	0.9
Transaminases increased						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Blood bilirubin increased						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Protein and chemistry analyses NEC						
<90	2 (0.6)	2	0.5	0		
90-<100	5 (1.9)	5	1.4	0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	4 (1.1)	4	0.8	4 (2.2)	4	1.8
C-reactive protein increased						
<90	2 (0.6)	2	0.5	0		
90-<100	5 (1.9)	5	1.4	0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	4 (1.1)	4	0.8	4 (2.2)	4	1.8
Gastrointestinal investigations						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	4 (1.5)	5	1.4	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	6 (1.6)	7	1.5	0		
Lipase increased						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	6 (1.6)	6	1.2	0		
Amylase increased						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Gastric pH						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Pancreatic enzymes increased						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Cardiac and vascular investigations (excl enzyme tests)						
<90	3 (0.9)	3	0.7	1 (0.6)	1	0.5
90-<100	2 (0.7)	3	0.9	1 (0.7)	1	0.5
100-<115	3 (0.9)	3	0.7	3 (1.8)	3	1.4
>=115	2 (0.5)	3	0.6	2 (1.1)	2	0.9
Heart rate increased						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
QRS axis abnormal						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Blood pressure abnormal						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Electrocardiogram T wave amplitude decreased						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Pulse abnormal						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Electrocardiogram ST segment depression						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Electrocardiogram T wave inversion						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Blood pressure decreased						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Blood pressure increased						
<90	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			1 (0.7)	1	0.5
100-<115	0			2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9
Cardiac murmur						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Electrocardiogram T wave abnormal						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Lipid analyses						
<90	2 (0.6)	4	0.9	0		
90-<100	4 (1.5)	9	2.6	2 (1.3)	3	1.6
100-<115	3 (0.9)	3	0.7	1 (0.6)	1	0.5
>=115	0			1 (0.6)	1	0.5
High density lipoprotein decreased						
<90	1 (0.3)	1	0.2	0		
90-<100	3 (1.1)	3	0.9	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Blood cholesterol increased						
<90	2 (0.6)	2	0.5	0		
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Low density lipoprotein increased						
<90	1 (0.3)	1	0.2	0		
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Lipids increased						
<90	0			0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	0			0		
Blood triglycerides increased						
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Very low density lipoprotein increased						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Endocrine investigations (incl sex hormones)						
<90	0			1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	0		
100-<115	3 (0.9)	5	1.2	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	3 (0.8)	3	0.6	1 (0.6)	1	0.5
Blood calcitonin increased						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	3 (0.8)	3	0.6	1 (0.6)	1	0.5
Blood thyroid stimulating hormone decreased						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Blood thyroid stimulating hormone abnormal						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Thyroxine free increased						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Thyroxine increased						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Blood thyroid stimulating hormone increased						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Physical examination and organ system status topics						
<90	4 (1.2)	4	0.9	0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	0			1 (0.6)	2	0.9
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9
Weight decreased						
<90	3 (0.9)	3	0.7	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Weight increased						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9
Body mass index decreased						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Respiratory rate increased						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Body temperature increased						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	2	0.9
>=115	0			0		
Enzyme investigations NEC						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	3 (2.0)	3	1.6
100-<115	2 (0.6)	2	0.5	3 (1.8)	3	1.4
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Blood creatine phosphokinase increased						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	3 (2.0)	3	1.6
100-<115	1 (0.3)	1	0.2	2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Enzyme level increased						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Blood alkaline phosphatase increased						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Renal and urinary tract investigations and urinalyses						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	1 (0.7)	1	0.5
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Blood creatinine increased						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Glomerular filtration rate decreased						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
White blood cells urine						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Blood urine present						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Microbiology and serology investigations						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	2 (0.5)	2	0.4	0		
HIV test positive						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Helicobacter test positive						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Human papilloma virus test positive						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Haematology investigations (incl blood groups)						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			2 (1.1)	5	2.3
Haemoglobin decreased						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Haematology test abnormal						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Haematocrit increased						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Haemoglobin increased						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Red blood cell count increased						
<90	0			0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Red cell distribution width increased						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Cytogenetic investigations						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Prostatic specific antigen increased						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Reproductive organ and breast investigations (excl hormone analyses)						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Biopsy breast						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Metabolic, nutritional and blood gas investigations						
<90	1 (0.3)	1	0.2	0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	1 (0.3)	1	0.2	3 (1.7)	3	1.4
Blood uric acid increased						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Blood glucose increased						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Glycosylated haemoglobin increased						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Vitamin D decreased						
<90	0			0		
90-<100	0			0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=115	0			1	(0.6)	1	0.5
Water, electrolyte and mineral investigations							
<90	1	(0.3)	1	0.2	0			
90-<100	0			3	(2.0)	3	1.6
100-<115	0			0			
>=115	1	(0.3)	1	0.2	0			
Blood potassium increased							
<90	1	(0.3)	1	0.2	0			
90-<100	0			0			
100-<115	0			0			
>=115	0			0			
Blood calcium decreased							
<90	0			0			
90-<100	0			0			
100-<115	0			0			
>=115	1	(0.3)	1	0.2	0			
Blood iron decreased							
<90	0			0			
90-<100	0			1	(0.7)	1	0.5
100-<115	0			0			
>=115	0			0			
Blood sodium increased							
<90	0			0			
90-<100	0			1	(0.7)	1	0.5
100-<115	0			0			
>=115	0			0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Serum ferritin decreased								
<90	0				0			
90-<100	0				1	(0.7)	1	0.5
100-<115	0				0			
>=115	0				0			
Investigations, imaging and histopathology procedures NEC								
<90	0				1	(0.6)	1	0.5
90-<100	0				0			
100-<115	0				0			
>=115	2	(0.5)	2	0.4	0			
Precancerous cells present								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Smear test								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Endoscopy								
<90	0				1	(0.6)	1	0.5
90-<100	0				0			
100-<115	0				0			
>=115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Musculoskeletal and soft tissue investigations (excl enzyme tests)								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Arthroscopy								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Immunology and allergy investigations								
<90	0				0			
90-<100	0				0			
100-<115	0				1	(0.6)	1	0.5
>=115	0				0			
Antinuclear antibody positive								
<90	0				0			
90-<100	0				0			
100-<115	0				1	(0.6)	1	0.5
>=115	0				0			
Vascular disorders								
<90	22	(6.5)	25	5.7	10	(6.2)	12	5.8
90-<100	13	(4.9)	13	3.7	12	(7.9)	12	6.3
100-<115	33	(10.0)	36	8.4	14	(8.6)	15	7.1
>=115	22	(6.0)	23	4.8	9	(5.0)	11	5.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Vascular hypertensive disorders						
<90	9 (2.7)	9	2.0	6 (3.7)	8	3.8
90-<100	5 (1.9)	5	1.4	7 (4.6)	7	3.7
100-<115	15 (4.5)	15	3.5	8 (4.9)	9	4.3
>=115	13 (3.5)	13	2.7	7 (3.9)	8	3.6
Hypertension						
<90	9 (2.7)	9	2.0	6 (3.7)	8	3.8
90-<100	5 (1.9)	5	1.4	6 (4.0)	6	3.2
100-<115	14 (4.2)	14	3.3	8 (4.9)	9	4.3
>=115	12 (3.3)	12	2.5	7 (3.9)	8	3.6
Essential hypertension						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Hypertensive emergency						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Hypertensive crisis						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Decreased and nonspecific blood pressure disorders and shock						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	7 (2.1)	8	1.8	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	0		
100-<115	6 (1.8)	7	1.6	1 (0.6)	1	0.5
>=115	4 (1.1)	4	0.8	0		
Hypotension						
<90	4 (1.2)	4	0.9	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	4 (1.2)	5	1.2	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Orthostatic hypotension						
<90	2 (0.6)	3	0.7	0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	2 (0.5)	2	0.4	0		
Circulatory collapse						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Vascular disorders NEC						
<90	4 (1.2)	5	1.1	0		
90-<100	1 (0.4)	1	0.3	2 (1.3)	2	1.1
100-<115	4 (1.2)	4	0.9	2 (1.2)	2	0.9
>=115	0			0		
Hot flush						
<90	4 (1.2)	4	0.9	0		
90-<100	1 (0.4)	1	0.3	2 (1.3)	2	1.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	3 (0.9)	3	0.7	1 (0.6)	1	0.5
>=115	0			0		
Flushing						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Arteriosclerosis, stenosis, vascular insufficiency and necrosis						
<90	0			1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	5 (1.5)	5	1.2	1 (0.6)	1	0.5
>=115	0			1 (0.6)	1	0.5
Peripheral venous disease						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	0			0		
Peripheral coldness						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Aortic arteriosclerosis						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Arteriosclerosis						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Raynaud's phenomenon						
<90	0			1 (0.6)	1	0.5
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Vascular haemorrhagic disorders						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	0		
Haematoma						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	2 (1.2)	2	0.9
>=115	1 (0.3)	1	0.2	0		
Venous varices						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	3 (0.8)	3	0.6	0		
Varicose vein						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	3 (0.8)	3	0.6	0		
Embolism and thrombosis						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9
Thrombosis						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Thrombophlebitis						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Deep vein thrombosis						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Thrombophlebitis superficial						
<90	0			0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Vascular infections and inflammations						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Arteritis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Phlebitis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Lymphatic vessel disorders						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Lymphoedema						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Cardiac disorders						
<90	9 (2.7)	10	2.3	9 (5.6)	12	5.8
90-<100	15 (5.6)	17	4.8	11 (7.3)	16	8.4
100-<115	11 (3.3)	12	2.8	11 (6.7)	13	6.2
>=115	19 (5.1)	23	4.8	2 (1.1)	3	1.4
Cardiac arrhythmias						
<90	4 (1.2)	4	0.9	4 (2.5)	4	1.9
90-<100	9 (3.4)	11	3.1	6 (4.0)	7	3.7
100-<115	7 (2.1)	7	1.6	5 (3.1)	7	3.3
>=115	12 (3.3)	16	3.3	2 (1.1)	3	1.4
Atrial fibrillation						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	2 (1.2)	3	1.4
>=115	3 (0.8)	6	1.2	1 (0.6)	1	0.5
Tachycardia						
<90	1 (0.3)	1	0.2	2 (1.2)	2	1.0
90-<100	2 (0.7)	2	0.6	2 (1.3)	2	1.1
100-<115	0			1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Atrioventricular block first degree						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	3 (0.8)	3	0.6	1 (0.6)	1	0.5
Arrhythmia						
<90	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Bundle branch block left						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Ventricular extrasystoles						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Sinus tachycardia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Atrial flutter						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Atrial tachycardia						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=115	0				0			
Atrioventricular block								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Bundle branch block right								
<90	0				0			
90-<100	1	(0.4)	1	0.3	2	(1.3)	2	1.1
100-<115	0				0			
>=115	0				0			
Defect conduction intraventricular								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Atrioventricular block second degree								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Bradycardia								
<90	0				0			
90-<100	0				1	(0.7)	1	0.5
100-<115	1	(0.3)	1	0.2	1	(0.6)	1	0.5
>=115	0				1	(0.6)	1	0.5
Cardiac flutter								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Nodal rhythm						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Sinus bradycardia						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Supraventricular extrasystoles						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Cardiac disorders, signs and symptoms NEC						
<90	4 (1.2)	4	0.9	5 (3.1)	7	3.4
90-<100	3 (1.1)	3	0.9	2 (1.3)	2	1.1
100-<115	3 (0.9)	3	0.7	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Palpitations						
<90	3 (0.9)	3	0.7	4 (2.5)	6	2.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	3 (1.1)	3	0.9	1 (0.7)	1	0.5
100-<115	3 (0.9)	3	0.7	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Cardiovascular disorder						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Hypertensive heart disease						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Coronary artery disorders						
<90	1 (0.3)	1	0.2	0		
90-<100	2 (0.7)	2	0.6	4 (2.6)	5	2.6
100-<115	0			3 (1.8)	3	1.4
>=115	4 (1.1)	4	0.8	0		
Acute myocardial infarction						
<90	1 (0.3)	1	0.2	0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Angina pectoris						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			3 (1.8)	3	1.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=115	2	(0.5)	2	0.4	0			
Arteriosclerosis coronary artery								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Coronary artery stenosis								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Angina unstable								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Coronary artery disease								
<90	0				0			
90-<100	0				1	(0.7)	1	0.5
100-<115	0				0			
>=115	0				0			
Myocardial infarction								
<90	0				0			
90-<100	0				2	(1.3)	2	1.1
100-<115	0				0			
>=115	0				0			
Cardiac valve disorders								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	2	1.1
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Aortic valve incompetence						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Aortic valve sclerosis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Mitral valve incompetence						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Tricuspid valve incompetence						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Cardiac neoplasms						
<90	0			0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Pericardial cyst						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Pericardial disorders						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Pericardial disease						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Myocardial disorders						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			2 (1.2)	2	0.9
>=115	0			0		
Left ventricular hypertrophy						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Cardiomegaly						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Cardiomyopathy						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Myocarditis						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
<90	14 (4.1)	14	3.2	8 (4.9)	8	3.8
90-<100	12 (4.5)	13	3.7	8 (5.3)	8	4.2
100-<115	9 (2.7)	12	2.8	3 (1.8)	5	2.4
>=115	11 (3.0)	13	2.7	6 (3.4)	6	2.7
Cutaneous neoplasms benign						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	2 (1.3)	2	1.1
100-<115	3 (0.9)	5	1.2	1 (0.6)	1	0.5
>=115	4 (1.1)	6	1.2	2 (1.1)	2	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Melanocytic naevus						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	3 (0.8)	4	0.8	1 (0.6)	1	0.5
Seborrhoeic keratosis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Acrochordon						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Skin papilloma						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Dysplastic naevus						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Pyogenic granuloma						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Reproductive neoplasms female benign						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Uterine leiomyoma						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	0			1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Ovarian adenoma						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Soft tissue neoplasms benign						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Lipoma						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	2 (0.5)	2	0.4	0		
Leiomyoma						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Breast neoplasms malignant and unspecified (incl nipple)						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Intraductal proliferative breast lesion						
<90	0			0		
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Breast cancer						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Invasive ductal breast carcinoma						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Lobular breast carcinoma in situ						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Phyllodes tumour						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Skin neoplasms malignant and unspecified						
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	2 (0.5)	2	0.4	2 (1.1)	2	0.9
Basal cell carcinoma						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Malignant melanoma						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Malignant melanoma in situ						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Neoplasm skin						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Gastrointestinal neoplasms benign						
<90	0			0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Colon adenoma						
<90	0			0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Breast neoplasms benign (incl nipple)						
<90	0			2 (1.2)	2	1.0
90-<100	2 (0.7)	2	0.6	0		
100-<115	0			0		
>=115	0			0		
Benign breast neoplasm						
<90	0			2 (1.2)	2	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	2 (0.7)	2	0.6	0		
100-<115	0			0		
>=115	0			0		
Miscellaneous and site unspecified neoplasms malignant and unspecified						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Neoplasm						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Squamous cell carcinoma						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Endocrine neoplasms benign						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Benign neoplasm of thyroid gland						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Parathyroid tumour benign						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Hepatic and biliary neoplasms benign						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Haemangioma of liver						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Endocrine neoplasms malignant and unspecified						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Papillary thyroid cancer						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=115	0				0			
Gastrointestinal neoplasms malignant and unspecified								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Gastrointestinal stromal tumour								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Hepatobiliary neoplasms malignant and unspecified								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Hepatic neoplasm								
<90	0				0			
90-<100	1	(0.4)	1	0.3	0			
100-<115	0				0			
>=115	0				0			
Skeletal neoplasms benign								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=115	0				0			
Haemangioma of bone								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Reproductive neoplasms female malignant and unspecified								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Cervix carcinoma stage 0								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Reproductive neoplasms male malignant and unspecified								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Prostate cancer								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=115	0				0			
Miscellaneous and site unspecified neoplasms benign								
<90	0				0			
90-<100	0				1	(0.7)	1	0.5
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Fibroma								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Adenoma benign								
<90	0				0			
90-<100	0				1	(0.7)	1	0.5
100-<115	0				0			
>=115	0				0			
Soft tissue neoplasms malignant and unspecified								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Dermatofibrosarcoma protuberans								
<90	0				0			
90-<100	0				0			
100-<115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	1 (0.3)	1	0.2	0		
Leukaemias						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Hairy cell leukaemia						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Nervous system neoplasms malignant and unspecified NEC						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Glioblastoma						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Ocular neoplasms						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Eyelid haemangioma						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Plasma cell neoplasms						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Paraproteinaemia						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Renal and urinary tract neoplasms benign						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Kidney angiomyolipoma						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Renal and urinary tract neoplasms malignant and unspecified						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Urinary tract neoplasm						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Ear and labyrinth disorders						
<90	15 (4.4)	16	3.6	8 (4.9)	9	4.3
90-<100	11 (4.1)	14	4.0	3 (2.0)	4	2.1
100-<115	9 (2.7)	11	2.6	4 (2.5)	6	2.8
>=115	10 (2.7)	15	3.1	9 (5.0)	10	4.5
Inner ear and VIIIth cranial nerve disorders						
<90	4 (1.2)	4	0.9	7 (4.3)	8	3.8
90-<100	7 (2.6)	9	2.6	3 (2.0)	4	2.1
100-<115	6 (1.8)	7	1.6	1 (0.6)	2	0.9
>=115	5 (1.4)	6	1.2	7 (3.9)	8	3.6
Vertigo						
<90	4 (1.2)	4	0.9	5 (3.1)	5	2.4
90-<100	6 (2.2)	6	1.7	2 (1.3)	2	1.1
100-<115	4 (1.2)	4	0.9	1 (0.6)	2	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	3 (0.8)	3	0.6	4 (2.2)	4	1.8
Tinnitus						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	2	0.6	1 (0.7)	2	1.1
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Vertigo positional						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	2	0.4	3 (1.7)	4	1.8
Meniere's disease						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Motion sickness						
<90	0			1 (0.6)	2	1.0
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Aural disorders NEC						
<90	4 (1.2)	4	0.9	1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	0		
100-<115	4 (1.2)	4	0.9	1 (0.6)	1	0.5
>=115	4 (1.1)	5	1.0	0		
Ear pain						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	3 (0.9)	3	0.7	1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	4 (1.1)	5	1.0	0		
Ear discomfort						
<90	0			0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Ear congestion						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Middle ear disorders (excl congenital)						
<90	3 (0.9)	4	0.9	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Eustachian tube dysfunction						
<90	2 (0.6)	3	0.7	0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Eustachian tube disorder						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	0			0		
>=115	0			0		
Tympanic membrane disorder						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Hearing disorders						
<90	2 (0.6)	2	0.5	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Deafness neurosensory						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Hypoacusis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Sudden hearing loss						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Deafness						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Hyperacusis						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
External ear disorders (excl congenital)						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Cerumen impaction						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Excessive cerumen production						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Eye disorders						
<90	14 (4.1)	23	5.2	4 (2.5)	4	1.9
90-<100	13 (4.9)	16	4.5	9 (6.0)	10	5.3
100-<115	7 (2.1)	7	1.6	1 (0.6)	1	0.5
>=115	10 (2.7)	12	2.5	10 (5.6)	16	7.3
Vision disorders						
<90	2 (0.6)	3	0.7	2 (1.2)	2	1.0
90-<100	4 (1.5)	6	1.7	1 (0.7)	1	0.5
100-<115	4 (1.2)	4	0.9	0		
>=115	4 (1.1)	4	0.8	1 (0.6)	1	0.5
Vision blurred						
<90	0			1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	1 (0.3)	1	0.2	0		
Myopia						
<90	0			0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Diplopia						
<90	1 (0.3)	2	0.5	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Astigmatism						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Photopsia						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Anisometropia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Visual impairment						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Scintillating scotoma						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Eye disorders NEC						
<90	3 (0.9)	3	0.7	1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	1 (0.3)	1	0.2	4 (2.2)	4	1.8
Dry eye						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			2 (1.1)	2	0.9
Eyelid disorder						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Eye pain						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Lacrimation increased						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Ocular discomfort						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Ocular infections, irritations and inflammations						
<90	3 (0.9)	4	0.9	0		
90-<100	2 (0.7)	2	0.6	3 (2.0)	4	2.1
100-<115	0			1 (0.6)	1	0.5
>=115	3 (0.8)	4	0.8	3 (1.7)	5	2.3
Eye pruritus						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Eye discharge						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Conjunctival irritation						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Conjunctivitis allergic						
<90	1 (0.3)	1	0.2	0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Ocular hyperaemia						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			
Eczema eyelids								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Eye allergy								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Meibomian gland dysfunction								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Swelling of eyelid								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Blepharitis								
<90	0				0			
90-<100	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
100-<115	0			0		
>=115	0			1	(0.6)	1 0.5
Conjunctival hyperaemia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1	(0.6)	1 0.5
Erythema of eyelid						
<90	0			0		
90-<100	0			1	(0.7)	1 0.5
100-<115	0			0		
>=115	0			0		
Eye inflammation						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1	(0.6)	2 0.9
Eye irritation						
<90	0			0		
90-<100	0			1	(0.7)	1 0.5
100-<115	0			0		
>=115	0			0		
Keratitis						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1	(0.6)	1 0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Ulcerative keratitis						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Anterior eye structural change, deposit and degeneration						
<90	6 (1.8)	7	1.6	0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			2 (1.1)	3	1.4
Cataract						
<90	5 (1.5)	6	1.4	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			1 (0.6)	2	0.9
Xerophthalmia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Ectropion						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Pterygium						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Glaucoma and ocular hypertension						
<90	3 (0.9)	3	0.7	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			1 (0.6)	2	0.9
Glaucoma						
<90	3 (0.9)	3	0.7	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			1 (0.6)	2	0.9
Ocular haemorrhages and vascular disorders NEC						
<90	0			0		
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Optic ischaemic neuropathy						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Eyelid haematoma						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Conjunctival haemorrhage						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Ocular structural change, deposit and degeneration NEC						
<90	2 (0.6)	3	0.7	0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Macular degeneration						
<90	2 (0.6)	3	0.7	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Vitreous detachment						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Retina, choroid and vitreous haemorrhages and vascular disorders						
<90	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Retinopathy						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Retinal aneurysm						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Ocular sensory symptoms NEC						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Asthenopia						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Ocular neuromuscular disorders						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	1 (0.3)	1	0.2	0		
Blepharospasm						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Hepatobiliary disorders						
<90	13 (3.8)	15	3.4	2 (1.2)	2	1.0
90-<100	6 (2.2)	10	2.8	3 (2.0)	4	2.1
100-<115	11 (3.3)	14	3.3	5 (3.1)	5	2.4
>=115	14 (3.8)	17	3.5	3 (1.7)	3	1.4
Gallbladder disorders						
<90	10 (2.9)	12	2.7	0		
90-<100	4 (1.5)	5	1.4	2 (1.3)	2	1.1
100-<115	7 (2.1)	8	1.9	1 (0.6)	1	0.5
>=115	10 (2.7)	13	2.7	2 (1.1)	2	0.9
Cholelithiasis						
<90	7 (2.1)	8	1.8	0		
90-<100	3 (1.1)	3	0.9	2 (1.3)	2	1.1
100-<115	6 (1.8)	6	1.4	0		
>=115	7 (1.9)	7	1.5	2 (1.1)	2	0.9
Cholecystitis acute						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Cholecystitis						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Gallbladder disorder						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Cholecystitis chronic						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Biliary dyskinesia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Hepatic and hepatobiliary disorders						
<90	3 (0.9)	3	0.7	2 (1.2)	2	1.0
90-<100	3 (1.1)	5	1.4	2 (1.3)	2	1.1
100-<115	3 (0.9)	4	0.9	4 (2.5)	4	1.9
>=115	4 (1.1)	4	0.8	1 (0.6)	1	0.5
Hepatic steatosis						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	4 (2.5)	4	1.9
>=115	2 (0.5)	2	0.4	1 (0.6)	1	0.5
Hepatic cyst						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Hepatic function abnormal						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Hepatic pain						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Hypertransaminasaemia						
<90	0			0		
90-<100	1 (0.4)	3	0.9	0		
100-<115	0			0		
>=115	0			0		
Nonalcoholic fatty liver disease						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=115	0				0			
Granulomatous liver disease								
<90	0				0			
90-<100	0				0			
100-<115	0				0			
>=115	1	(0.3)	1	0.2	0			
Portal vein thrombosis								
<90	0				0			
90-<100	0				1	(0.7)	1	0.5
100-<115	0				0			
>=115	0				0			
Bile duct disorders								
<90	0				0			
90-<100	0				0			
100-<115	2	(0.6)	2	0.5	0			
>=115	0				0			
Bile duct stone								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			
Biliary colic								
<90	0				0			
90-<100	0				0			
100-<115	1	(0.3)	1	0.2	0			
>=115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Renal and urinary disorders						
<90	11 (3.2)	15	3.4	3 (1.9)	3	1.4
90-<100	8 (3.0)	9	2.6	4 (2.6)	4	2.1
100-<115	13 (3.9)	17	4.0	7 (4.3)	8	3.8
>=115	9 (2.4)	10	2.1	8 (4.5)	9	4.1
Urinary tract signs and symptoms						
<90	6 (1.8)	7	1.6	1 (0.6)	1	0.5
90-<100	5 (1.9)	6	1.7	1 (0.7)	1	0.5
100-<115	9 (2.7)	10	2.3	2 (1.2)	2	0.9
>=115	6 (1.6)	6	1.2	4 (2.2)	5	2.3
Dysuria						
<90	3 (0.9)	4	0.9	0		
90-<100	3 (1.1)	4	1.1	0		
100-<115	2 (0.6)	2	0.5	0		
>=115	1 (0.3)	1	0.2	0		
Haematuria						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	0			0		
Stress urinary incontinence						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Pollakiuria						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Renal pain						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Chromaturia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Nocturia						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Renal colic						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	2	0.5	0		
>=115	0			0		
Urine odour abnormal						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			1 (0.6)	1	0.5
Bladder pain						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Micturition urgency						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Urine flow decreased						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Polyuria						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Urinary incontinence						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Urinary retention						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Urolithiases						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	3 (1.1)	3	0.9	0		
100-<115	4 (1.2)	5	1.2	3 (1.8)	3	1.4
>=115	3 (0.8)	3	0.6	2 (1.1)	2	0.9
Nephrolithiasis						
<90	1 (0.3)	1	0.2	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	0		
100-<115	3 (0.9)	3	0.7	3 (1.8)	3	1.4
>=115	3 (0.8)	3	0.6	2 (1.1)	2	0.9
Calculus urinary						
<90	0			0		
90-<100	2 (0.7)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Ureterolithiasis						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Renal disorders (excl nephropathies)						
<90	4 (1.2)	6	1.4	1 (0.6)	1	0.5
90-<100	0			2 (1.3)	2	1.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
100-<115	2 (0.6)	2	0.5	2 (1.2)	3	1.4
>=115	1 (0.3)	1	0.2	2 (1.1)	2	0.9
Acute kidney injury						
<90	2 (0.6)	2	0.5	0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Renal cyst						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	0			1 (0.7)	1	0.5
100-<115	0			1 (0.6)	1	0.5
>=115	0			1 (0.6)	1	0.5
Hydronephrosis						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Chronic kidney disease						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Renal impairment						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Nephrectasia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Hypertensive nephropathy						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Bladder and bladder neck disorders (excl calculi)						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Cystitis noninfective						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Urethral disorders (excl calculi)						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Urethritis noninfective						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Blood and lymphatic system disorders						
<90	12 (3.5)	12	2.7	6 (3.7)	9	4.3
90-<100	5 (1.9)	7	2.0	3 (2.0)	5	2.6
100-<115	9 (2.7)	9	2.1	4 (2.5)	4	1.9
>=115	9 (2.4)	9	1.9	3 (1.7)	3	1.4
Anaemias nonhaemolytic and marrow depression						
<90	12 (3.5)	12	2.7	4 (2.5)	5	2.4
90-<100	4 (1.5)	5	1.4	1 (0.7)	1	0.5
100-<115	5 (1.5)	5	1.2	3 (1.8)	3	1.4
>=115	3 (0.8)	3	0.6	2 (1.1)	2	0.9
Anaemia						
<90	9 (2.7)	9	2.0	4 (2.5)	5	2.4
90-<100	4 (1.5)	5	1.4	0		
100-<115	4 (1.2)	4	0.9	3 (1.8)	3	1.4
>=115	2 (0.5)	2	0.4	2 (1.1)	2	0.9
Iron deficiency anaemia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Blood loss anaemia						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Hypochromic anaemia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Pernicious anaemia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Pancytopenia						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Spleen, lymphatic and reticuloendothelial system disorders						
<90	0			1 (0.6)	2	1.0
90-<100	2 (0.7)	2	0.6	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	0		
>=115	3 (0.8)	3	0.6	1 (0.6)	1	0.5
Lymphadenopathy						
<90	0			1 (0.6)	2	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	2 (0.7)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Splenomegaly						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Hypersplenism						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Splenic haemorrhage						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
White blood cell disorders						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	0		
>=115	1 (0.3)	1	0.2	0		
Leukocytosis						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	1 (0.3)	1	0.2	0		
Eosinophilia						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Platelet disorders						
<90	0			1 (0.6)	1	0.5
90-<100	0			2 (1.3)	2	1.1
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Thrombocytopenia						
<90	0			1 (0.6)	1	0.5
90-<100	0			2 (1.3)	2	1.1
100-<115	0			1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		
Red blood cell disorders						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Polycythaemia						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Microcytosis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Immune system disorders						
<90	5 (1.5)	5	1.1	2 (1.2)	2	1.0
90-<100	4 (1.5)	4	1.1	5 (3.3)	5	2.6
100-<115	12 (3.6)	12	2.8	8 (4.9)	10	4.7
>=115	7 (1.9)	7	1.5	6 (3.4)	6	2.7
Allergic conditions						
<90	5 (1.5)	5	1.1	2 (1.2)	2	1.0
90-<100	4 (1.5)	4	1.1	5 (3.3)	5	2.6
100-<115	11 (3.3)	11	2.6	8 (4.9)	10	4.7
>=115	7 (1.9)	7	1.5	6 (3.4)	6	2.7
Seasonal allergy						
<90	3 (0.9)	3	0.7	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	4 (2.6)	4	2.1
100-<115	7 (2.1)	7	1.6	6 (3.7)	6	2.8
>=115	4 (1.1)	4	0.8	3 (1.7)	3	1.4
Hypersensitivity						
<90	0			1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	3 (1.8)	3	1.4
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Allergy to arthropod bite						
<90	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Food allergy						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Drug hypersensitivity						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Rubber sensitivity						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Allergy to arthropod sting						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Mite allergy						
<90	0			0		
90-<100	0			0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			1 (0.6)	1	0.5
Multiple allergies						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Immune disorders NEC						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Immunisation reaction						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Surgical and medical procedures						
<90	5 (1.5)	5	1.1	1 (0.6)	1	0.5
90-<100	5 (1.9)	5	1.4	3 (2.0)	3	1.6
100-<115	6 (1.8)	7	1.6	2 (1.2)	2	0.9
>=115	2 (0.5)	2	0.4	2 (1.1)	2	0.9
Head and neck therapeutic procedures						
<90	0			0		
90-<100	3 (1.1)	3	0.9	0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Dental operation						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Tooth extraction						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	1 (0.3)	1	0.2	0		
Dental implantation						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Sinus operation						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Therapeutic procedures and supportive care NEC						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	2 (0.6)	2	0.5	0		
>=115	0			0		
Polypectomy						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<90	1 (0.3)	1	0.2	0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Cyst removal						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Spinal anaesthesia						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Skin and subcutaneous tissue therapeutic procedures						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Acrochordon excision						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Skin neoplasm excision						
<90	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Bone and joint therapeutic procedures						
<90	0			0		
90-<100	1 (0.4)	1	0.3	1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Synovial cyst removal						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Bone prosthesis insertion						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Hip surgery						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Hepatobiliary therapeutic procedures						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Cholecystectomy						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Obstetric and gynaecological therapeutic procedures						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Abortion induced						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Ovarian operation						
<90	0			0		
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Eye therapeutic procedures						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Glaucoma surgery						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Nervous system, skull and spine therapeutic procedures						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Intervertebral disc operation						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Soft tissue therapeutic procedures						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Lipoma excision						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Gastrointestinal therapeutic procedures						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Gastric bypass						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Abdominoplasty						
<90	0			1 (0.6)	1	0.5
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Endocrine disorders						
<90	5 (1.5)	5	1.1	1 (0.6)	1	0.5
90-<100	4 (1.5)	6	1.7	3 (2.0)	3	1.6
100-<115	3 (0.9)	3	0.7	0		
>=115	2 (0.5)	2	0.4	2 (1.1)	3	1.4
Thyroid gland disorders						
<90	5 (1.5)	5	1.1	1 (0.6)	1	0.5
90-<100	4 (1.5)	6	1.7	3 (2.0)	3	1.6
100-<115	2 (0.6)	2	0.5	0		
>=115	2 (0.5)	2	0.4	2 (1.1)	2	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hypothyroidism						
<90	2 (0.6)	2	0.5	1 (0.6)	1	0.5
90-<100	1 (0.4)	1	0.3	2 (1.3)	2	1.1
100-<115	1 (0.3)	1	0.2	0		
>=115	0			1 (0.6)	1	0.5
Hyperthyroidism						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	2	0.6	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Goitre						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Thyroid mass						
<90	1 (0.3)	1	0.2	0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
Thyroid cyst						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	0			0		
Primary hyperthyroidism						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	0			1 (0.7)	1	0.5
100-<115	0			0		
>=115	0			0		
Adrenal gland disorders						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Hyperadrenocorticism						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Endocrine disorders of gonadal function						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Hypogonadism						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	0			1 (0.6)	1	0.5
Social circumstances						
<90	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
90-<100	2 (0.7)	2	0.6	0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	2 (0.5)	2	0.4	0		
Age related factors						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Menopause						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Economic and housing issues						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Stress at work						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	1 (0.3)	1	0.2	1 (0.6)	1	0.5
>=115	0			0		
Family issues						
<90	0			0		
90-<100	0			0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	1 (0.3)	1	0.2	0		
Family stress						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Lifestyle issues						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Bedridden						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Pregnancy, puerperium and perinatal conditions						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	4 (1.1)	4	0.8	0		
Abortions and stillbirth						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	2 (0.5)	2	0.4	0		
Abortion spontaneous						
<90	0			0		
90-<100	1 (0.4)	1	0.3	0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Abortion						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Maternal complications of pregnancy						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	2 (0.5)	2	0.4	0		
Ectopic pregnancy						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		
Morning sickness						
<90	0			0		
90-<100	0			0		
100-<115	0			0		
>=115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Congenital, familial and genetic disorders						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	2 (0.6)	2	0.5	1 (0.6)	1	0.5
>=115	0			0		
Metabolic and nutritional disorders congenital						
<90	2 (0.6)	2	0.5	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Type V hyperlipidaemia						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Gilbert's syndrome						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Musculoskeletal and connective tissue disorders congenital						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=115	0			0		
Carpus curvus						
<90	0			0		
90-<100	0			0		
100-<115	1 (0.3)	1	0.2	0		
>=115	0			0		
Skin and subcutaneous tissue disorders congenital						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Dermoid cyst						
<90	0			0		
90-<100	0			0		
100-<115	0			1 (0.6)	1	0.5
>=115	0			0		
Product issues						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		
>=115	0			0		
Device issues						
<90	1 (0.3)	1	0.2	0		
90-<100	0			0		
100-<115	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=115	0				0			
Device expulsion								
<90	1	(0.3)	1	0.2	0			
90-<100	0				0			
100-<115	0				0			
>=115	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

15 Adverse events by body weight at baseline - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
<90	150	196.0			147	194.9			141	184.1		
90-<100	85	111.5			77	100.4			78	103.3		
100-<115	81	103.1			91	118.8			94	128.3		
>=115	86	119.1			88	119.0			89	112.6		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Events												
<90	127	(84.7)	649	331.1	133	(90.5)	835	428.5	104	(73.8)	416	225.9
90-<100	64	(75.3)	414	371.3	64	(83.1)	383	381.5	60	(76.9)	257	248.7
100-<115	66	(81.5)	362	351.0	81	(89.0)	525	441.9	75	(79.8)	363	283.0
>=115	72	(83.7)	434	364.3	75	(85.2)	454	381.5	70	(78.7)	352	312.7
Serious												
Yes												
<90	10	(6.7)	16	8.2	15	(10.2)	22	11.3	10	(7.1)	13	7.1
90-<100	5	(5.9)	13	11.7	6	(7.8)	9	9.0	7	(9.0)	9	8.7
100-<115	7	(8.6)	9	8.7	6	(6.6)	23	19.4	8	(8.5)	12	9.4
>=115	9	(10.5)	15	12.6	13	(14.8)	17	14.3	12	(13.5)	19	16.9
No												
<90	126	(84.0)	633	323.0	133	(90.5)	813	417.2	102	(72.3)	403	218.9
90-<100	63	(74.1)	401	359.6	64	(83.1)	374	372.6	60	(76.9)	248	240.0
100-<115	65	(80.2)	353	342.3	81	(89.0)	502	422.5	75	(79.8)	351	273.6
>=115	72	(83.7)	419	351.7	74	(84.1)	437	367.3	70	(78.7)	333	295.8
Severity												
Severe												
<90	8	(5.3)	10	5.1	8	(5.4)	14	7.2	9	(6.4)	12	6.5

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by body weight at baseline - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Severity									
Severe									
90-<100	7 (8.2)	19	17.0	4 (5.2)	6	6.0	4 (5.1)	7	6.8
100-<115	2 (2.5)	4	3.9	4 (4.4)	16	13.5	4 (4.3)	4	3.1
>=115	5 (5.8)	10	8.4	11 (12.5)	15	12.6	11 (12.4)	16	14.2
Moderate									
<90	46 (30.7)	102	52.0	66 (44.9)	174	89.3	39 (27.7)	70	38.0
90-<100	30 (35.3)	93	83.4	27 (35.1)	90	89.7	24 (30.8)	59	57.1
100-<115	28 (34.6)	61	59.1	38 (41.8)	115	96.8	27 (28.7)	52	40.5
>=115	31 (36.0)	59	49.5	42 (47.7)	129	108.4	28 (31.5)	83	73.7
Mild									
<90	118 (78.7)	537	274.0	121 (82.3)	647	332.0	88 (62.4)	334	181.4
90-<100	61 (71.8)	302	270.8	60 (77.9)	287	285.9	55 (70.5)	191	184.8
100-<115	59 (72.8)	297	288.0	77 (84.6)	394	331.6	72 (76.6)	307	239.3
>=115	68 (79.1)	365	306.4	70 (79.5)	310	260.5	64 (71.9)	253	224.8
Relationship to trial product									
Missing									
<90	2 (1.3)	2	1.0	1 (0.7)	1	0.5	0		
90-<100	2 (2.4)	3	2.7	2 (2.6)	2	2.0	2 (2.6)	2	1.9
100-<115	1 (1.2)	1	1.0	4 (4.4)	4	3.4	2 (2.1)	2	1.6
>=115	5 (5.8)	5	4.2	3 (3.4)	3	2.5	2 (2.2)	3	2.7
Probable									
<90	55 (36.7)	136	69.4	65 (44.2)	180	92.4	24 (17.0)	50	27.2
90-<100	30 (35.3)	94	84.3	30 (39.0)	77	76.7	14 (17.9)	17	16.5
100-<115	24 (29.6)	49	47.5	41 (45.1)	134	112.8	15 (16.0)	17	13.3
>=115	24 (27.9)	65	54.6	33 (37.5)	65	54.6	9 (10.1)	16	14.2
Possible									
<90	60 (40.0)	144	73.5	73 (49.7)	240	123.2	27 (19.1)	53	28.8
90-<100	30 (35.3)	85	76.2	30 (39.0)	77	76.7	15 (19.2)	27	26.1

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by body weight at baseline - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Relationship to trial product									
Possible									
100-<115	32 (39.5)	104	100.8	40 (44.0)	93	78.3	30 (31.9)	55	42.9
>=115	31 (36.0)	74	62.1	39 (44.3)	124	104.2	21 (23.6)	35	31.1
Unlikely									
<90	114 (76.0)	367	187.3	110 (74.8)	414	212.5	94 (66.7)	313	170.0
90-<100	55 (64.7)	232	208.1	56 (72.7)	227	226.1	57 (73.1)	211	204.2
100-<115	63 (77.8)	208	201.7	67 (73.6)	294	247.5	71 (75.5)	289	225.3
>=115	64 (74.4)	290	243.4	68 (77.3)	262	220.2	67 (75.3)	298	264.7
Outcome									
Fatal									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Recovered									
<90	122 (81.3)	537	274.0	128 (87.1)	720	369.5	95 (67.4)	319	173.2
90-<100	64 (75.3)	333	298.6	61 (79.2)	310	308.8	55 (70.5)	197	190.6
100-<115	62 (76.5)	293	284.1	75 (82.4)	424	356.9	69 (73.4)	270	210.5
>=115	67 (77.9)	340	285.4	69 (78.4)	358	300.9	66 (74.2)	268	238.1
Recovering									
<90	7 (4.7)	8	4.1	2 (1.4)	2	1.0	3 (2.1)	3	1.6
90-<100	4 (4.7)	4	3.6	6 (7.8)	10	10.0	4 (5.1)	6	5.8
100-<115	3 (3.7)	7	6.8	6 (6.6)	10	8.4	6 (6.4)	6	4.7
>=115	5 (5.8)	13	10.9	3 (3.4)	4	3.4	4 (4.5)	4	3.6
Recovered With Sequelae									
<90	1 (0.7)	1	0.5	0			1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	2 (2.5)	2	1.9	1 (1.1)	1	0.8	0		

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by body weight at baseline - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Outcome									
Recovered With Sequelae									
>=115	2 (2.3)	2	1.7	3 (3.4)	3	2.5	0		
Not Recovered									
<90	51 (34.0)	103	52.6	54 (36.7)	109	55.9	48 (34.0)	91	49.4
90-<100	28 (32.9)	77	69.1	27 (35.1)	62	61.8	27 (34.6)	53	51.3
100-<115	32 (39.5)	60	58.2	45 (49.5)	89	74.9	46 (48.9)	87	67.8
>=115	36 (41.9)	79	66.3	37 (42.0)	85	71.4	35 (39.3)	79	70.2
Unknown									
<90	0			1 (0.7)	4	2.1	1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			2 (2.3)	3	2.5	1 (1.1)	1	0.9
Leading to									
Permanent treatment discontinuation									
<90	9 (6.0)	10	5.1	8 (5.4)	9	4.6	7 (5.0)	9	4.9
90-<100	6 (7.1)	7	6.3	5 (6.5)	5	5.0	3 (3.8)	3	2.9
100-<115	4 (4.9)	5	4.8	8 (8.8)	14	11.8	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	4 (4.5)	6	5.0	3 (3.4)	5	4.4
Temporary interruption of trial product									
<90	11 (7.3)	20	10.2	13 (8.8)	26	13.3	3 (2.1)	3	1.6
90-<100	3 (3.5)	7	6.3	3 (3.9)	4	4.0	5 (6.4)	5	4.8
100-<115	7 (8.6)	13	12.6	9 (9.9)	37	31.1	5 (5.3)	9	7.0
>=115	5 (5.8)	7	5.9	12 (13.6)	23	19.3	2 (2.2)	3	2.7
Dose reduction of trial product									
<90	3 (2.0)	4	2.0	17 (11.6)	35	18.0	1 (0.7)	1	0.5
90-<100	8 (9.4)	11	9.9	5 (6.5)	12	12.0	0		
100-<115	4 (4.9)	7	6.8	4 (4.4)	6	5.1	1 (1.1)	1	0.8
>=115	3 (3.5)	6	5.0	9 (10.2)	13	10.9	1 (1.1)	1	0.9

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

16 Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N		PYE		N		PYE		N		PYE	
<90	150		196.0		147		194.9		141		184.1	
90-<100	85		111.5		77		100.4		78		103.3	
100-<115	81		103.1		91		118.8		94		128.3	
>=115	86		119.1		88		119.0		89		112.6	
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Adverse events												
<90	127	(84.7)	649	331.1	133	(90.5)	835	428.5	104	(73.8)	416	225.9
90-<100	64	(75.3)	414	371.3	64	(83.1)	383	381.5	60	(76.9)	257	248.7
100-<115	66	(81.5)	362	351.0	81	(89.0)	525	441.9	75	(79.8)	363	283.0
>=115	72	(83.7)	434	364.3	75	(85.2)	454	381.5	70	(78.7)	352	312.7
Gastrointestinal disorders												
<90	98	(65.3)	260	132.7	102	(69.4)	365	187.3	48	(34.0)	98	53.2
90-<100	48	(56.5)	186	166.8	44	(57.1)	162	161.4	21	(26.9)	38	36.8
100-<115	43	(53.1)	152	147.4	59	(64.8)	213	179.3	36	(38.3)	66	51.5
>=115	42	(48.8)	126	105.8	51	(58.0)	184	154.6	33	(37.1)	60	53.3
Gastrointestinal signs and symptoms												
<90	81	(54.0)	172	87.8	78	(53.1)	260	133.4	25	(17.7)	46	25.0
90-<100	41	(48.2)	95	85.2	35	(45.5)	92	91.7	13	(16.7)	13	12.6
100-<115	35	(43.2)	94	91.1	42	(46.2)	134	112.8	20	(21.3)	32	24.9
>=115	30	(34.9)	71	59.6	45	(51.1)	115	96.6	18	(20.2)	24	21.3
Nausea												
<90	63	(42.0)	86	43.9	52	(35.4)	101	51.8	16	(11.3)	22	11.9
90-<100	25	(29.4)	39	35.0	20	(26.0)	36	35.9	4	(5.1)	4	3.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	24 (29.6)	45	43.6	30 (33.0)	61	51.3	10 (10.6)	10	7.8
>=115	17 (19.8)	28	23.5	34 (38.6)	51	42.9	7 (7.9)	9	8.0
Vomiting									
<90	20 (13.3)	32	16.3	37 (25.2)	103	52.9	2 (1.4)	2	1.1
90-<100	14 (16.5)	25	22.4	16 (20.8)	22	21.9	2 (2.6)	2	1.9
100-<115	11 (13.6)	25	24.2	18 (19.8)	39	32.8	4 (4.3)	5	3.9
>=115	9 (10.5)	11	9.2	17 (19.3)	24	20.2	3 (3.4)	3	2.7
Abdominal distension									
<90	3 (2.0)	6	3.1	7 (4.8)	9	4.6	6 (4.3)	6	3.3
90-<100	1 (1.2)	1	0.9	6 (7.8)	7	7.0	3 (3.8)	3	2.9
100-<115	2 (2.5)	2	1.9	5 (5.5)	6	5.1	2 (2.1)	4	3.1
>=115	3 (3.5)	3	2.5	6 (6.8)	8	6.7	0		
Dyspepsia									
<90	12 (8.0)	12	6.1	11 (7.5)	12	6.2	2 (1.4)	2	1.1
90-<100	6 (7.1)	6	5.4	3 (3.9)	3	3.0	0		
100-<115	3 (3.7)	3	2.9	4 (4.4)	6	5.1	1 (1.1)	1	0.8
>=115	6 (7.0)	6	5.0	7 (8.0)	9	7.6	2 (2.2)	2	1.8
Abdominal pain upper									
<90	2 (1.3)	2	1.0	3 (2.0)	4	2.1	2 (1.4)	3	1.6
90-<100	2 (2.4)	2	1.8	6 (7.8)	9	9.0	0		
100-<115	2 (2.5)	2	1.9	6 (6.6)	6	5.1	5 (5.3)	6	4.7
>=115	5 (5.8)	5	4.2	1 (1.1)	2	1.7	4 (4.5)	4	3.6
Flatulence									
<90	4 (2.7)	5	2.6	3 (2.0)	3	1.5	3 (2.1)	4	2.2
90-<100	5 (5.9)	7	6.3	2 (2.6)	2	2.0	1 (1.3)	1	1.0
100-<115	5 (6.2)	5	4.8	5 (5.5)	7	5.9	1 (1.1)	1	0.8
>=115	7 (8.1)	8	6.7	6 (6.8)	9	7.6	2 (2.2)	3	2.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Eructation									
<90	4 (2.7)	5	2.6	7 (4.8)	9	4.6	0		
90-<100	2 (2.4)	4	3.6	2 (2.6)	3	3.0	1 (1.3)	1	1.0
100-<115	2 (2.5)	2	1.9	3 (3.3)	3	2.5	0		
>=115	3 (3.5)	5	4.2	4 (4.5)	6	5.0	0		
Abdominal pain									
<90	9 (6.0)	10	5.1	4 (2.7)	6	3.1	1 (0.7)	1	0.5
90-<100	4 (4.7)	4	3.6	5 (6.5)	5	5.0	1 (1.3)	1	1.0
100-<115	3 (3.7)	4	3.9	1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	1 (1.2)	2	1.7	3 (3.4)	3	2.5	1 (1.1)	1	0.9
Abdominal discomfort									
<90	9 (6.0)	11	5.6	5 (3.4)	7	3.6	4 (2.8)	4	2.2
90-<100	3 (3.5)	3	2.7	3 (3.9)	3	3.0	0		
100-<115	2 (2.5)	2	1.9	4 (4.4)	4	3.4	2 (2.1)	2	1.6
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	1 (1.1)	1	0.9
Regurgitation									
<90	0			2 (1.4)	2	1.0	0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	0		
Abdominal pain lower									
<90	0			2 (1.4)	2	1.0	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Aerophagia									
<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
90-<100	0				1	(1.3)	1	1.0	0			
100-<115	0				0				0			
>=115	0				0				0			
Gastrointestinal pain												
<90	0				0				0			
90-<100	0				1	(1.3)	1	1.0	0			
100-<115	0				0				0			
>=115	1	(1.2)	1	0.8	0				0			
Abnormal faeces												
<90	0				0				0			
90-<100	0				0				0			
100-<115	1	(1.2)	1	1.0	0				0			
>=115	0				1	(1.1)	1	0.8	0			
Epigastric discomfort												
<90	0				1	(0.7)	1	0.5	0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				0				0			
Gastrointestinal sounds abnormal												
<90	0				1	(0.7)	1	0.5	0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				0				0			
Abdominal rigidity												
<90	0				0				0			
90-<100	1	(1.2)	1	0.9	0				0			
100-<115	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=115	0			0			0		
Anal incontinence									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			0		
>=115	0			0			0		
Breath odour									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Dysphagia									
<90	2	(1.3)	2 1.0	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Faeces discoloured									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Faeces soft									
<90	1	(0.7)	1 0.5	0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Retching									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<90	0			0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			0		
>=115	0			0			0		
Gastrointestinal motility and defaecation conditions									
<90	41	(27.3)	63 32.1	48	(32.7)	77 39.5	20	(14.2)	31 16.8
90-<100	31	(36.5)	79 70.8	28	(36.4)	47 46.8	15	(19.2)	22 21.3
100-<115	26	(32.1)	51 49.4	38	(41.8)	61 51.3	14	(14.9)	21 16.4
>=115	27	(31.4)	50 42.0	29	(33.0)	54 45.4	21	(23.6)	27 24.0
Diarrhoea									
<90	28	(18.7)	41 20.9	27	(18.4)	49 25.1	13	(9.2)	19 10.3
90-<100	21	(24.7)	53 47.5	19	(24.7)	27 26.9	12	(15.4)	16 15.5
100-<115	18	(22.2)	32 31.0	19	(20.9)	37 31.1	10	(10.6)	14 10.9
>=115	22	(25.6)	32 26.9	21	(23.9)	28 23.5	13	(14.6)	17 15.1
Constipation									
<90	14	(9.3)	19 9.7	22	(15.0)	23 11.8	8	(5.7)	8 4.3
90-<100	16	(18.8)	21 18.8	13	(16.9)	16 15.9	3	(3.8)	5 4.8
100-<115	10	(12.3)	15 14.5	19	(20.9)	21 17.7	4	(4.3)	6 4.7
>=115	11	(12.8)	15 12.6	16	(18.2)	22 18.5	7	(7.9)	7 6.2
Gastrooesophageal reflux disease									
<90	3	(2.0)	3 1.5	5	(3.4)	5 2.6	3	(2.1)	3 1.6
90-<100	4	(4.7)	4 3.6	2	(2.6)	2 2.0	1	(1.3)	1 1.0
100-<115	3	(3.7)	4 3.9	3	(3.3)	3 2.5	1	(1.1)	1 0.8
>=115	3	(3.5)	3 2.5	2	(2.3)	3 2.5	2	(2.2)	2 1.8
Change of bowel habit									
<90	0			0			1	(0.7)	1 0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Gastrointestinal motility disorder									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Irritable bowel syndrome									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Gastrointestinal hypermotility									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Gastrooesophageal sphincter insufficiency									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Gastrointestinal conditions NEC									
<90	4 (2.7)	5	2.6	6 (4.1)	9	4.6	4 (2.8)	4	2.2
90-<100	0			5 (6.5)	5	5.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	1 (1.2)	1	1.0	4 (4.4)	4	3.4	1 (1.1)	1	0.8
>=115	2 (2.3)	2	1.7	3 (3.4)	3	2.5	1 (1.1)	1	0.9
Hyperchlorhydria									
<90	3 (2.0)	4	2.0	6 (4.1)	9	4.6	2 (1.4)	2	1.1
90-<100	0			3 (3.9)	3	3.0	0		
100-<115	1 (1.2)	1	1.0	2 (2.2)	2	1.7	0		
>=115	1 (1.2)	1	0.8	0			0		
Food poisoning									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	2 (2.3)	2	1.7	0		
Gastrointestinal disorder									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	0		
Barrett's oesophagus									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Gastric disorder									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gastrointestinal melanosis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Gastrointestinal inflammatory conditions									
<90	6 (4.0)	6	3.1	7 (4.8)	7	3.6	3 (2.1)	4	2.2
90-<100	1 (1.2)	1	0.9	6 (7.8)	9	9.0	1 (1.3)	1	1.0
100-<115	2 (2.5)	2	1.9	2 (2.2)	2	1.7	2 (2.1)	3	2.3
>=115	0			2 (2.3)	2	1.7	0		
Gastritis									
<90	4 (2.7)	4	2.0	6 (4.1)	6	3.1	2 (1.4)	3	1.6
90-<100	1 (1.2)	1	0.9	3 (3.9)	5	5.0	0		
100-<115	1 (1.2)	1	1.0	0			2 (2.1)	3	2.3
>=115	0			2 (2.3)	2	1.7	0		
Enteritis									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			1 (1.3)	1	1.0	1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Enterocolitis									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Chronic gastritis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Duodenitis									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Colitis									
<90	2 (1.3)	2	1.0	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Gastrointestinal vascular conditions									
<90	2 (1.3)	4	2.0	1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			4 (4.4)	4	3.4	0		
>=115	0			3 (3.4)	3	2.5	1 (1.1)	1	0.9
Haemorrhoids									
<90	1 (0.7)	2	1.0	1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			4 (4.4)	4	3.4	0		
>=115	0			3 (3.4)	3	2.5	1 (1.1)	1	0.9
Haemorrhoids thrombosed									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	0			0			0		
Varices oesophageal									
<90	1 (0.7)	1	0.5	0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Dental and gingival conditions									
<90	3 (2.0)	4	2.0	6 (4.1)	7	3.6	2 (1.4)	2	1.1
90-<100	3 (3.5)	3	2.7	2 (2.6)	2	2.0	0		
100-<115	1 (1.2)	1	1.0	2 (2.2)	2	1.7	3 (3.2)	3	2.3
>=115	1 (1.2)	1	0.8	0			2 (2.2)	2	1.8
Toothache									
<90	2 (1.3)	3	1.5	3 (2.0)	3	1.5	1 (0.7)	1	0.5
90-<100	2 (2.4)	2	1.8	0			0		
100-<115	0			2 (2.2)	2	1.7	0		
>=115	0			0			1 (1.1)	1	0.9
Dental caries									
<90	0			3 (2.0)	3	1.5	1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	0			3 (3.2)	3	2.3
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Gingival swelling									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Tooth deposit									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Periodontal disease									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Salivary gland conditions									
<90	0			0			1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			2 (2.2)	2	1.7	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	1 (1.1)	2	1.7	0		
Dry mouth									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			2 (2.2)	2	1.7	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			0		
Parotid gland enlargement									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Salivary hypersecretion									
<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	2	1.7	0		
Noninfective sialoadenitis									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Abdominal hernias and other abdominal wall conditions									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	4 (2.8)	4	2.2
90-<100	0			2 (2.6)	2	2.0	0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Abdominal wall haematoma									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Umbilical hernia									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Abdominal hernia									
<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Hiatus hernia									
<90	0			1 (0.7)	1	0.5	2 (1.4)	2	1.1
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Inguinal hernia									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Gastrointestinal haemorrhages NEC									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	1 (1.2)	1	0.8	2 (2.3)	2	1.7	2 (2.2)	2	1.8
Upper gastrointestinal haemorrhage									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Haematochezia									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Mallory-Weiss syndrome									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Intra-abdominal haemorrhage									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Intra-abdominal haematoma									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Rectal haemorrhage									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Benign neoplasms gastrointestinal									
<90	3 (2.0)	3	1.5	1 (0.7)	1	0.5	2 (1.4)	2	1.1
90-<100	2 (2.4)	3	2.7	1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	0			0			0		
Gastric polyps									
<90	1 (0.7)	1	0.5	0			1 (0.7)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Large intestine polyp									
<90	2 (1.3)	2	1.0	1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	2 (2.4)	2	1.8	0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Oral soft tissue conditions									
<90	0			1 (0.7)	1	0.5	3 (2.1)	3	1.6
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Mouth ulceration									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Stomatitis									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Aphthous ulcer									
<90	0			0			2 (1.4)	2	1.1
90-<100	0			0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
>=115	0				0				0			
Lip swelling												
<90	0				0				0			
90-<100	0				0				1	(1.3)	1	1.0
100-<115	0				0				0			
>=115	0				0				0			
Odynophagia												
<90	0				0				1	(0.7)	1	0.5
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				0				0			
Gastrointestinal ulceration and perforation												
<90	0				0				0			
90-<100	1	(1.2)	1	0.9	1	(1.3)	1	1.0	1	(1.3)	1	1.0
100-<115	0				0				0			
>=115	0				0				0			
Gastritis erosive												
<90	0				0				0			
90-<100	0				1	(1.3)	1	1.0	0			
100-<115	0				0				0			
>=115	0				0				0			
Diverticular perforation												
<90	0				0				0			
90-<100	0				0				1	(1.3)	1	1.0
100-<115	0				0				0			
>=115	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Gastric ulcer									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Diverticular disorders									
<90	1	(0.7)	1 0.5	0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			1	(1.1)	1 0.8	2	(2.2)	2 1.8
Diverticulum intestinal									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1	(1.1)	1 0.8	0		
Diverticulum									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			2	(2.2)	2 1.8
Exocrine pancreas conditions									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			1	(1.1)	1 0.8
>=115	0			1	(1.1)	1 0.8	0		
Pancreatitis acute									
<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1	(1.1)	1 0.8	0		
Obstructive pancreatitis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			0		
Pancreatic cyst									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			0		
>=115	0			0			0		
Gastrointestinal stenosis and obstruction									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1	(1.1)	1 0.8	0		
Small intestinal obstruction									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1	(1.1)	1 0.8	0		
Anal and rectal conditions NEC									
<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
100-<115	0			1	(1.1)	1 0.8	0		
>=115	0			0			0		
Anal fissure									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1	(1.1)	1 0.8	0		
>=115	0			0			0		
Malabsorption conditions									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Malabsorption									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Peritoneal and retroperitoneal conditions									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Retroperitoneal mass									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			0			0		
Tongue conditions									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Glossodynia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Infections and infestations									
<90	58 (38.7)	119	60.7	68 (46.3)	131	67.2	51 (36.2)	103	55.9
90-<100	33 (38.8)	64	57.4	32 (41.6)	74	73.7	39 (50.0)	67	64.8
100-<115	31 (38.3)	46	44.6	41 (45.1)	74	62.3	42 (44.7)	85	66.3
>=115	44 (51.2)	89	74.7	38 (43.2)	66	55.5	43 (48.3)	104	92.4
Infections - pathogen unspecified									
<90	53 (35.3)	94	48.0	61 (41.5)	109	55.9	46 (32.6)	90	48.9
90-<100	28 (32.9)	46	41.3	31 (40.3)	65	64.8	31 (39.7)	51	49.4
100-<115	27 (33.3)	40	38.8	37 (40.7)	61	51.3	29 (30.9)	59	46.0
>=115	38 (44.2)	70	58.8	33 (37.5)	54	45.4	41 (46.1)	81	72.0
Nasopharyngitis									
<90	18 (12.0)	29	14.8	27 (18.4)	43	22.1	23 (16.3)	38	20.6
90-<100	10 (11.8)	13	11.7	15 (19.5)	27	26.9	13 (16.7)	17	16.5
100-<115	6 (7.4)	9	8.7	10 (11.0)	22	18.5	12 (12.8)	21	16.4
>=115	13 (15.1)	18	15.1	16 (18.2)	23	19.3	11 (12.4)	16	14.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Upper respiratory tract infection									
<90	8 (5.3)	15	7.7	14 (9.5)	18	9.2	12 (8.5)	17	9.2
90-<100	6 (7.1)	10	9.0	6 (7.8)	6	6.0	8 (10.3)	11	10.6
100-<115	5 (6.2)	7	6.8	12 (13.2)	13	10.9	5 (5.3)	6	4.7
>=115	18 (20.9)	22	18.5	10 (11.4)	11	9.2	13 (14.6)	16	14.2
Sinusitis									
<90	3 (2.0)	3	1.5	3 (2.0)	3	1.5	2 (1.4)	3	1.6
90-<100	0			5 (6.5)	9	9.0	0		
100-<115	1 (1.2)	1	1.0	3 (3.3)	4	3.4	3 (3.2)	4	3.1
>=115	2 (2.3)	2	1.7	3 (3.4)	3	2.5	6 (6.7)	6	5.3
Bronchitis									
<90	5 (3.3)	5	2.6	3 (2.0)	3	1.5	4 (2.8)	4	2.2
90-<100	1 (1.2)	1	0.9	1 (1.3)	2	2.0	2 (2.6)	2	1.9
100-<115	1 (1.2)	1	1.0	6 (6.6)	6	5.1	2 (2.1)	3	2.3
>=115	3 (3.5)	4	3.4	4 (4.5)	5	4.2	5 (5.6)	6	5.3
Gastroenteritis									
<90	8 (5.3)	11	5.6	7 (4.8)	7	3.6	4 (2.8)	5	2.7
90-<100	6 (7.1)	7	6.3	3 (3.9)	3	3.0	2 (2.6)	2	1.9
100-<115	6 (7.4)	6	5.8	2 (2.2)	2	1.7	4 (4.3)	4	3.1
>=115	4 (4.7)	4	3.4	2 (2.3)	3	2.5	3 (3.4)	4	3.6
Urinary tract infection									
<90	9 (6.0)	12	6.1	6 (4.1)	9	4.6	5 (3.5)	8	4.3
90-<100	3 (3.5)	3	2.7	3 (3.9)	3	3.0	1 (1.3)	2	1.9
100-<115	3 (3.7)	3	2.9	2 (2.2)	2	1.7	2 (2.1)	2	1.6
>=115	2 (2.3)	3	2.5	2 (2.3)	2	1.7	4 (4.5)	4	3.6
Pneumonia									
<90	2 (1.3)	2	1.0	0			1 (0.7)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			1 (1.3)	2	2.0	2 (2.6)	2	1.9
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			2 (2.3)	2	1.7	2 (2.2)	2	1.8
Conjunctivitis									
<90	0			3 (2.0)	3	1.5	0		
90-<100	0			0			2 (2.6)	2	1.9
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	2 (2.3)	4	3.4	1 (1.1)	1	0.8	1 (1.1)	2	1.8
Cystitis									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	2 (2.2)	2	1.7	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			2 (2.2)	4	3.6
Tonsillitis									
<90	0			1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	2 (2.6)	2	1.9
100-<115	0			2 (2.2)	2	1.7	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Paronychia									
<90	0			3 (2.0)	3	1.5	2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Pharyngitis									
<90	0			1 (0.7)	1	0.5	3 (2.1)	3	1.6
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			1 (1.1)	1	0.8	2 (2.2)	2	1.8
Gastrointestinal infection									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			1 (1.3)	2	2.0	1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Lower respiratory tract infection									
<90	2 (1.3)	2	1.0	2 (1.4)	2	1.0	1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	0			1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	3 (3.4)	3	2.7
Acute sinusitis									
<90	1 (0.7)	1	0.5	0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	2 (2.1)	4	3.1
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	1 (1.1)	1	0.9
Tooth infection									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	1 (1.2)	2	1.9	1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	1 (1.1)	1	0.9
Otitis externa									
<90	1 (0.7)	1	0.5	0			0		
90-<100	2 (2.4)	2	1.8	0			0		
100-<115	1 (1.2)	1	1.0	2 (2.2)	2	1.7	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			0		
Localised infection									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Appendicitis									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Kidney infection									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Post procedural infection									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Skin infection									
<90	0			0			0		
90-<100	0			1 (1.3)	2	2.0	0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Vulvovaginitis									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	1 (1.3)	2	2.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
100-<115	0			0			0		
>=115	0			0			0		
Chronic sinusitis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1	(1.1)	1 0.8	0		
>=115	0			0			0		
Abscess									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Breast abscess									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Diverticulitis									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			2	(2.6)	2 1.9
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			1	(1.1)	1 0.9
Implant site infection									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Infected dermal cyst									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Mastitis									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Otitis media acute									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Periodontitis									
<90	0			1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			1 (1.1)	2	1.6
>=115	0			0			0		
Respiratory tract infection									
<90	0			1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			4 (4.3)	4	3.1
>=115	0			0			0		
Rhinitis									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	1 (0.7)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			2 (2.2)	2	1.8
Tooth abscess									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	1 (0.7)	2	1.1
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	1 (1.2)	1	0.8	0			0		
Urosepsis									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Colonic abscess									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Ear infection									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Empyema									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=115	0			0			1	(1.1)	1 0.9
Eye infection									
<90	2	(1.3)	2 1.0	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Gingival abscess									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Gingivitis									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			2	(2.6)	2 1.9
100-<115	0			0			0		
>=115	0			0			0		
Hordeolum									
<90	0			0			0		
90-<100	0			0			1	(1.3)	1 1.0
100-<115	1	(1.2)	1 1.0	0			0		
>=115	0			0			0		
Joint abscess									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Labyrinthitis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Laryngitis									
<90	1 (0.7)	1	0.5	0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	1 (1.2)	2	1.7	0			0		
Mastoiditis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Osteomyelitis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Otitis media									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Otitis media chronic									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
100-<115	0			0			0		
>=115	0			0			0		
Pericoronitis									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Postoperative wound infection									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			0		
Pulpitis dental									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Pyelonephritis acute									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Sepsis									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			0		
>=115	1	(1.2)	1 0.8	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Sialoadenitis												
<90	1	(0.7)	1	0.5	0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				0				0			
Sinobronchitis												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				0				1	(1.1)	1	0.8
>=115	0				0				0			
Subcutaneous abscess												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				0				1	(1.1)	1	0.8
>=115	0				0				0			
Tracheitis												
<90	1	(0.7)	1	0.5	0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				0				0			
Tracheobronchitis												
<90	1	(0.7)	1	0.5	0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				0				0			
Vaginal infection												
<90	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Wound infection									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Viral infectious disorders									
<90	13 (8.7)	14	7.1	11 (7.5)	13	6.7	8 (5.7)	8	4.3
90-<100	10 (11.8)	12	10.8	5 (6.5)	5	5.0	7 (9.0)	7	6.8
100-<115	2 (2.5)	3	2.9	11 (12.1)	13	10.9	13 (13.8)	17	13.3
>=115	10 (11.6)	12	10.1	9 (10.2)	10	8.4	8 (9.0)	10	8.9
Influenza									
<90	4 (2.7)	4	2.0	4 (2.7)	4	2.1	4 (2.8)	4	2.2
90-<100	5 (5.9)	6	5.4	2 (2.6)	2	2.0	4 (5.1)	4	3.9
100-<115	2 (2.5)	3	2.9	6 (6.6)	7	5.9	7 (7.4)	10	7.8
>=115	6 (7.0)	6	5.0	3 (3.4)	3	2.5	3 (3.4)	4	3.6
Gastroenteritis viral									
<90	3 (2.0)	3	1.5	1 (0.7)	2	1.0	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	2 (2.6)	2	2.0	1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	1 (1.2)	1	0.8	2 (2.3)	2	1.7	3 (3.4)	3	2.7
Viral infection									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	2 (2.4)	2	1.8	0			0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			2 (2.3)	3	2.5	1 (1.1)	2	1.8
Herpes zoster									
<90	3 (2.0)	3	1.5	3 (2.0)	3	1.5	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	0		
Viral diarrhoea									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Viral pharyngitis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Herpes simplex									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Herpes virus infection									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Oral herpes									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	2 (1.3)	3	1.5	0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Respiratory tract infection viral									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	2 (2.3)	2	1.7	0			0		
Gastroenteritis norovirus									
<90	0			1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Ophthalmic herpes zoster									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Pneumonia influenzal									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Chikungunya virus infection									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	0			0			0		
Ear infection viral									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Rhinovirus infection									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Viral upper respiratory tract infection									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	2 (2.3)	3	2.5	0			1 (1.1)	1	0.9
Bacterial infectious disorders									
<90	3 (2.0)	3	1.5	4 (2.7)	4	2.1	1 (0.7)	1	0.5
90-<100	3 (3.5)	5	4.5	3 (3.9)	3	3.0	4 (5.1)	6	5.8
100-<115	2 (2.5)	2	1.9	0			4 (4.3)	6	4.7
>=115	2 (2.3)	3	2.5	1 (1.1)	1	0.8	3 (3.4)	5	4.4
Cellulitis									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	0		
90-<100	2 (2.4)	2	1.8	0			2 (2.6)	2	1.9
100-<115	1 (1.2)	1	1.0	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	1 (1.2)	2	1.7	0			2 (2.2)	3	2.7
Bacterial vaginosis									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Breast cellulitis									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Ear infection bacterial									
<90	0			0			0		
90-<100	1 (1.2)	3	2.7	1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Pharyngitis streptococcal									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			2 (2.1)	3	2.3
>=115	0			1 (1.1)	1	0.8	0		
Furuncle									
<90	0			1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Staphylococcal infection									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	2	1.6
>=115	0			0			1 (1.1)	1	0.9
Clostridium difficile colitis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Helicobacter gastritis									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Helicobacter infection									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Wound infection staphylococcal									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Fungal infectious disorders									
<90	8 (5.3)	8	4.1	5 (3.4)	5	2.6	4 (2.8)	4	2.2
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	3 (3.8)	3	2.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	1 (1.2)	1	1.0	0			2 (2.1)	2	1.6
>=115	4 (4.7)	4	3.4	1 (1.1)	1	0.8	6 (6.7)	8	7.1
Onychomycosis									
<90	0			2 (1.4)	2	1.0	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Tinea pedis									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			1 (1.1)	1	0.9
Fungal infection									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			1 (1.1)	1	0.8	0		
Fungal skin infection									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Vulvovaginal candidiasis									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			3 (3.4)	4	3.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Vulvovaginal mycotic infection									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	2 (1.4)	2	1.1
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Balanitis candida									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Candida infection									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Dermatophytosis of nail									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Genital candidiasis									
<90	2 (1.3)	2	1.0	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Genital infection fungal									
<90	1 (0.7)	1	0.5	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Skin candida									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Tinea infection									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	1	(1.2)	1 0.8	0			1	(1.1)	1 0.9
Tinea versicolour									
<90	1	(0.7)	1 0.5	0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Ectoparasitic disorders									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			0		
Acarodermatitis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			0			0		
Musculoskeletal and connective tissue disorders									
<90	37 (24.7)	52	26.5	38 (25.9)	64	32.8	21 (14.9)	28	15.2
90-<100	20 (23.5)	28	25.1	17 (22.1)	24	23.9	21 (26.9)	40	38.7
100-<115	22 (27.2)	37	35.9	20 (22.0)	34	28.6	20 (21.3)	27	21.0
>=115	20 (23.3)	30	25.2	23 (26.1)	29	24.4	22 (24.7)	31	27.5
Musculoskeletal and connective tissue disorders NEC									
<90	22 (14.7)	26	13.3	25 (17.0)	29	14.9	7 (5.0)	8	4.3
90-<100	12 (14.1)	14	12.6	9 (11.7)	10	10.0	11 (14.1)	11	10.6
100-<115	11 (13.6)	11	10.7	11 (12.1)	12	10.1	6 (6.4)	7	5.5
>=115	12 (14.0)	15	12.6	11 (12.5)	15	12.6	9 (10.1)	12	10.7
Back pain									
<90	11 (7.3)	12	6.1	9 (6.1)	11	5.6	4 (2.8)	5	2.7
90-<100	8 (9.4)	9	8.1	6 (7.8)	6	6.0	4 (5.1)	4	3.9
100-<115	5 (6.2)	5	4.8	6 (6.6)	6	5.1	2 (2.1)	2	1.6
>=115	4 (4.7)	4	3.4	6 (6.8)	7	5.9	4 (4.5)	4	3.6
Pain in extremity									
<90	4 (2.7)	4	2.0	7 (4.8)	7	3.6	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	4 (5.1)	4	3.9
100-<115	1 (1.2)	1	1.0	3 (3.3)	3	2.5	0		
>=115	6 (7.0)	6	5.0	5 (5.7)	5	4.2	5 (5.6)	5	4.4
Neck pain									
<90	2 (1.3)	2	1.0	3 (2.0)	3	1.5	0		
90-<100	0			1 (1.3)	1	1.0	1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			2 (2.2)	2	1.7	2 (2.1)	2	1.6
>=115	0			2 (2.3)	2	1.7	0		
Musculoskeletal pain									
<90	0			5 (3.4)	5	2.6	1 (0.7)	1	0.5
90-<100	2 (2.4)	2	1.8	1 (1.3)	1	1.0	2 (2.6)	2	1.9
100-<115	4 (4.9)	4	3.9	1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	2 (2.3)	2	1.7	0			1 (1.1)	1	0.9
Musculoskeletal chest pain									
<90	1 (0.7)	2	1.0	0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	0			1 (1.1)	1	0.8
>=115	3 (3.5)	3	2.5	0			0		
Flank pain									
<90	3 (2.0)	3	1.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Muscle contracture									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Neck mass									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Rheumatic disorder									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Axillary mass									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Limb mass									
<90	0			0			0		
90-<100	1	(1.2)	2 1.8	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Musculoskeletal discomfort									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Musculoskeletal stiffness									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Plantar fasciitis									
<90	2	(1.3)	2 1.0	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Joint disorders									
<90	14 (9.3)	16	8.2	15 (10.2)	19	9.8	11 (7.8)	12	6.5
90-<100	5 (5.9)	5	4.5	8 (10.4)	10	10.0	7 (9.0)	13	12.6
100-<115	10 (12.3)	14	13.6	13 (14.3)	19	16.0	10 (10.6)	11	8.6
>=115	9 (10.5)	11	9.2	8 (9.1)	9	7.6	13 (14.6)	13	11.5
Arthralgia									
<90	8 (5.3)	9	4.6	7 (4.8)	8	4.1	8 (5.7)	8	4.3
90-<100	2 (2.4)	2	1.8	4 (5.2)	4	4.0	2 (2.6)	2	1.9
100-<115	6 (7.4)	7	6.8	8 (8.8)	13	10.9	6 (6.4)	6	4.7
>=115	8 (9.3)	9	7.6	4 (4.5)	4	3.4	4 (4.5)	4	3.6
Osteoarthritis									
<90	1 (0.7)	1	0.5	4 (2.7)	6	3.1	1 (0.7)	1	0.5
90-<100	0			3 (3.9)	3	3.0	4 (5.1)	5	4.8
100-<115	0			2 (2.2)	2	1.7	2 (2.1)	2	1.6
>=115	1 (1.2)	1	0.8	2 (2.3)	3	2.5	5 (5.6)	5	4.4
Rotator cuff syndrome									
<90	2 (1.3)	3	1.5	0			0		
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	2 (2.5)	3	2.9	1 (1.1)	2	1.7	0		
>=115	0			1 (1.1)	1	0.8	0		
Periarthritis									
<90	1 (0.7)	1	0.5	2 (1.4)	3	1.5	0		
90-<100	0			1 (1.3)	2	2.0	1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	1 (1.2)	1	0.8	0			0		
Arthritis									
<90	1 (0.7)	1	0.5	0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	0		
Spinal osteoarthritis									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	2 (1.4)	2	1.1
90-<100	0			0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			3 (3.4)	3	2.7
Joint swelling									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Arthritis climacteric									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Arthropathy									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Femoroacetabular impingement									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<90	0			0			0		
90-<100	0			0			1	(1.3)	1 1.0
100-<115	0			0			0		
>=115	0			0			0		
Gouty arthritis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Joint effusion									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Neuropathic arthropathy									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			0		
Psoriatic arthropathy									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			0		
Rheumatoid arthritis									
<90	0			0			0		
90-<100	0			0			1	(1.3)	2 1.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	0			0			0		
Sacroiliitis									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Muscle disorders									
<90	4 (2.7)	4	2.0	6 (4.1)	8	4.1	3 (2.1)	4	2.2
90-<100	4 (4.7)	6	5.4	1 (1.3)	1	1.0	1 (1.3)	1	1.0
100-<115	3 (3.7)	5	4.8	1 (1.1)	1	0.8	3 (3.2)	3	2.3
>=115	1 (1.2)	1	0.8	2 (2.3)	2	1.7	1 (1.1)	1	0.9
Myalgia									
<90	3 (2.0)	3	1.5	2 (1.4)	4	2.1	1 (0.7)	2	1.1
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	1 (1.3)	1	1.0
100-<115	2 (2.5)	4	3.9	1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	0			1 (1.1)	1	0.8	0		
Muscle spasms									
<90	1 (0.7)	1	0.5	4 (2.7)	4	2.1	1 (0.7)	1	0.5
90-<100	4 (4.7)	5	4.5	0			0		
100-<115	1 (1.2)	1	1.0	0			1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		
Diastasis recti abdominis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Muscular weakness									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Tendon, ligament and cartilage disorders									
<90	0			2 (1.4)	2	1.0	2 (1.4)	2	1.1
90-<100	2 (2.4)	2	1.8	1 (1.3)	1	1.0	3 (3.8)	4	3.9
100-<115	2 (2.5)	2	1.9	1 (1.1)	1	0.8	3 (3.2)	3	2.3
>=115	2 (2.3)	2	1.7	1 (1.1)	1	0.8	1 (1.1)	1	0.9
Trigger finger									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	0		
Osteochondrosis									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Tendonitis									
<90	0			0			2 (1.4)	2	1.1
90-<100	0			0			3 (3.8)	3	2.9
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			0		
Tendon disorder									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Costochondritis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			1 (1.1)	1	0.8
>=115	0			0			0		
Ligament calcification									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Meniscal degeneration									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Tendon pain									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Synovial and bursal disorders									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	0		
90-<100	0			0			2 (2.6)	2	1.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	1 (1.2)	1	1.0	0			2 (2.1)	3	2.3
>=115	0			2 (2.3)	2	1.7	1 (1.1)	1	0.9
Bursitis									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	0		
90-<100	0			0			2 (2.6)	2	1.9
100-<115	1 (1.2)	1	1.0	0			2 (2.1)	3	2.3
>=115	0			2 (2.3)	2	1.7	1 (1.1)	1	0.9
Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	2 (2.6)	2	2.0	4 (5.1)	5	4.8
100-<115	2 (2.5)	2	1.9	0			0		
>=115	1 (1.2)	1	0.8	0			2 (2.2)	2	1.8
Intervertebral disc protrusion									
<90	0			1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	0			2 (2.6)	2	2.0	1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			1 (1.1)	1	0.9
Foot deformity									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			1 (1.3)	2	1.9
100-<115	0			0			0		
>=115	0			0			0		
Intervertebral disc degeneration									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	0			0			0		
Scoliosis									
<90	0			0			0		
90-<100	0			0			2 (2.6)	2	1.9
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Spinal flattening									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Spondylolisthesis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Bone disorders (excl congenital and fractures)									
<90	4 (2.7)	4	2.0	2 (1.4)	3	1.5	0		
90-<100	0			0			4 (5.1)	4	3.9
100-<115	2 (2.5)	2	1.9	1 (1.1)	1	0.8	0		
>=115	0			0			0		
Exostosis									
<90	2 (1.3)	2	1.0	0			0		
90-<100	0			0			2 (2.6)	2	1.9
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=115	0			0			0		
Bone lesion									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Osteopenia									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			0		
>=115	0			0			0		
Osteoporosis									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			1	(1.3)	1 1.0
100-<115	0			0			0		
>=115	0			0			0		
Bone pain									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Metatarsalgia									
<90	0			0			0		
90-<100	0			0			1	(1.3)	1 1.0
100-<115	0			0			0		
>=115	0			0			0		
Osteitis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Connective tissue disorders (excl congenital)									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Polymyalgia rheumatica									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Nervous system disorders									
<90	22 (14.7)	29	14.8	29 (19.7)	44	22.6	17 (12.1)	22	11.9
90-<100	13 (15.3)	20	17.9	19 (24.7)	21	20.9	13 (16.7)	14	13.5
100-<115	10 (12.3)	24	23.3	18 (19.8)	28	23.6	17 (18.1)	32	24.9
>=115	18 (20.9)	32	26.9	16 (18.2)	25	21.0	16 (18.0)	24	21.3
Headaches									
<90	16 (10.7)	18	9.2	13 (8.8)	18	9.2	10 (7.1)	10	5.4
90-<100	7 (8.2)	10	9.0	8 (10.4)	9	9.0	3 (3.8)	4	3.9
100-<115	5 (6.2)	15	14.5	8 (8.8)	9	7.6	6 (6.4)	9	7.0
>=115	8 (9.3)	13	10.9	8 (9.1)	10	8.4	5 (5.6)	9	8.0
Headache									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	15 (10.0)	16	8.2	9 (6.1)	14	7.2	9 (6.4)	9	4.9
90-<100	7 (8.2)	9	8.1	7 (9.1)	8	8.0	2 (2.6)	3	2.9
100-<115	5 (6.2)	14	13.6	7 (7.7)	8	6.7	5 (5.3)	8	6.2
>=115	6 (7.0)	9	7.6	8 (9.1)	10	8.4	4 (4.5)	7	6.2
Migraine									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Migraine with aura									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Tension headache									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	2 (2.3)	2	1.7	0			1 (1.1)	1	0.9
Occipital neuralgia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Sinus headache									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	1 (1.2)	2	1.7	0			0		
Neurological disorders NEC									
<90	6 (4.0)	6	3.1	13 (8.8)	17	8.7	8 (5.7)	10	5.4
90-<100	6 (7.1)	8	7.2	8 (10.4)	8	8.0	7 (9.0)	7	6.8
100-<115	6 (7.4)	7	6.8	6 (6.6)	9	7.6	9 (9.6)	14	10.9
>=115	10 (11.6)	12	10.1	9 (10.2)	12	10.1	7 (7.9)	7	6.2
Dizziness									
<90	5 (3.3)	5	2.6	6 (4.1)	6	3.1	5 (3.5)	5	2.7
90-<100	6 (7.1)	7	6.3	4 (5.2)	4	4.0	1 (1.3)	1	1.0
100-<115	2 (2.5)	2	1.9	2 (2.2)	2	1.7	6 (6.4)	8	6.2
>=115	5 (5.8)	7	5.9	7 (8.0)	8	6.7	1 (1.1)	1	0.9
Paraesthesia									
<90	1 (0.7)	1	0.5	3 (2.0)	3	1.5	1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	2 (2.6)	2	1.9
100-<115	0			1 (1.1)	3	2.5	2 (2.1)	3	2.3
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Hypoaesthesia									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			2 (2.6)	2	2.0	0		
100-<115	0			0			2 (2.1)	2	1.6
>=115	0			0			0		
Dysgeusia									
<90	0			3 (2.0)	7	3.6	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Hyperaesthesia									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	0			0		
Syncope									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	2 (2.3)	2	1.7	2 (2.3)	2	1.7	0		
Dizziness postural									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	2	1.9	1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	0		
Somnolence									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.9
Ageusia									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Aphasia									
<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			0		
Coordination abnormal									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Dysaesthesia									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Head discomfort									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			0		
>=115	0			0			0		
Hypogeusia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			0		
>=115	0			0			0		
Lethargy									
<90	0			0			0		
90-<100	0			0			1	(1.3)	1 1.0
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=115	0			0			1	(1.1)	1 0.9
Loss of consciousness									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Neuralgia									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			1	(1.3)	1 1.0
100-<115	0			0			0		
>=115	0			0			0		
Phantom limb syndrome									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			0		
>=115	0			0			0		
Presyncope									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			1	(1.1)	1 0.9
Restless legs syndrome									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Central nervous system vascular disorders									
<90	0			3 (2.0)	4	2.1	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	2 (2.6)	2	2.0	0		
100-<115	0			2 (2.2)	3	2.5	1 (1.1)	2	1.6
>=115	1 (1.2)	1	0.8	1 (1.1)	2	1.7	0		
Carotid artery stenosis									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Carotid arteriosclerosis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	0		
Cerebrovascular accident									
<90	0			2 (1.4)	2	1.0	1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Cerebral artery stenosis									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Spinal epidural haematoma									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Subarachnoid haemorrhage									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Cerebral artery thrombosis									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Cerebral infarction									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Ischaemic stroke									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	2	1.6
>=115	1 (1.2)	1	0.8	0			0		
Peripheral neuropathies									
<90	4 (2.7)	4	2.0	1 (0.7)	1	0.5	0		
90-<100	0			0			1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	1 (1.2)	1	1.0	3 (3.3)	3	2.5	5 (5.3)	5	3.9
>=115	1 (1.2)	2	1.7	0			1 (1.1)	2	1.8
Diabetic neuropathy									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Meralgia paraesthetica									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Neuropathy peripheral									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			1 (1.1)	2	1.8
Carpal tunnel syndrome									
<90	2 (1.3)	2	1.0	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			2 (2.1)	2	1.6
>=115	1 (1.2)	2	1.7	0			0		
Nerve compression									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Polyneuropathy									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Encephalopathies									
<90	0			0			0		
90-<100	0			2 (2.6)	2	2.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Hepatic encephalopathy									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Hyponatraemic encephalopathy									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Spinal cord and nerve root disorders									
<90	0			2 (1.4)	2	1.0	0		
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	1 (1.1)	2	1.7	1 (1.1)	1	0.8
>=115	3 (3.5)	3	2.5	0			2 (2.2)	2	1.8
Sciatica									
<90	0			2 (1.4)	2	1.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	0			1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			0		
Radiculopathy									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Sacral radiculopathy									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Cervical radiculopathy									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Cervicobrachial syndrome									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Lumbar radiculopathy									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	1 (1.2)	1	0.8	0			2 (2.2)	2	1.8
Cranial nerve disorders (excl neoplasms)									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Facial paralysis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Anosmia									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Mental impairment disorders									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	0			2 (2.2)	2	1.8
Memory impairment									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Amnesia									
<90	0			0			0		
90-<100	0			0			1	(1.3)	1 1.0
100-<115	0			0			0		
>=115	0			0			2	(2.2)	2 1.8
Dementia Alzheimer's type									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Vascular dementia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			0		
Structural brain disorders									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1	(1.1)	1 0.8	0		
>=115	0			0			0		
Cerebral ventricle dilatation									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1	(1.1)	1 0.8	0		
>=115	0			0			0		
Sleep disturbances (incl subtypes)									
<90	0			1	(0.7)	1 0.5	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Hypersomnia									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Movement disorders (incl parkinsonism)									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Tremor									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Neurological disorders of the eye									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			1	(1.1)	1 0.9
Visual field defect									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			0			1 (1.1)	1	0.9
Seizures (incl subtypes)									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Partial seizures									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
General disorders and administration site conditions									
<90	16 (10.7)	24	12.2	32 (21.8)	37	19.0	14 (9.9)	22	11.9
90-<100	17 (20.0)	23	20.6	9 (11.7)	12	12.0	5 (6.4)	5	4.8
100-<115	5 (6.2)	7	6.8	16 (17.6)	23	19.4	10 (10.6)	14	10.9
>=115	13 (15.1)	15	12.6	12 (13.6)	21	17.6	17 (19.1)	20	17.8
General system disorders NEC									
<90	14 (9.3)	20	10.2	25 (17.0)	28	14.4	5 (3.5)	5	2.7
90-<100	15 (17.6)	19	17.0	9 (11.7)	12	12.0	4 (5.1)	4	3.9
100-<115	3 (3.7)	4	3.9	15 (16.5)	18	15.2	8 (8.5)	9	7.0
>=115	8 (9.3)	9	7.6	8 (9.1)	10	8.4	11 (12.4)	12	10.7
Fatigue									
<90	10 (6.7)	15	7.7	13 (8.8)	13	6.7	2 (1.4)	2	1.1
90-<100	6 (7.1)	6	5.4	6 (7.8)	7	7.0	0		
100-<115	1 (1.2)	2	1.9	4 (4.4)	4	3.4	1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	2 (2.3)	3	2.5	5 (5.7)	5	4.2	1 (1.1)	1	0.9
Asthenia									
<90	2 (1.3)	2	1.0	4 (2.7)	4	2.1	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			3 (3.3)	4	3.4	0		
>=115	1 (1.2)	1	0.8	0			0		
Influenza like illness									
<90	0			1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			2 (2.2)	3	2.5	2 (2.1)	2	1.6
>=115	0			2 (2.3)	2	1.7	1 (1.1)	1	0.9
Malaise									
<90	1 (0.7)	2	1.0	2 (1.4)	2	1.0	1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Early satiety									
<90	0			2 (1.4)	2	1.0	0		
90-<100	3 (3.5)	3	2.7	0			0		
100-<115	0			2 (2.2)	2	1.7	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Pain									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	3 (3.5)	3	2.7	1 (1.3)	1	1.0	2 (2.6)	2	1.9
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Non-cardiac chest pain									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			2 (2.2)	2	1.7	0		
>=115	1 (1.2)	1	0.8	0			0		
Oedema peripheral									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	4 (4.5)	4	3.6
Peripheral swelling									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			2 (2.1)	2	1.6
>=115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.9
Face oedema									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Feeling cold									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Swelling									
<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Thirst decreased									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Chest discomfort									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Chest pain									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			2 (2.2)	3	2.7
Hunger									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Chills									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Discomfort									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Inflammation									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Polyp									
<90	0			0			0		
90-<100	1 (1.2)	2	1.8	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Sensation of foreign body									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Thirst									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Administration site reactions									
<90	2 (1.3)	2	1.0	3 (2.0)	4	2.1	4 (2.8)	10	5.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	4 (4.4)	5	4.2	3 (3.2)	5	3.9
>=115	3 (3.5)	4	3.4	6 (6.8)	10	8.4	3 (3.4)	3	2.7
Injection site pain									
<90	1 (0.7)	1	0.5	1 (0.7)	2	1.0	2 (1.4)	4	2.2
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	2 (2.2)	3	2.5	1 (1.1)	3	2.3
>=115	2 (2.3)	2	1.7	4 (4.5)	4	3.4	0		
Injection site erythema									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			2 (2.2)	2	1.7	0		
>=115	0			1 (1.1)	1	0.8	0		
Injection site bruising									
<90	1 (0.7)	1	0.5	0			3 (2.1)	4	2.2
90-<100	0			0			0		
100-<115	0			0			2 (2.1)	2	1.6
>=115	2 (2.3)	2	1.7	2 (2.3)	2	1.7	0		
Injection site reaction									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Injection site mass									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			1 (1.1)	2	1.7	1 (1.1)	1	0.9
Implant site pain									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Injection site discomfort									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Injection site haemorrhage									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Injection site urticaria									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Body temperature conditions									
<90	2 (1.3)	2	1.0	4 (2.7)	4	2.1	5 (3.5)	7	3.8
90-<100	3 (3.5)	3	2.7	0			0		
100-<115	2 (2.5)	2	1.9	0			0		
>=115	2 (2.3)	2	1.7	0			4 (4.5)	5	4.4
Pyrexia									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	2 (1.3)	2	1.0	4 (2.7)	4	2.1	5 (3.5)	7	3.8
90-<100	3 (3.5)	3	2.7	0			0		
100-<115	2 (2.5)	2	1.9	0			0		
>=115	2 (2.3)	2	1.7	0			4 (4.5)	5	4.4
Therapeutic and nontherapeutic effects (excl toxicity)									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Drug intolerance									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Tissue disorders NEC									
<90	0			1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Mass									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Nodule									
<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Complications associated with device									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Complication associated with device									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Metabolism and nutrition disorders									
<90	16 (10.7)	24	12.2	32 (21.8)	36	18.5	18 (12.8)	20	10.9
90-<100	10 (11.8)	13	11.7	14 (18.2)	17	16.9	10 (12.8)	12	11.6
100-<115	8 (9.9)	9	8.7	4 (4.4)	6	5.1	13 (13.8)	14	10.9
>=115	14 (16.3)	22	18.5	6 (6.8)	7	5.9	12 (13.5)	15	13.3
Appetite and general nutritional disorders									
<90	14 (9.3)	20	10.2	25 (17.0)	27	13.9	8 (5.7)	8	4.3
90-<100	7 (8.2)	9	8.1	11 (14.3)	14	13.9	4 (5.1)	4	3.9
100-<115	6 (7.4)	6	5.8	3 (3.3)	3	2.5	1 (1.1)	1	0.8
>=115	5 (5.8)	5	4.2	2 (2.3)	2	1.7	3 (3.4)	5	4.4
Decreased appetite									
<90	13 (8.7)	16	8.2	25 (17.0)	27	13.9	8 (5.7)	8	4.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	7 (8.2)	9	8.1	9 (11.7)	10	10.0	4 (5.1)	4	3.9
100-<115	5 (6.2)	5	4.8	2 (2.2)	2	1.7	1 (1.1)	1	0.8
>=115	4 (4.7)	4	3.4	2 (2.3)	2	1.7	2 (2.2)	4	3.6
Hyperphagia									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Increased appetite									
<90	3 (2.0)	4	2.0	0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Overweight									
<90	0			0			0		
90-<100	0			1 (1.3)	2	2.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Cachexia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Obesity									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			0			1 (1.1)	1	0.9
Electrolyte and fluid balance conditions									
<90	0			3 (2.0)	3	1.5	1 (0.7)	1	0.5
90-<100	3 (3.5)	3	2.7	1 (1.3)	1	1.0	1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	3 (3.5)	4	3.4	2 (2.3)	2	1.7	0		
Hypokalaemia									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	2 (2.3)	3	2.5	2 (2.3)	2	1.7	0		
Dehydration									
<90	0			2 (1.4)	2	1.0	0		
90-<100	2 (2.4)	2	1.8	0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			0		
Hyponatraemia									
<90	0			1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Hyperkalaemia									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Lipid metabolism disorders									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	5 (3.5)	5	2.7
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			0			3 (3.2)	3	2.3
>=115	2 (2.3)	2	1.7	2 (2.3)	2	1.7	1 (1.1)	1	0.9
Dyslipidaemia									
<90	0			0			4 (2.8)	4	2.2
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			2 (2.1)	2	1.6
>=115	2 (2.3)	2	1.7	2 (2.3)	2	1.7	0		
Hyperlipidaemia									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Hypertriglyceridaemia									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Hypercholesterolaemia									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Vitamin related disorders									
<90	1 (0.7)	1	0.5	0			1 (0.7)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Folate deficiency									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Vitamin B complex deficiency									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Vitamin D deficiency									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Purine and pyrimidine metabolism disorders									
<90	0			1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	2	1.9
100-<115	1 (1.2)	1	1.0	0			0		
>=115	2 (2.3)	3	2.5	1 (1.1)	1	0.8	1 (1.1)	2	1.8
Gout									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			1 (1.3)	2	1.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	1 (1.2)	1	1.0	0			0		
>=115	2 (2.3)	3	2.5	1 (1.1)	1	0.8	1 (1.1)	2	1.8
Hyperuricaemia									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Bone, calcium, magnesium and phosphorus metabolism disorders									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	4 (4.7)	4	3.4	0			0		
Hypomagnesaemia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	0			0		
Hypercalcaemia									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	2 (2.3)	2	1.7	0			0		
Hypercalcitoninaemia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	1 (1.2)	1	0.8	0			0		
Hypocalcaemia									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Acid-base disorders									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Ketoacidosis									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Lactic acidosis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Diabetic complications									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Diabetic ketoacidosis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Diabetic metabolic decompensation									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Glucose metabolism disorders (incl diabetes mellitus)									
<90	2 (1.3)	2	1.0	1 (0.7)	1	0.5	3 (2.1)	3	1.6
90-<100	0			0			4 (5.1)	4	3.9
100-<115	0			0			7 (7.4)	7	5.5
>=115	1 (1.2)	2	1.7	0			6 (6.7)	6	5.3
Diabetes mellitus									
<90	0			1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	0			0			2 (2.6)	2	1.9
100-<115	0			0			2 (2.1)	2	1.6
>=115	0			0			1 (1.1)	1	0.9
Diabetes mellitus inadequate control									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			3 (3.2)	3	2.3
>=115	1 (1.2)	2	1.7	0			1 (1.1)	1	0.9
Hyperglycaemia									
<90	1 (0.7)	1	0.5	0			1 (0.7)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
100-<115	0			0			2	(2.1)	2 1.6
>=115	0			0			2	(2.2)	2 1.8
Hyperinsulinaemia									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Hypoglycaemia									
<90	0			0			0		
90-<100	0			0			1	(1.3)	1 1.0
100-<115	0			0			0		
>=115	0			0			0		
Type 2 diabetes mellitus									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			2	(2.2)	2 1.8
Iron and trace metal metabolism disorders									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			0		
Iron deficiency									
<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Metabolism disorders NEC									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	2	1.9	0			0		
>=115	0			0			0		
Hyperamylasaemia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Hyperlipasaemia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Eye disorders									
<90	23 (15.3)	33	16.8	16 (10.9)	23	11.8	16 (11.3)	21	11.4
90-<100	5 (5.9)	6	5.4	9 (11.7)	15	14.9	7 (9.0)	7	6.8
100-<115	11 (13.6)	15	14.5	15 (16.5)	20	16.8	12 (12.8)	19	14.8
>=115	7 (8.1)	11	9.2	10 (11.4)	11	9.2	7 (7.9)	9	8.0
Retina, choroid and vitreous haemorrhages and vascular disorders									
<90	7 (4.7)	7	3.6	8 (5.4)	8	4.1	5 (3.5)	6	3.3
90-<100	1 (1.2)	2	1.8	3 (3.9)	5	5.0	2 (2.6)	2	1.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	3 (3.7)	3	2.9	7 (7.7)	7	5.9	2 (2.1)	2	1.6
>=115	1 (1.2)	1	0.8	3 (3.4)	3	2.5	2 (2.2)	2	1.8
Diabetic retinopathy									
<90	6 (4.0)	6	3.1	7 (4.8)	7	3.6	5 (3.5)	6	3.3
90-<100	1 (1.2)	2	1.8	2 (2.6)	3	3.0	2 (2.6)	2	1.9
100-<115	3 (3.7)	3	2.9	4 (4.4)	4	3.4	2 (2.1)	2	1.6
>=115	1 (1.2)	1	0.8	2 (2.3)	2	1.7	2 (2.2)	2	1.8
Non-proliferative retinopathy									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Retinal haemorrhage									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Retinopathy hypertensive									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	0		
Retinal artery occlusion									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Retinopathy									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Anterior eye structural change, deposit and degeneration									
<90	4 (2.7)	4	2.0	1 (0.7)	2	1.0	4 (2.8)	5	2.7
90-<100	0			2 (2.6)	2	2.0	2 (2.6)	2	1.9
100-<115	4 (4.9)	4	3.9	5 (5.5)	6	5.1	4 (4.3)	5	3.9
>=115	0			1 (1.1)	1	0.8	2 (2.2)	3	2.7
Cataract									
<90	3 (2.0)	3	1.5	1 (0.7)	2	1.0	3 (2.1)	4	2.2
90-<100	0			1 (1.3)	1	1.0	2 (2.6)	2	1.9
100-<115	2 (2.5)	2	1.9	2 (2.2)	2	1.7	2 (2.1)	2	1.6
>=115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.9
Dermatochalasis									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	0			2 (2.1)	2	1.6
>=115	0			0			0		
Cataract cortical									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Cataract subcapsular									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Narrow anterior chamber angle									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	2	1.7	0		
>=115	0			0			0		
Cataract nuclear									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			1 (1.1)	2	1.8
Pinguecula									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Posterior capsule opacification									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Ocular infections, irritations and inflammations									
<90	9 (6.0)	9	4.6	4 (2.7)	4	2.1	1 (0.7)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			2 (2.6)	2	2.0	1 (1.3)	1	1.0
100-<115	0			1 (1.1)	2	1.7	3 (3.2)	3	2.3
>=115	4 (4.7)	4	3.4	1 (1.1)	2	1.7	1 (1.1)	1	0.9
Macular oedema									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	2	1.7	0		
>=115	0			0			0		
Blepharitis									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			2 (2.1)	2	1.6
>=115	2 (2.3)	2	1.7	1 (1.1)	2	1.7	0		
Ocular hyperaemia									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Eyelid rash									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Keratitis									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=115	0			0			0		
Meibomian gland dysfunction									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Conjunctivitis allergic									
<90	2	(1.3)	2 1.0	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			0		
Episcleritis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Eye pruritus									
<90	0			0			0		
90-<100	0			0			1	(1.3)	1 1.0
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			0		
Punctate keratitis									
<90	2	(1.3)	2 1.0	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Swelling of eyelid									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Uveitis									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Eye disorders NEC									
<90	2 (1.3)	2	1.0	4 (2.7)	4	2.1	2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	2 (2.6)	2	2.0	1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	2 (2.2)	2	1.7	3 (3.2)	3	2.3
>=115	4 (4.7)	4	3.4	0			1 (1.1)	1	0.9
Dry eye									
<90	1 (0.7)	1	0.5	3 (2.0)	3	1.5	2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	2 (2.6)	2	2.0	1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	2 (2.3)	2	1.7	0			1 (1.1)	1	0.9
Vitreous disorder									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			0		
Lacrimation increased									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Eyelid disorder									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Retinal disorder									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Ocular structural change, deposit and degeneration NEC									
<90	5 (3.3)	6	3.1	1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	3 (3.9)	3	3.0	0		
100-<115	4 (4.9)	5	4.8	0			2 (2.1)	3	2.3
>=115	0			2 (2.3)	2	1.7	0		
Detachment of retinal pigment epithelium									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Macular fibrosis									
<90	1 (0.7)	2	1.0	0			0		
90-<100	0			1 (1.3)	1	1.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
100-<115	0			0			0		
>=115	0			0			0		
Retinal degeneration									
<90	0			0			0		
90-<100	0			1	(1.3)	1 1.0	0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			0		
Retinal depigmentation									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1	(1.1)	1 0.8	0		
Vitreous detachment									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	2 1.9	0			1	(1.1)	1 0.8
>=115	0			1	(1.1)	1 0.8	0		
Optic disc disorder									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Age-related macular degeneration									
<90	0			0			0		
90-<100	0			0			0		
100-<115	2	(2.5)	2 1.9	0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Choroidal dystrophy									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Macular degeneration									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Optic atrophy									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Retinal drusen									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Vitreous floaters									
<90	1 (0.7)	1	0.5	0			1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Vision disorders									
<90	3 (2.0)	3	1.5	0			4 (2.8)	4	2.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	1 (1.3)	1	1.0
100-<115	2 (2.5)	2	1.9	2 (2.2)	2	1.7	2 (2.1)	2	1.6
>=115	2 (2.3)	2	1.7	2 (2.3)	2	1.7	1 (1.1)	1	0.9
Vision blurred									
<90	2 (1.3)	2	1.0	0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	2 (2.3)	2	1.7	2 (2.3)	2	1.7	1 (1.1)	1	0.9
Myopia									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Visual impairment									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Astigmatism									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Hypermetropia									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			0			0		
Pathologic myopia									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Presbyopia									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Glaucoma and ocular hypertension									
<90	1 (0.7)	1	0.5	1 (0.7)	2	1.0	1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Glaucoma									
<90	1 (0.7)	1	0.5	1 (0.7)	2	1.0	1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Ocular neuromuscular disorders									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Eyelid ptosis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Ocular haemorrhages and vascular disorders NEC									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Eye haemorrhage									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Conjunctival haemorrhage									
<90	1 (0.7)	1	0.5	0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Optic disc haemorrhage									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Ocular sensory symptoms NEC									
<90	0			1 (0.7)	1	0.5	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Asthenopia									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Injury, poisoning and procedural complications									
<90	18 (12.0)	21	10.7	16 (10.9)	21	10.8	15 (10.6)	16	8.7
90-<100	8 (9.4)	11	9.9	6 (7.8)	12	12.0	11 (14.1)	16	15.5
100-<115	9 (11.1)	11	10.7	14 (15.4)	22	18.5	14 (14.9)	18	14.0
>=115	16 (18.6)	28	23.5	12 (13.6)	13	10.9	9 (10.1)	11	9.8
Injuries NEC									
<90	12 (8.0)	12	6.1	9 (6.1)	10	5.1	9 (6.4)	9	4.9
90-<100	6 (7.1)	7	6.3	4 (5.2)	8	8.0	8 (10.3)	10	9.7
100-<115	7 (8.6)	7	6.8	12 (13.2)	14	11.8	11 (11.7)	13	10.1
>=115	12 (14.0)	23	19.3	7 (8.0)	7	5.9	8 (9.0)	8	7.1
Muscle strain									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	1 (0.7)	1	0.5
90-<100	2 (2.4)	2	1.8	2 (2.6)	2	2.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	2 (2.3)	2	1.7	3 (3.4)	3	2.5	0		
Fall									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			1 (1.3)	2	2.0	1 (1.3)	2	1.9
100-<115	2 (2.5)	2	1.9	0			0		
>=115	5 (5.8)	5	4.2	2 (2.3)	2	1.7	1 (1.1)	1	0.9
Skin laceration									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			2 (2.2)	2	1.7	2 (2.1)	2	1.6
>=115	2 (2.3)	2	1.7	1 (1.1)	1	0.8	0		
Ligament sprain									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	3 (3.2)	3	2.3
>=115	4 (4.7)	6	5.0	0			0		
Limb injury									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	1 (1.2)	1	1.0	2 (2.2)	2	1.7	0		
>=115	0			0			0		
Contusion									
<90	0			0			2 (1.4)	2	1.1
90-<100	0			2 (2.6)	3	3.0	1 (1.3)	1	1.0
100-<115	0			0			3 (3.2)	4	3.1
>=115	0			0			2 (2.2)	2	1.8
Bone contusion									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			1 (1.1)	1	0.8	0		
Animal bite									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Epicondylitis									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	0			0		
Muscle injury									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Post-traumatic pain									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Road traffic accident									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	0			0		
Tooth fracture									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	1 (0.7)	1	0.5	0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	2 (2.3)	2	1.7	0			1 (1.1)	1	0.9
Traumatic haemothorax									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Arthropod sting									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Face injury									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Head injury									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Skin abrasion									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Abdominal injury									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Arthropod bite									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Chest injury									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Craniocerebral injury									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Foreign body in eye									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Injury corneal									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Ligament rupture									
<90	2 (1.3)	2	1.0	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Muscle rupture									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Post-traumatic neck syndrome									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Soft tissue injury									
<90	0			0			0		
90-<100	0			0			0		
100-<115	3 (3.7)	3	2.9	0			0		
>=115	2 (2.3)	2	1.7	0			0		
Spinal column injury									
<90	1 (0.7)	1	0.5	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Subdural haematoma									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Tendon injury									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Tendon rupture									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Wound									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			1 (1.1)	1	0.9
Bone and joint injuries									
<90	3 (2.0)	3	1.5	4 (2.7)	4	2.1	7 (5.0)	7	3.8
90-<100	3 (3.5)	4	3.6	3 (3.9)	3	3.0	3 (3.8)	3	2.9
100-<115	2 (2.5)	2	1.9	3 (3.3)	7	5.9	1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			4 (4.5)	5	4.2	2 (2.2)	2	1.8
Foot fracture									
<90	0			1 (0.7)	1	0.5	2 (1.4)	2	1.1
90-<100	0			1 (1.3)	1	1.0	1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			2 (2.3)	2	1.7	0		
Rib fracture									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			3 (3.3)	3	2.5	0		
>=115	0			0			0		
Humerus fracture									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Meniscus injury									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Joint injury									
<90	0			0			2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.9
Stress fracture									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
<90	0				0				0			
90-<100	1	(1.2)	1	0.9	0				0			
100-<115	0				0				0			
>=115	0				1	(1.1)	1	0.8	0			
Wrist fracture												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				1	(1.1)	1	0.8	0			
Cervical vertebral fracture												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				0			
Spinal compression fracture												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				0			
Thoracic vertebral fracture												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				0			
Upper limb fracture												
<90	0				0				0			
90-<100	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
100-<115	0			1	(1.1)	1 0.8	0		
>=115	0			0			0		
Radius fracture									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Ankle fracture									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Bone fissure									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Cartilage injury									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Hand fracture									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Hip fracture									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Joint dislocation									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Lisfranc fracture									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Spinal fracture									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Sternal fracture									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Procedural related injuries and complications NEC									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	1 (0.7)	1	0.5	3 (2.0)	3	1.5	0		
90-<100	0			1 (1.3)	1	1.0	3 (3.8)	3	2.9
100-<115	1 (1.2)	1	1.0	0			1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.9
Post procedural haemorrhage									
<90	0			2 (1.4)	2	1.0	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Procedural pain									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			1 (1.1)	1	0.9
Anaemia postoperative									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Graft complication									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Dental restoration failure									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	0			0			0		
Incision site pain									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Post procedural complication									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Surgical skin tear									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Injuries by physical agents									
<90	1 (0.7)	1	0.5	3 (2.0)	3	1.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Hypobarism									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Sunburn									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Thermal burn									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Heat illness									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Medication errors and other product use errors and issues									
<90	2 (1.3)	4	2.0	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	2 (2.1)	3	2.3
>=115	2 (2.3)	3	2.5	0			0		
Accidental overdose									
<90	2 (1.3)	4	2.0	0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	2 (2.1)	3	2.3
>=115	0			0			0		
Extra dose administered									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
<90	0				1	(0.7)	1	0.5	0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				0				0			
Dose calculation error												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	1	(1.2)	1	0.8	0				0			
Incorrect dose administered												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	1	(1.2)	2	1.7	0				0			
Overdoses and underdoses NEC												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	1	(1.2)	1	0.8	0				0			
Intentional overdose												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	1	(1.2)	1	0.8	0				0			
Respiratory, thoracic and mediastinal disorders												

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	7 (4.7)	7	3.6	16 (10.9)	19	9.8	7 (5.0)	7	3.8
90-<100	8 (9.4)	10	9.0	5 (6.5)	5	5.0	5 (6.4)	8	7.7
100-<115	10 (12.3)	13	12.6	15 (16.5)	22	18.5	12 (12.8)	15	11.7
>=115	11 (12.8)	14	11.8	11 (12.5)	16	13.4	12 (13.5)	13	11.5
Respiratory tract signs and symptoms									
<90	2 (1.3)	2	1.0	6 (4.1)	6	3.1	4 (2.8)	4	2.2
90-<100	3 (3.5)	3	2.7	2 (2.6)	2	2.0	0		
100-<115	4 (4.9)	4	3.9	8 (8.8)	8	6.7	3 (3.2)	3	2.3
>=115	4 (4.7)	4	3.4	3 (3.4)	3	2.5	2 (2.2)	2	1.8
Oropharyngeal pain									
<90	1 (0.7)	1	0.5	3 (2.0)	3	1.5	4 (2.8)	4	2.2
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	4 (4.9)	4	3.9	3 (3.3)	3	2.5	2 (2.1)	2	1.6
>=115	3 (3.5)	3	2.5	0			0		
Rhinorrhoea									
<90	0			1 (0.7)	1	0.5	0		
90-<100	2 (2.4)	2	1.8	1 (1.3)	1	1.0	0		
100-<115	0			2 (2.2)	2	1.7	0		
>=115	1 (1.2)	1	0.8	0			0		
Dysphonia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			2 (2.3)	2	1.7	0		
Painful respiration									
<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
100-<115	0				0				0			
>=115	0				1	(1.1)	1	0.8	0			
Hiccups												
<90	1	(0.7)	1	0.5	0				0			
90-<100	1	(1.2)	1	0.9	0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				0			
Oropharyngeal discomfort												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				1	(1.1)	1	0.9
Upper respiratory tract congestion												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				0			
Aphonia												
<90	0				1	(0.7)	1	0.5	0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				0				0			
Dry throat												
<90	0				1	(0.7)	1	0.5	0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Nasal discomfort									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Upper-airway cough syndrome									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Respiratory disorders NEC									
<90	4 (2.7)	4	2.0	8 (5.4)	8	4.1	1 (0.7)	1	0.5
90-<100	3 (3.5)	3	2.7	1 (1.3)	1	1.0	3 (3.8)	5	4.8
100-<115	3 (3.7)	3	2.9	5 (5.5)	5	4.2	4 (4.3)	4	3.1
>=115	6 (7.0)	7	5.9	4 (4.5)	5	4.2	7 (7.9)	8	7.1
Cough									
<90	3 (2.0)	3	1.5	3 (2.0)	3	1.5	1 (0.7)	1	0.5
90-<100	2 (2.4)	2	1.8	0			2 (2.6)	2	1.9
100-<115	0			4 (4.4)	4	3.4	2 (2.1)	2	1.6
>=115	5 (5.8)	6	5.0	2 (2.3)	2	1.7	2 (2.2)	3	2.7
Pulmonary mass									
<90	0			1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			2 (2.3)	2	1.7	0		
Productive cough									
<90	1 (0.7)	1	0.5	3 (2.0)	3	1.5	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Respiratory disorder									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			1	(1.3)	1 1.0
100-<115	1	(1.2)	1 1.0	0			1	(1.1)	1 0.8
>=115	1	(1.2)	1 0.8	1	(1.1)	1 0.8	1	(1.1)	1 0.9
Sleep apnoea syndrome									
<90	0			0			0		
90-<100	0			1	(1.3)	1 1.0	0		
100-<115	1	(1.2)	1 1.0	0			1	(1.1)	1 0.8
>=115	0			0			3	(3.4)	3 2.7
Acute respiratory failure									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	1	(1.1)	1 0.8	0		
>=115	0			0			0		
Dyspnoea									
<90	0			0			0		
90-<100	0			0			1	(1.3)	1 1.0
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Hypoxia									
<90	0			0			0		
90-<100	0			0			1	(1.3)	1 1.0
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			0			0		
Upper respiratory tract disorders (excl infections)									
<90	0			1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	2 (2.6)	2	2.0	1 (1.3)	1	1.0
100-<115	3 (3.7)	4	3.9	4 (4.4)	5	4.2	4 (4.3)	5	3.9
>=115	2 (2.3)	2	1.7	3 (3.4)	4	3.4	2 (2.2)	2	1.8
Epistaxis									
<90	0			1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	0			2 (2.2)	2	1.7	2 (2.1)	2	1.6
>=115	0			1 (1.1)	2	1.7	2 (2.2)	2	1.8
Rhinitis allergic									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		
Sinus congestion									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	2 (2.5)	2	1.9	0			1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	0		
Nasal congestion									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	1 (1.2)	2	1.9	2 (2.2)	2	1.7	1 (1.1)	2	1.6
>=115	1 (1.2)	1	0.8	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Bronchial disorders (excl neoplasms)									
<90	1 (0.7)	1	0.5	2 (1.4)	3	1.5	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	2 (2.5)	2	1.9	3 (3.3)	3	2.5	3 (3.2)	3	2.3
>=115	1 (1.2)	1	0.8	2 (2.3)	3	2.5	1 (1.1)	1	0.9
Asthma									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	3 (3.3)	3	2.5	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	1 (1.1)	2	1.7	1 (1.1)	1	0.9
Bronchospasm									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	0		
Chronic obstructive pulmonary disease									
<90	0			1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Childhood asthma									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Lower respiratory tract disorders (excl obstruction and infection)									
<90	0			1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	2	1.8	0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Atelectasis									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Idiopathic interstitial pneumonia									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Emphysema									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Pleural disorders									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Pneumothorax									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
<90	0			0			0					
90-<100	0			0			0					
100-<115	0			1	(1.1)	1	0.8	0				
>=115	0			0			0					
Skin and subcutaneous tissue disorders												
<90	15	(10.0)	16	8.2	16	(10.9)	20	10.3	11	(7.8)	13	7.1
90-<100	7	(8.2)	9	8.1	8	(10.4)	10	10.0	6	(7.7)	7	6.8
100-<115	10	(12.3)	10	9.7	8	(8.8)	12	10.1	11	(11.7)	13	10.1
>=115	6	(7.0)	8	6.7	8	(9.1)	12	10.1	9	(10.1)	9	8.0
Epidermal and dermal conditions												
<90	8	(5.3)	8	4.1	11	(7.5)	14	7.2	5	(3.5)	6	3.3
90-<100	4	(4.7)	5	4.5	6	(7.8)	7	7.0	5	(6.4)	5	4.8
100-<115	6	(7.4)	6	5.8	5	(5.5)	6	5.1	7	(7.4)	7	5.5
>=115	5	(5.8)	6	5.0	5	(5.7)	8	6.7	5	(5.6)	5	4.4
Rash												
<90	2	(1.3)	2	1.0	3	(2.0)	4	2.1	1	(0.7)	1	0.5
90-<100	1	(1.2)	1	0.9	1	(1.3)	1	1.0	2	(2.6)	2	1.9
100-<115	2	(2.5)	2	1.9	2	(2.2)	2	1.7	1	(1.1)	1	0.8
>=115	0				1	(1.1)	3	2.5	0			
Eczema												
<90	1	(0.7)	1	0.5	1	(0.7)	1	0.5	1	(0.7)	1	0.5
90-<100	0				1	(1.3)	1	1.0	1	(1.3)	1	1.0
100-<115	2	(2.5)	2	1.9	1	(1.1)	1	0.8	0			
>=115	1	(1.2)	1	0.8	1	(1.1)	1	0.8	0			
Blister												
<90	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			2 (2.6)	3	3.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Dry skin									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Rash pruritic									
<90	0			1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	2	1.8	0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Decubitus ulcer									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Dermatitis contact									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Dermatitis allergic									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			1 (1.1)	1	0.8	0		
Skin exfoliation									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Skin lesion									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	1 (1.1)	1	0.9
Drug eruption									
<90	0			0			2 (1.4)	3	1.6
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Pruritus									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			2 (2.2)	2	1.8
Intertrigo									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Pain of skin									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Perioral dermatitis									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Psoriasis									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			0		
>=115	0			0			1	(1.1)	1 0.9
Sensitive skin									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Skin burning sensation									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Dermatitis									
<90	2	(1.3)	2 1.0	0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			2 (2.1)	2	1.6
>=115	0			0			0		
Erythema									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	2	1.7	0			0		
Neurodermatitis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Parapsoriasis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Rash erythematous									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Stasis dermatitis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Xanthelasma									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Skin appendage conditions									
<90	5 (3.3)	5	2.6	2 (1.4)	3	1.5	3 (2.1)	3	1.6
90-<100	2 (2.4)	2	1.8	2 (2.6)	3	3.0	0		
100-<115	2 (2.5)	2	1.9	2 (2.2)	2	1.7	2 (2.1)	2	1.6
>=115	2 (2.3)	2	1.7	3 (3.4)	4	3.4	3 (3.4)	3	2.7
Alopecia									
<90	4 (2.7)	4	2.0	0			2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	2 (2.6)	3	3.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	0		
Ingrowing nail									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.9
Onychomadesis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	2	1.7	0		
Acne									
<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	0			0		
Alopecia areata									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Hyperhidrosis									
<90	1 (0.7)	1	0.5	1 (0.7)	2	1.0	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			1 (1.1)	1	0.9
Miliaria									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			1 (1.1)	1	0.9
Nail dystrophy									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Skin and subcutaneous tissue disorders NEC									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	1 (1.2)	1	1.0	1 (1.1)	4	3.4	1 (1.1)	1	0.8
>=115	0			0			0		
Diabetic foot									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	3	2.5	0		
>=115	0			0			0		
Skin ulcer									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Angioedema and urticaria									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			2 (2.6)	2	1.9
100-<115	0			0			0		
>=115	0			0			0		
Urticaria									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			2 (2.6)	2	1.9
100-<115	0			0			0		
>=115	0			0			0		
Chronic spontaneous urticaria									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Cornification and dystrophic skin disorders									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			1 (1.1)	1	0.8
>=115	0			0			1 (1.1)	1	0.9
Actinic keratosis									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Dermatitis papillaris capillitii									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Hyperkeratosis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			1 (1.1)	1	0.9
Punctate keratosis									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Cutaneous neoplasms benign									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			1 (0.7)	1	0.5	2 (1.4)	3	1.6
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Dermal cyst									
<90	0			1 (0.7)	1	0.5	2 (1.4)	3	1.6
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Skin vascular abnormalities									
<90	1 (0.7)	1	0.5	0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Ecchymosis									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Haemorrhage subcutaneous									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Investigations									
<90	5 (3.3)	8	4.1	15 (10.2)	16	8.2	10 (7.1)	12	6.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	5 (5.9)	7	6.3	4 (5.2)	6	6.0	6 (7.7)	10	9.7
100-<115	3 (3.7)	3	2.9	10 (11.0)	12	10.1	11 (11.7)	11	8.6
>=115	5 (5.8)	5	4.2	11 (12.5)	14	11.8	6 (6.7)	9	8.0
Cardiac and vascular investigations (excl enzyme tests)									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	0		
90-<100	0			1 (1.3)	2	2.0	1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	2 (2.2)	2	1.7	2 (2.1)	2	1.6
>=115	0			3 (3.4)	3	2.5	1 (1.1)	1	0.9
Heart rate increased									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			2 (2.3)	2	1.7	0		
Cardiac murmur									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Carotid pulse decreased									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Blood pressure decreased									
<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
100-<115	0				0				0			
>=115	0				1	(1.1)	1	0.8	0			
Cardiac stress test abnormal												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				0			
Electrocardiogram Q waves												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				0			
Blood pressure increased												
<90	0				1	(0.7)	1	0.5	0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				0				0			
Electrocardiogram QT prolonged												
<90	0				1	(0.7)	1	0.5	0			
90-<100	0				0				0			
100-<115	0				0				1	(1.1)	1	0.8
>=115	0				0				0			
Electrocardiogram PR prolongation												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				0				1	(1.1)	1	0.8
>=115	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Electrocardiogram ST-T segment abnormal									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Gastrointestinal investigations									
<90	2 (1.3)	2	1.0	3 (2.0)	3	1.5	2 (1.4)	3	1.6
90-<100	1 (1.2)	1	0.9	2 (2.6)	2	2.0	0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	1 (1.1)	1	0.9
Lipase increased									
<90	2 (1.3)	2	1.0	2 (1.4)	2	1.0	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			1 (1.1)	1	0.9
Occult blood									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Colonoscopy normal									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Occult blood positive									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Amylase increased									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Faecal volume increased									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Pancreatic enzymes increased									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Renal and urinary tract investigations and urinalyses									
<90	0			5 (3.4)	5	2.6	0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Glomerular filtration rate decreased									
<90	0			2 (1.4)	2	1.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
100-<115	0			1	(1.1)	1 0.8	0		
>=115	0			0			0		
Urine albumin/creatinine ratio increased									
<90	0			2	(1.4)	2 1.0	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Urine albumin/creatinine ratio abnormal									
<90	0			1	(0.7)	1 0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Haematology investigations (incl blood groups)									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			2	(2.2)	3 2.5	0		
>=115	0			2	(2.3)	3 2.5	0		
Haemoglobin decreased									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			2	(2.2)	2 1.7	0		
>=115	0			1	(1.1)	1 0.8	0		
Haematocrit decreased									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	0		
Platelet count decreased									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Endocrine investigations (incl sex hormones)									
<90	0			2 (1.4)	2	1.0	2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		
Blood thyroid stimulating hormone increased									
<90	0			1 (0.7)	1	0.5	2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Blood thyroid stimulating hormone decreased									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Blood parathyroid hormone increased									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Enzyme investigations NEC									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	2 (2.2)	2	1.7	0		
>=115	0			1 (1.1)	1	0.8	0		
Blood creatine phosphokinase increased									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	2 (2.2)	2	1.7	0		
>=115	0			1 (1.1)	1	0.8	0		
Hepatobiliary investigations									
<90	1 (0.7)	1	0.5	0			0		
90-<100	1 (1.2)	2	1.8	0			2 (2.6)	4	3.9
100-<115	0			2 (2.2)	2	1.7	2 (2.1)	2	1.6
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	3 (3.4)	4	3.6
Liver function test increased									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	0		
Hepatic enzyme increased									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Liver function test abnormal									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Alanine aminotransferase increased									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			2 (2.6)	2	1.9
100-<115	0			0			0		
>=115	0			0			2 (2.2)	2	1.8
Aspartate aminotransferase increased									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			2 (2.6)	2	1.9
100-<115	0			0			0		
>=115	0			0			0		
Blood bilirubin increased									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Transaminases increased									
<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Lipid analyses									
<90	0			2 (1.4)	2	1.0	1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Lipids abnormal									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Low density lipoprotein increased									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Blood cholesterol increased									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Blood triglycerides increased									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Physical examination and organ system status topics												
<90	0				0				0			
90-<100	0				1	(1.3)	1	1.0	1	(1.3)	1	1.0
100-<115	0				0				0			
>=115	0				0				0			
Weight decreased												
<90	0				0				0			
90-<100	0				1	(1.3)	1	1.0	0			
100-<115	0				0				0			
>=115	0				0				0			
Weight increased												
<90	0				0				0			
90-<100	0				0				1	(1.3)	1	1.0
100-<115	0				0				0			
>=115	0				0				0			
Investigations, imaging and histopathology procedures NEC												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				1	(1.1)	1	0.8	0			
Endoscopy abnormal												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				1	(1.1)	1	0.8	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Neurological, special senses and psychiatric investigations									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	2	1.7	0		
Intraocular pressure increased									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	2	1.7	0		
Reproductive organ and breast investigations (excl hormone analyses)									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Mammogram abnormal									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Metabolic, nutritional and blood gas investigations									
<90	2 (1.3)	2	1.0	0			4 (2.8)	5	2.7
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	2 (2.1)	2	1.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=115	0			0			1	(1.1)	1 0.9
Vitamin B12 decreased									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1	(1.1)	1 0.8	1	(1.1)	1 0.8
>=115	0			0			0		
Blood glucose decreased									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Blood glucose increased									
<90	0			0			3	(2.1)	3 1.6
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Blood uric acid increased									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Brain natriuretic peptide increased									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			0		
Glycosylated haemoglobin increased									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	1 (0.7)	1	0.5	0			2 (1.4)	2	1.1
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Protein and chemistry analyses NEC									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	3 (3.2)	3	2.3
>=115	1 (1.2)	1	0.8	0			0		
C-reactive protein increased									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	3 (3.2)	3	2.3
>=115	1 (1.2)	1	0.8	0			0		
Microbiology and serology investigations									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Helicobacter test positive									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Water, electrolyte and mineral investigations									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			0		
Blood potassium increased									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Blood potassium decreased									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Blood sodium increased									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Cytogenetic investigations									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Prostatic specific antigen increased									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Immunology and allergy investigations									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Antinuclear antibody increased									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Renal and urinary disorders									
<90	7 (4.7)	7	3.6	9 (6.1)	11	5.6	9 (6.4)	11	6.0
90-<100	1 (1.2)	1	0.9	4 (5.2)	4	4.0	6 (7.7)	8	7.7
100-<115	5 (6.2)	6	5.8	8 (8.8)	9	7.6	4 (4.3)	5	3.9
>=115	6 (7.0)	8	6.7	10 (11.4)	13	10.9	9 (10.1)	10	8.9
Urinary tract signs and symptoms									
<90	2 (1.3)	2	1.0	3 (2.0)	3	1.5	4 (2.8)	5	2.7
90-<100	0			2 (2.6)	2	2.0	5 (6.4)	7	6.8
100-<115	0			7 (7.7)	7	5.9	1 (1.1)	1	0.8
>=115	5 (5.8)	5	4.2	5 (5.7)	5	4.2	6 (6.7)	6	5.3
Microalbuminuria									
<90	2 (1.3)	2	1.0	0			1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			2 (2.2)	2	1.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		
Dysuria									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			3 (3.3)	3	2.5	1 (1.1)	1	0.8
>=115	0			0			1 (1.1)	1	0.9
Haematuria									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.9
Renal colic									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Proteinuria									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	2 (2.3)	2	1.7	1 (1.1)	1	0.9
Nocturia									
<90	0			2 (1.4)	2	1.0	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Pollakiuria									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	3 (3.5)	3	2.5	1 (1.1)	1	0.8	2 (2.2)	2	1.8
Lower urinary tract symptoms									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Micturition disorder									
<90	0			0			0		
90-<100	0			0			1 (1.3)	2	1.9
100-<115	0			0			0		
>=115	0			0			0		
Polyuria									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Urethral pain									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Urinary incontinence									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	0			0			0		
Renal disorders (excl nephropathies)									
<90	0			1 (0.7)	2	1.0	3 (2.1)	3	1.6
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	2 (2.5)	2	1.9	1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	2 (2.3)	2	1.7	4 (4.5)	5	4.2	1 (1.1)	1	0.9
Acute kidney injury									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	2 (2.3)	3	2.5	0		
Renal cyst									
<90	0			0			2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	1 (1.2)	1	1.0	0			1 (1.1)	1	0.8
>=115	0			2 (2.3)	2	1.7	0		
Chronic kidney disease									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Renal impairment									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Hydronephrosis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Kidney fibrosis									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Nephropathies									
<90	1 (0.7)	1	0.5	3 (2.0)	3	1.5	1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	1 (1.2)	1	0.8	2 (2.3)	2	1.7	0		
Diabetic nephropathy									
<90	1 (0.7)	1	0.5	3 (2.0)	3	1.5	1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		
Nephropathy									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			1 (1.1)	1	0.8	0		
Urolithiases									
<90	4 (2.7)	4	2.0	2 (1.4)	2	1.0	2 (1.4)	2	1.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	2 (2.5)	3	2.9	0			2 (2.1)	2	1.6
>=115	0			1 (1.1)	1	0.8	2 (2.2)	2	1.8
Nephrolithiasis									
<90	4 (2.7)	4	2.0	1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	2 (2.5)	3	2.9	0			2 (2.1)	2	1.6
>=115	0			0			1 (1.1)	1	0.9
Calculus urinary									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Stag horn calculus									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Ureterolithiasis									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Bladder and bladder neck disorders (excl calculi)									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			1 (1.1)	1	0.9
Bladder outlet obstruction									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Hypertonic bladder									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Bladder hypertrophy									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Vascular disorders									
<90	6 (4.0)	6	3.1	6 (4.1)	7	3.6	5 (3.5)	5	2.7
90-<100	5 (5.9)	5	4.5	4 (5.2)	4	4.0	3 (3.8)	3	2.9
100-<115	5 (6.2)	5	4.8	9 (9.9)	9	7.6	12 (12.8)	13	10.1
>=115	6 (7.0)	7	5.9	5 (5.7)	6	5.0	10 (11.2)	11	9.8
Vascular hypertensive disorders									
<90	3 (2.0)	3	1.5	2 (1.4)	2	1.0	2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	3 (3.9)	3	3.0	0		
100-<115	4 (4.9)	4	3.9	4 (4.4)	4	3.4	10 (10.6)	11	8.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	1 (1.2)	1	0.8	1 (1.1)	2	1.7	3 (3.4)	3	2.7
Hypertension									
<90	3 (2.0)	3	1.5	2 (1.4)	2	1.0	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	3 (3.9)	3	3.0	0		
100-<115	4 (4.9)	4	3.9	4 (4.4)	4	3.4	8 (8.5)	8	6.2
>=115	1 (1.2)	1	0.8	1 (1.1)	2	1.7	3 (3.4)	3	2.7
Hypertensive crisis									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			2 (2.1)	2	1.6
>=115	0			0			0		
Hypertensive urgency									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Decreased and nonspecific blood pressure disorders and shock									
<90	1 (0.7)	1	0.5	2 (1.4)	3	1.5	2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	3 (3.5)	4	3.4	0			0		
Hypotension									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	0		
>=115	3 (3.5)	4	3.4	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Blood pressure inadequately controlled									
<90	0			0			0		
90-<100	0			1	(1.3)	1 1.0	0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			0		
Orthostatic hypotension									
<90	0			1	(0.7)	2 1.0	2	(1.4)	2 1.1
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Shock									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Vascular disorders NEC									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			1	(1.3)	1 1.0
100-<115	0			2	(2.2)	2 1.7	0		
>=115	1	(1.2)	1 0.8	1	(1.1)	1 0.8	0		
Aortic dilatation									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1	(1.1)	1 0.8	0		
Aortic rupture									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				0			
Hot flush												
<90	0				0				1	(0.7)	1	0.5
90-<100	0				0				1	(1.3)	1	1.0
100-<115	0				1	(1.1)	1	0.8	0			
>=115	1	(1.2)	1	0.8	0				0			
Vascular haemorrhagic disorders												
<90	0				2	(1.4)	2	1.0	0			
90-<100	0				0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				1	(1.1)	1	0.9
Haematoma												
<90	0				2	(1.4)	2	1.0	0			
90-<100	0				0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				1	(1.1)	1	0.9
Aneurysms and artery dissections												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				1	(1.1)	1	0.8	0			
Aortic aneurysm												
<90	0				0				0			
90-<100	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Arteriosclerosis, stenosis, vascular insufficiency and necrosis									
<90	2 (1.3)	2	1.0	0			0		
90-<100	3 (3.5)	3	2.7	0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	0			1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	3 (3.4)	4	3.6
Aortic arteriosclerosis									
<90	1 (0.7)	1	0.5	0			0		
90-<100	2 (2.4)	2	1.8	0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Arteriosclerosis									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Peripheral arterial occlusive disease									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Peripheral artery stenosis									
<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Peripheral coldness									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	1	(1.2)	1 1.0	0			0		
>=115	0			0			0		
Peripheral venous disease									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			2	(2.2)	3 2.7
Embolism and thrombosis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1	(1.1)	1 0.8	1	(1.1)	1 0.9
Post thrombotic syndrome									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1	(1.1)	1 0.8	0		
Deep vein thrombosis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Vascular infections and inflammations									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1	(1.1)	1 0.8	0		
>=115	0			0			0		
Temporal arteritis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1	(1.1)	1 0.8	0		
>=115	0			0			0		
Lymphatic vessel disorders									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Lymphoedema									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Venous varices									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			1	(1.1)	1 0.9
Varicose vein									
<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Psychiatric disorders									
<90	7 (4.7)	7	3.6	5 (3.4)	7	3.6	6 (4.3)	6	3.3
90-<100	5 (5.9)	7	6.3	1 (1.3)	1	1.0	4 (5.1)	4	3.9
100-<115	3 (3.7)	4	3.9	12 (13.2)	13	10.9	3 (3.2)	4	3.1
>=115	8 (9.3)	10	8.4	6 (6.8)	8	6.7	2 (2.2)	2	1.8
Sleep disorders and disturbances									
<90	3 (2.0)	3	1.5	2 (1.4)	2	1.0	2 (1.4)	2	1.1
90-<100	0			0			0		
100-<115	0			6 (6.6)	6	5.1	1 (1.1)	1	0.8
>=115	3 (3.5)	3	2.5	2 (2.3)	2	1.7	1 (1.1)	1	0.9
Insomnia									
<90	3 (2.0)	3	1.5	1 (0.7)	1	0.5	2 (1.4)	2	1.1
90-<100	0			0			0		
100-<115	0			5 (5.5)	5	4.2	1 (1.1)	1	0.8
>=115	3 (3.5)	3	2.5	1 (1.1)	1	0.8	1 (1.1)	1	0.9
Abnormal dreams									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Middle insomnia									
<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Sleep disorder									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Depressed mood disorders and disturbances									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	1 (0.7)	1	0.5
90-<100	2 (2.4)	2	1.8	1 (1.3)	1	1.0	2 (2.6)	2	1.9
100-<115	1 (1.2)	1	1.0	3 (3.3)	3	2.5	2 (2.1)	2	1.6
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		
Depressed mood									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	2 (2.2)	2	1.7	0		
>=115	1 (1.2)	1	0.8	0			0		
Depression									
<90	0			0			1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	0			2 (2.6)	2	1.9
100-<115	0			1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	0			1 (1.1)	1	0.8	0		
Anhedonia									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			0			0		
Major depression									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Anxiety disorders and symptoms									
<90	2 (1.3)	2	1.0	1 (0.7)	1	0.5	3 (2.1)	3	1.6
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	2 (2.5)	2	1.9	2 (2.2)	2	1.7	1 (1.1)	1	0.8
>=115	5 (5.8)	6	5.0	2 (2.3)	2	1.7	1 (1.1)	1	0.9
Anxiety									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	1	1.0
100-<115	2 (2.5)	2	1.9	0			1 (1.1)	1	0.8
>=115	4 (4.7)	5	4.2	2 (2.3)	2	1.7	1 (1.1)	1	0.9
Anxiety disorder due to a general medical condition									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Stress									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Generalised anxiety disorder									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Nervousness									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Post-traumatic stress disorder									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Adjustment disorders (incl subtypes)									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	0		
Adjustment disorder with depressed mood									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			1 (1.1)	1	0.8	0		
Grief reaction									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Mood disorders and disturbances NEC									
<90	1 (0.7)	1	0.5	1 (0.7)	2	1.0	0		
90-<100	1 (1.2)	1	0.9	0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Irritability									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Mood altered									
<90	0			1 (0.7)	2	1.0	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Mood swings									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Suicidal and self-injurious behaviours NEC									
<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				1	(1.1)	1	0.8	0			
Suicidal ideation												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				1	(1.1)	1	0.8	0			
Changes in physical activity												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				0			
Restlessness												
<90	0				0				0			
90-<100	0				0				0			
100-<115	0				1	(1.1)	1	0.8	0			
>=115	0				0				0			
Psychiatric disorders NEC												
<90	0				0				0			
90-<100	1	(1.2)	1	0.9	0				0			
100-<115	0				0				0			
>=115	0				0				0			
Mental status changes												
<90	0				0				0			
90-<100	1	(1.2)	1	0.9	0				0			
100-<115	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			0			0		
Sexual dysfunctions, disturbances and gender identity disorders									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Libido decreased									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Cardiac disorders									
<90	8 (5.3)	9	4.6	8 (5.4)	12	6.2	5 (3.5)	6	3.3
90-<100	5 (5.9)	8	7.2	2 (2.6)	3	3.0	1 (1.3)	4	3.9
100-<115	3 (3.7)	3	2.9	6 (6.6)	6	5.1	3 (3.2)	3	2.3
>=115	4 (4.7)	4	3.4	6 (6.8)	7	5.9	4 (4.5)	4	3.6
Cardiac arrhythmias									
<90	6 (4.0)	7	3.6	5 (3.4)	7	3.6	1 (0.7)	1	0.5
90-<100	2 (2.4)	3	2.7	1 (1.3)	1	1.0	1 (1.3)	2	1.9
100-<115	1 (1.2)	1	1.0	3 (3.3)	3	2.5	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	4 (4.5)	5	4.2	1 (1.1)	1	0.9
Atrial fibrillation									
<90	2 (1.3)	2	1.0	1 (0.7)	1	0.5	0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			2 (2.3)	2	1.7	1 (1.1)	1	0.9
Supraventricular extrasystoles									
<90	0			3 (2.0)	3	1.5	0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Tachycardia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	0		
Atrioventricular block first degree									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Supraventricular tachycardia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		
Bundle branch block right									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Sinus tachycardia									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	2 (2.4)	2	1.8	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Ventricular extrasystoles									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Atrial flutter									
<90	0			0			0		
90-<100	0			0			1 (1.3)	2	1.9
100-<115	0			0			0		
>=115	0			0			0		
Bradycardia									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Bundle branch block left									
<90	2 (1.3)	2	1.0	0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Coronary artery disorders									
<90	0			2 (1.4)	2	1.0	1 (0.7)	1	0.5
90-<100	3 (3.5)	3	2.7	1 (1.3)	1	1.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	2 (2.5)	2	1.9	2 (2.2)	2	1.7	0		
>=115	2 (2.3)	2	1.7	2 (2.3)	2	1.7	3 (3.4)	3	2.7
Angina pectoris									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	0			2 (2.2)	2	1.8
Acute myocardial infarction									
<90	0			0			1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Coronary artery disease									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			1 (1.1)	1	0.8	0		
Myocardial infarction									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			1 (1.1)	1	0.8	0		
Myocardial ischaemia									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			1 (1.1)	1	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Angina unstable									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Arteriosclerosis coronary artery									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Cardiac disorders, signs and symptoms NEC									
<90	2 (1.3)	2	1.0	2 (1.4)	3	1.5	2 (1.4)	2	1.1
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	1 (1.2)	1	0.8	0			0		
Palpitations									
<90	2 (1.3)	2	1.0	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	1 (1.2)	1	0.8	0			0		
Cardiovascular disorder									
<90	0			1 (0.7)	2	1.0	1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Hypertensive heart disease									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Heart failures									
<90	0			0			1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	1 (1.3)	2	1.9
100-<115	0			0			0		
>=115	0			0			0		
Cardiac failure congestive									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Cardiac failure acute									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Left ventricular failure									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Myocardial disorders									
<90	0			0			1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	0			0			0		
Cardiac hypertrophy									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Left ventricular hypertrophy									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Ear and labyrinth disorders									
<90	2 (1.3)	2	1.0	7 (4.8)	7	3.6	4 (2.8)	4	2.2
90-<100	3 (3.5)	5	4.5	2 (2.6)	2	2.0	5 (6.4)	6	5.8
100-<115	2 (2.5)	3	2.9	6 (6.6)	6	5.1	2 (2.1)	2	1.6
>=115	4 (4.7)	4	3.4	5 (5.7)	5	4.2	1 (1.1)	2	1.8
Inner ear and VIIIth cranial nerve disorders									
<90	0			3 (2.0)	3	1.5	2 (1.4)	2	1.1
90-<100	3 (3.5)	5	4.5	2 (2.6)	2	2.0	4 (5.1)	4	3.9
100-<115	2 (2.5)	3	2.9	3 (3.3)	3	2.5	1 (1.1)	1	0.8
>=115	3 (3.5)	3	2.5	2 (2.3)	2	1.7	1 (1.1)	2	1.8
Vertigo									
<90	0			2 (1.4)	2	1.0	2 (1.4)	2	1.1
90-<100	2 (2.4)	4	3.6	2 (2.6)	2	2.0	2 (2.6)	2	1.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	1 (1.2)	1	1.0	2 (2.2)	2	1.7	1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	1 (1.1)	2	1.8
Vertigo positional									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	0		
Motion sickness									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	1 (1.2)	2	1.9	0			0		
>=115	0			0			0		
Tinnitus									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	3 (3.5)	3	2.5	0			0		
Aural disorders NEC									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			2 (2.2)	2	1.7	1 (1.1)	1	0.8
>=115	0			3 (3.4)	3	2.5	0		
Ear pain									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			2 (2.2)	2	1.7	1 (1.1)	1	0.8
>=115	0			3 (3.4)	3	2.5	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Ear pruritus									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Ear discomfort									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Hearing disorders									
<90	1 (0.7)	1	0.5	2 (1.4)	2	1.0	1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Hypoacusis									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Deafness bilateral									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Deafness unilateral									
<90	1 (0.7)	1	0.5	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Mixed deafness									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
External ear disorders (excl congenital)									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Cerumen impaction									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Excessive cerumen production									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Reproductive system and breast disorders									
<90	5 (3.3)	6	3.1	2 (1.4)	2	1.0	2 (1.4)	2	1.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	2 (2.4)	3	2.7	2 (2.6)	2	2.0	2 (2.6)	3	2.9
100-<115	4 (4.9)	4	3.9	4 (4.4)	4	3.4	3 (3.2)	4	3.1
>=115	4 (4.7)	7	5.9	4 (4.5)	4	3.4	2 (2.2)	2	1.8
Vulvovaginal disorders (excl infections and inflammations)									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		
Vulva cyst									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Vulvovaginal pruritus									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Vulval disorder									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Vaginal disorder									
<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Vaginal haemorrhage									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Vulvovaginal dryness									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Menstrual cycle and uterine bleeding disorders									
<90	0			1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	1 (1.3)	2	1.9
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		
Metrorrhagia									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Dysmenorrhoea									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			1 (1.1)	1	0.8	0		
Oligomenorrhoea									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Menorrhagia									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Menstruation irregular									
<90	0			0			0		
90-<100	0			0			1 (1.3)	2	1.9
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Sexual function and fertility disorders									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		
Erectile dysfunction									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Breast disorders									
<90	2 (1.3)	2	1.0	0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			1 (1.1)	1	0.8	0		
Breast mass									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Breast cyst									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Breast pain									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Menopause related conditions									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Atrophic vulvovaginitis									
<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	0			0			0		
Uterine, pelvic and broad ligament disorders									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Uterine polyp									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Adenomyosis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Endometriosis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Reproductive tract disorders NEC									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	1 (1.2)	1	0.9	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
100-<115	0			0			0		
>=115	0			0			0		
Pruritus genital									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Pelvic pain									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Male reproductive tract infections and inflammations									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	2 (2.5)	2	1.9	0			1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			0		
Balanoposthitis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	2 (2.5)	2	1.9	0			0		
>=115	1 (1.2)	1	0.8	0			0		
Prostatitis									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=115	0			0			0		
Ovarian and fallopian tube disorders									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	2	(2.3)	2 1.7	0			0		
Haemorrhagic ovarian cyst									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			0		
Ovarian cyst									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			0		
Penile and scrotal disorders (excl infections and inflammations)									
<90	1	(0.7)	2 1.0	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Penile erosion									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Peyronie's disease									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Prostatic disorders (excl infections and inflammations)									
<90	1 (0.7)	1	0.5	0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Benign prostatic hyperplasia									
<90	1 (0.7)	1	0.5	0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Testicular and epididymal disorders									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Testicular disorder									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Hepatobiliary disorders									
<90	5 (3.3)	5	2.6	2 (1.4)	2	1.0	3 (2.1)	4	2.2
90-<100	1 (1.2)	1	0.9	3 (3.9)	4	4.0	0		
100-<115	2 (2.5)	3	2.9	2 (2.2)	2	1.7	3 (3.2)	6	4.7
>=115	2 (2.3)	2	1.7	3 (3.4)	5	4.2	3 (3.4)	4	3.6
Hepatic and hepatobiliary disorders									
<90	3 (2.0)	3	1.5	1 (0.7)	1	0.5	3 (2.1)	4	2.2
90-<100	1 (1.2)	1	0.9	2 (2.6)	3	3.0	0		
100-<115	0			2 (2.2)	2	1.7	3 (3.2)	3	2.3
>=115	2 (2.3)	2	1.7	3 (3.4)	3	2.5	3 (3.4)	3	2.7
Hepatic steatosis									
<90	2 (1.3)	2	1.0	0			2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			2 (2.2)	2	1.7	2 (2.1)	2	1.6
>=115	0			2 (2.3)	2	1.7	1 (1.1)	1	0.9
Hepatic lesion									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Non-alcoholic steatohepatitis									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Nonalcoholic fatty liver disease									
<90	1 (0.7)	1	0.5	0			0		

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Portal vein thrombosis									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Hepatic cyst									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Drug-induced liver injury									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Hepatic cirrhosis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Hepatomegaly									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	1 (1.2)	1	0.8	0			0		
Liver disorder									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Portal hypertension									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Gallbladder disorders									
<90	2 (1.3)	2	1.0	1 (0.7)	1	0.5	0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	2 (2.5)	3	2.9	0			2 (2.1)	3	2.3
>=115	0			1 (1.1)	2	1.7	1 (1.1)	1	0.9
Gallbladder polyp									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Cholecystitis chronic									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Cholelithiasis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	2 (2.5)	2	1.9	0			2 (2.1)	2	1.6
>=115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.9
Cholecystitis acute									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Blood and lymphatic system disorders									
<90	4 (2.7)	4	2.0	7 (4.8)	7	3.6	4 (2.8)	4	2.2
90-<100	2 (2.4)	2	1.8	2 (2.6)	2	2.0	2 (2.6)	2	1.9
100-<115	1 (1.2)	1	1.0	3 (3.3)	4	3.4	3 (3.2)	4	3.1
>=115	2 (2.3)	2	1.7	0			1 (1.1)	1	0.9
Anaemias nonhaemolytic and marrow depression									
<90	4 (2.7)	4	2.0	7 (4.8)	7	3.6	3 (2.1)	3	1.6
90-<100	2 (2.4)	2	1.8	1 (1.3)	1	1.0	1 (1.3)	1	1.0
100-<115	1 (1.2)	1	1.0	2 (2.2)	3	2.5	2 (2.1)	2	1.6
>=115	1 (1.2)	1	0.8	0			0		
Anaemia									
<90	2 (1.3)	2	1.0	6 (4.1)	6	3.1	2 (1.4)	2	1.1
90-<100	1 (1.2)	1	0.9	1 (1.3)	1	1.0	0		
100-<115	0			2 (2.2)	2	1.7	2 (2.1)	2	1.6
>=115	1 (1.2)	1	0.8	0			0		
Pancytopenia									

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Iron deficiency anaemia									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Hypochromic anaemia									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Microcytic anaemia									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Normocytic anaemia									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Spleen, lymphatic and reticuloendothelial system disorders									
<90	0			0			1 (0.7)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			1 (1.1)	1	0.9
Splenomegaly									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	0			0			0		
Lymphadenopathy									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			1 (1.1)	1	0.9
Platelet disorders									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Thrombocytosis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
White blood cell disorders									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	1 (1.2)	1	0.8	0			0		
Leukocytosis									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Lymphopenia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)									
<90	6 (4.0)	6	3.1	0			4 (2.8)	6	3.3
90-<100	3 (3.5)	4	3.6	0			1 (1.3)	1	1.0
100-<115	3 (3.7)	3	2.9	4 (4.4)	4	3.4	3 (3.2)	3	2.3
>=115	1 (1.2)	3	2.5	5 (5.7)	6	5.0	4 (4.5)	4	3.6
Gastrointestinal neoplasms benign									
<90	1 (0.7)	1	0.5	0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	1 (1.2)	2	1.7	1 (1.1)	1	0.8	2 (2.2)	2	1.8
Gastrointestinal tract adenoma									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			1 (1.1)	1	0.8	0		
Benign duodenal neoplasm									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Colon adenoma									
<90	1 (0.7)	1	0.5	0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	1 (1.2)	2	1.7	0			2 (2.2)	2	1.8
Leukaemias									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			1 (1.1)	1	0.8	0		
Chronic lymphocytic leukaemia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Myeloid leukaemia									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Cutaneous neoplasms benign									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	1 (0.7)	1	0.5	0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Anogenital warts									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Melanocytic naevus									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Miscellaneous and site unspecified neoplasms malignant and unspecified									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Squamous cell carcinoma									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Respiratory and mediastinal neoplasms malignant and unspecified									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	1 (1.1)	1	0.9
Nasal cavity cancer									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Keratinising squamous cell carcinoma of nasopharynx									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1 (1.1)	1	0.9
Skeletal neoplasms benign									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Osteochondroma									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Lymphomas non-Hodgkin's unspecified histology									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Gastrointestinal lymphoma									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Soft tissue neoplasms benign									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	0		
>=115	0			0			1 (1.1)	1	0.9
Lipoma									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	0		
>=115	0			0			1 (1.1)	1	0.9
Breast neoplasms malignant and unspecified (incl nipple)									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Invasive ductal breast carcinoma									
<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Endocrine neoplasms benign									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Pituitary tumour benign									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Endocrine neoplasms malignant and unspecified									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Neuroendocrine tumour									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Gastrointestinal neoplasms malignant and unspecified									
<90	3 (2.0)	3	1.5	0			2 (1.4)	2	1.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Adenocarcinoma gastric									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Adenocarcinoma of colon									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Gastric cancer									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Gastric cancer stage IV									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Gastrointestinal stromal tumour									
<90	0			0			0		
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=115	0			0			0		
Gastrointestinal submucosal tumour									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Oral neoplasm									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Hepatobiliary neoplasms malignant and unspecified									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Hepatocellular carcinoma									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Metastases									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Metastases to liver												
<90	0				0				0			
90-<100	1	(1.2)	1	0.9	0				0			
100-<115	0				0				0			
>=115	0				0				0			
Reproductive neoplasms female benign												
<90	0				0				0			
90-<100	0				0				0			
100-<115	1	(1.2)	1	1.0	0				0			
>=115	0				0				0			
Uterine leiomyoma												
<90	0				0				0			
90-<100	0				0				0			
100-<115	1	(1.2)	1	1.0	0				0			
>=115	0				0				0			
Reproductive neoplasms female malignant and unspecified												
<90	1	(0.7)	1	0.5	0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				0				0			
Uterine cancer												
<90	1	(0.7)	1	0.5	0				0			
90-<100	0				0				0			
100-<115	0				0				0			
>=115	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Reproductive neoplasms male malignant and unspecified									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Prostate cancer									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Skin neoplasms malignant and unspecified									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Basal cell carcinoma									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			0		
Immune system disorders									
<90	2 (1.3)	2	1.0	2 (1.4)	2	1.0	2 (1.4)	3	1.6
90-<100	0			2 (2.6)	2	2.0	2 (2.6)	2	1.9
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	2 (2.1)	2	1.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	3 (3.5)	3	2.5	1 (1.1)	1	0.8	0		
Allergic conditions									
<90	2 (1.3)	2	1.0	2 (1.4)	2	1.0	2 (1.4)	3	1.6
90-<100	0			2 (2.6)	2	2.0	2 (2.6)	2	1.9
100-<115	0			1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	3 (3.5)	3	2.5	1 (1.1)	1	0.8	0		
Seasonal allergy									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	2 (1.4)	3	1.6
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	2 (2.1)	2	1.6
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	0		
Hypersensitivity									
<90	0			0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Allergy to arthropod sting									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Allergy to chemicals									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			0		
Drug hypersensitivity									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Multiple allergies									
<90	0			0			0		
90-<100	0			0			1 (1.3)	1	1.0
100-<115	0			0			0		
>=115	0			0			0		
Immune disorders NEC									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Immunisation reaction									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Endocrine disorders									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	2 (2.2)	2	1.8
Thyroid gland disorders									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	1 (0.7)	1	0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	1 (1.2)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	1 (1.1)	1	0.8	2 (2.2)	2	1.8
Hypothyroidism									
<90	1 (0.7)	1	0.5	0			0		
90-<100	0			1 (1.3)	1	1.0	0		
100-<115	0			1 (1.1)	1	0.8	0		
>=115	0			0			0		
Primary hyperthyroidism									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			1 (1.1)	1	0.8	0		
Thyroid cyst									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Autoimmune thyroiditis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1 (1.2)	1	0.8	0			1 (1.1)	1	0.9
Goitre									
<90	0			0			1 (0.7)	1	0.5
90-<100	0			0			0		
100-<115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=115	0			0			0		
Silent thyroiditis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1 (1.2)	1	1.0	0			0		
>=115	0			0			0		
Thyroid mass									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	0			0			1 (1.1)	1	0.9
Surgical and medical procedures									
<90	1 (0.7)	1	0.5	1 (0.7)	1	0.5	1 (0.7)	1	0.5
90-<100	1 (1.2)	1	0.9	0			0		
100-<115	0			0			1 (1.1)	1	0.8
>=115	1 (1.2)	1	0.8	0			3 (3.4)	4	3.6
Endocrine gland therapeutic procedures									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Thyroidectomy									
<90	0			1 (0.7)	1	0.5	0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Bone and joint therapeutic procedures									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Bone graft									
<90	0			0			0		
90-<100	1	(1.2)	1 0.9	0			0		
100-<115	0			0			0		
>=115	0			0			0		
Joint injection									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Cardiac therapeutic procedures									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			0		
Cardiac pacemaker replacement									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			0		
Eye therapeutic procedures									
<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Cataract operation									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Head and neck therapeutic procedures									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Tooth extraction									
<90	1	(0.7)	1 0.5	0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Male genital tract therapeutic procedures									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			0		
Sperm aspiration									
<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			0		
Therapeutic procedures and supportive care NEC									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			2	(2.2)	2 1.8
Cyst removal									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Nerve block									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			1	(1.1)	1 0.9
Stent placement									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Congenital, familial and genetic disorders									
<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	1	(1.2)	1 0.8	0			1	(1.1)	1 0.9
Reproductive tract and breast disorders congenital									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			1	(1.1)	1 0.9
Phimosis									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			1	(1.1)	1 0.8
>=115	0			0			1	(1.1)	1 0.9
Respiratory disorders congenital									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			0		
Laryngeal web									
<90	0			0			0		
90-<100	0			0			0		
100-<115	0			0			0		
>=115	1	(1.2)	1 0.8	0			0		
Pregnancy, puerperium and perinatal conditions									
<90	0			0			1	(0.7)	1 0.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Abortions and stillbirth									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Abortion spontaneous									
<90	0			0			1	(0.7)	1 0.5
90-<100	0			0			0		
100-<115	0			0			0		
>=115	0			0			0		
Social circumstances									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			0		
>=115	1	(1.2)	1 0.8	0			0		
Economic and housing issues									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			0		
>=115	1	(1.2)	1 0.8	0			0		
Stress at work									
<90	0			0			0		
90-<100	0			0			0		
100-<115	1	(1.2)	1 1.0	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
>=115	1	(1.2)	1	0.8	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

17 Adverse events by body weight at baseline - overview - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
<80	31	43.7			73	101.6			24	33.2		
80-<90	37	49.0			63	87.6			36	50.3		
90-<100	17	23.3			28	38.9			23	32.7		
>=100	15	20.3			35	46.9			18	25.7		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Events												
<80	25	(80.6)	123	281.7	64	(87.7)	330	324.8	19	(79.2)	52	156.8
80-<90	30	(81.1)	118	241.1	54	(85.7)	259	295.8	29	(80.6)	94	187.0
90-<100	12	(70.6)	67	287.1	23	(82.1)	89	228.7	16	(69.6)	53	161.9
>=100	15	(100)	175	863.8	30	(85.7)	156	332.4	16	(88.9)	36	140.3
Serious												
Yes												
<80	2	(6.5)	2	4.6	4	(5.5)	5	4.9	1	(4.2)	1	3.0
80-<90	2	(5.4)	2	4.1	3	(4.8)	4	4.6	4	(11.1)	4	8.0
90-<100	2	(11.8)	2	8.6	1	(3.6)	1	2.6	1	(4.3)	1	3.1
>=100	1	(6.7)	4	19.7	2	(5.7)	2	4.3	1	(5.6)	1	3.9
No												
<80	25	(80.6)	121	277.1	64	(87.7)	325	319.9	19	(79.2)	51	153.8
80-<90	30	(81.1)	116	237.0	54	(85.7)	255	291.2	28	(77.8)	90	179.0
90-<100	12	(70.6)	65	278.5	23	(82.1)	88	226.1	15	(65.2)	52	158.8
>=100	15	(100)	171	844.0	29	(82.9)	154	328.1	16	(88.9)	35	136.4
Severity												
Severe												
<80	1	(3.2)	1	2.3	2	(2.7)	3	3.0	1	(4.2)	1	3.0

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by body weight at baseline - overview - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Severity									
Severe									
80-<90	1 (2.7)	1	2.0	0			3 (8.3)	3	6.0
90-<100	1 (5.9)	1	4.3	0			1 (4.3)	1	3.1
>=100	0			1 (2.9)	1	2.1	0		
Moderate									
<80	2 (6.5)	3	6.9	8 (11.0)	13	12.8	3 (12.5)	5	15.1
80-<90	6 (16.2)	10	20.4	8 (12.7)	12	13.7	6 (16.7)	6	11.9
90-<100	3 (17.6)	13	55.7	4 (14.3)	8	20.6	0		
>=100	3 (20.0)	37	182.6	5 (14.3)	9	19.2	2 (11.1)	2	7.8
Mild									
<80	25 (80.6)	119	272.6	64 (87.7)	314	309.1	18 (75.0)	46	138.7
80-<90	28 (75.7)	107	218.6	53 (84.1)	247	282.1	27 (75.0)	85	169.1
90-<100	12 (70.6)	53	227.1	22 (78.6)	81	208.1	15 (65.2)	52	158.8
>=100	14 (93.3)	138	681.1	29 (82.9)	146	311.1	16 (88.9)	34	132.5
Relationship to trial product									
Missing									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Probable									
<80	7 (22.6)	11	25.2	18 (24.7)	57	56.1	4 (16.7)	5	15.1
80-<90	8 (21.6)	13	26.6	20 (31.7)	61	69.7	4 (11.1)	6	11.9
90-<100	5 (29.4)	7	30.0	7 (25.0)	12	30.8	0		
>=100	5 (33.3)	30	148.1	10 (28.6)	28	59.7	2 (11.1)	5	19.5
Possible									
<80	18 (58.1)	32	73.3	33 (45.2)	79	77.8	1 (4.2)	2	6.0
80-<90	19 (51.4)	36	73.5	26 (41.3)	62	70.8	6 (16.7)	11	21.9

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by body weight at baseline - overview - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Relationship to trial product									
Possible									
90-<100	7 (41.2)	16	68.6	9 (32.1)	25	64.2	2 (8.7)	3	9.2
>=100	11 (73.3)	106	523.2	16 (45.7)	40	85.2	1 (5.6)	1	3.9
Unlikely									
<80	25 (80.6)	80	183.2	58 (79.5)	193	190.0	18 (75.0)	45	135.7
80-<90	27 (73.0)	69	141.0	46 (73.0)	136	155.3	25 (69.4)	77	153.2
90-<100	12 (70.6)	44	188.5	21 (75.0)	52	133.6	16 (69.6)	50	152.7
>=100	9 (60.0)	39	192.5	27 (77.1)	88	187.5	15 (83.3)	30	116.9
Outcome									
Recovered									
<80	24 (77.4)	100	229.0	61 (83.6)	294	289.4	18 (75.0)	40	120.6
80-<90	28 (75.7)	92	187.9	50 (79.4)	221	252.4	29 (80.6)	81	161.1
90-<100	12 (70.6)	54	231.4	23 (82.1)	81	208.1	13 (56.5)	36	110.0
>=100	14 (93.3)	163	804.5	30 (85.7)	133	283.4	15 (83.3)	29	113.0
Recovering									
<80	1 (3.2)	2	4.6	6 (8.2)	7	6.9	1 (4.2)	1	3.0
80-<90	4 (10.8)	6	12.3	3 (4.8)	5	5.7	1 (2.8)	1	2.0
90-<100	2 (11.8)	4	17.1	1 (3.6)	1	2.6	1 (4.3)	1	3.1
>=100	2 (13.3)	4	19.7	6 (17.1)	8	17.0	2 (11.1)	2	7.8
Not Recovered									
<80	13 (41.9)	21	48.1	20 (27.4)	29	28.5	5 (20.8)	11	33.2
80-<90	13 (35.1)	20	40.9	20 (31.7)	33	37.7	8 (22.2)	12	23.9
90-<100	4 (23.5)	9	38.6	5 (17.9)	7	18.0	8 (34.8)	16	48.9
>=100	5 (33.3)	8	39.5	9 (25.7)	15	32.0	5 (27.8)	5	19.5
Leading to									
Permanent treatment discontinuation									
<80	1 (3.2)	1	2.3	3 (4.1)	6	5.9	0		

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by body weight at baseline - overview - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Leading to												
Permanent treatment discontinuation												
80-<90	1	(2.7)	4	8.2	1	(1.6)	2	2.3	1	(2.8)	1	2.0
90-<100	0				1	(3.6)	1	2.6	0			
>=100	1	(6.7)	1	4.9	0				0			
Temporary interruption of trial product												
<80	0				6	(8.2)	6	5.9	1	(4.2)	1	3.0
80-<90	2	(5.4)	3	6.1	5	(7.9)	14	16.0	2	(5.6)	2	4.0
90-<100	2	(11.8)	2	8.6	2	(7.1)	4	10.3	1	(4.3)	1	3.1
>=100	3	(20.0)	4	19.7	1	(2.9)	2	4.3	1	(5.6)	1	3.9
Dose reduction of trial product												
<80	0				7	(9.6)	10	9.8	0			
80-<90	1	(2.7)	1	2.0	3	(4.8)	3	3.4	0			
90-<100	1	(5.9)	1	4.3	3	(10.7)	5	12.8	0			
>=100	1	(6.7)	1	4.9	1	(2.9)	1	2.1	0			

Adverse events with onset prior to randomisation are not included.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

18 Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N		PYE		N		PYE		N		PYE	
<80	31		43.7		73		101.6		24		33.2	
80-<90	37		49.0		63		87.6		36		50.3	
90-<100	17		23.3		28		38.9		23		32.7	
>=100	15		20.3		35		46.9		18		25.7	
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Adverse events												
<80	25	(80.6)	123	281.7	64	(87.7)	330	324.8	19	(79.2)	52	156.8
80-<90	30	(81.1)	118	241.1	54	(85.7)	259	295.8	29	(80.6)	94	187.0
90-<100	12	(70.6)	67	287.1	23	(82.1)	89	228.7	16	(69.6)	53	161.9
>=100	15	(100)	175	863.8	30	(85.7)	156	332.4	16	(88.9)	36	140.3
Gastrointestinal disorders												
<80	23	(74.2)	47	107.6	44	(60.3)	132	129.9	9	(37.5)	14	42.2
80-<90	19	(51.4)	49	100.1	37	(58.7)	109	124.5	10	(27.8)	12	23.9
90-<100	8	(47.1)	21	90.0	16	(57.1)	34	87.4	4	(17.4)	5	15.3
>=100	14	(93.3)	139	686.1	21	(60.0)	68	144.9	7	(38.9)	12	46.8
Gastrointestinal motility and defaecation conditions												
<80	15	(48.4)	15	34.4	29	(39.7)	42	41.3	3	(12.5)	3	9.0
80-<90	14	(37.8)	21	42.9	24	(38.1)	40	45.7	3	(8.3)	3	6.0
90-<100	4	(23.5)	6	25.7	10	(35.7)	10	25.7	3	(13.0)	3	9.2
>=100	8	(53.3)	42	207.3	15	(42.9)	27	57.5	0			
Constipation												
<80	7	(22.6)	7	16.0	22	(30.1)	26	25.6	1	(4.2)	1	3.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	9 (24.3)	12	24.5	16 (25.4)	18	20.6	0		
90-<100	1 (5.9)	1	4.3	5 (17.9)	5	12.8	2 (8.7)	2	6.1
>=100	2 (13.3)	2	9.9	9 (25.7)	11	23.4	0		
Diarrhoea									
<80	7 (22.6)	7	16.0	10 (13.7)	14	13.8	2 (8.3)	2	6.0
80-<90	6 (16.2)	8	16.3	10 (15.9)	20	22.8	3 (8.3)	3	6.0
90-<100	3 (17.6)	5	21.4	3 (10.7)	3	7.7	1 (4.3)	1	3.1
>=100	6 (40.0)	39	192.5	9 (25.7)	15	32.0	0		
Gastrooesophageal reflux disease									
<80	1 (3.2)	1	2.3	2 (2.7)	2	2.0	0		
80-<90	0			2 (3.2)	2	2.3	0		
90-<100	0			2 (7.1)	2	5.1	0		
>=100	1 (6.7)	1	4.9	0			0		
Gastrointestinal motility disorder									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Irritable bowel syndrome									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Gastrointestinal signs and symptoms									
<80	16 (51.6)	25	57.3	27 (37.0)	71	69.9	4 (16.7)	5	15.1
80-<90	9 (24.3)	19	38.8	20 (31.7)	47	53.7	3 (8.3)	4	8.0
90-<100	5 (29.4)	11	47.1	13 (46.4)	22	56.5	1 (4.3)	1	3.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	9 (60.0)	96	473.8	11 (31.4)	29	61.8	3 (16.7)	7	27.3
Nausea									
<80	7 (22.6)	8	18.3	14 (19.2)	31	30.5	1 (4.2)	1	3.0
80-<90	5 (13.5)	5	10.2	11 (17.5)	15	17.1	2 (5.6)	2	4.0
90-<100	1 (5.9)	1	4.3	3 (10.7)	7	18.0	0		
>=100	5 (33.3)	13	64.2	7 (20.0)	13	27.7	1 (5.6)	1	3.9
Vomiting									
<80	5 (16.1)	5	11.5	6 (8.2)	12	11.8	0		
80-<90	0			3 (4.8)	6	6.9	2 (5.6)	2	4.0
90-<100	1 (5.9)	1	4.3	4 (14.3)	6	15.4	0		
>=100	4 (26.7)	28	138.2	4 (11.4)	5	10.7	0		
Abdominal discomfort									
<80	5 (16.1)	6	13.7	4 (5.5)	5	4.9	0		
80-<90	3 (8.1)	3	6.1	5 (7.9)	7	8.0	0		
90-<100	1 (5.9)	1	4.3	2 (7.1)	3	7.7	1 (4.3)	1	3.1
>=100	2 (13.3)	2	9.9	1 (2.9)	1	2.1	0		
Abdominal pain									
<80	0			5 (6.8)	6	5.9	0		
80-<90	1 (2.7)	1	2.0	4 (6.3)	7	8.0	0		
90-<100	1 (5.9)	2	8.6	2 (7.1)	2	5.1	0		
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	0		
Dyspepsia									
<80	0			1 (1.4)	1	1.0	0		
80-<90	2 (5.4)	2	4.1	3 (4.8)	6	6.9	0		
90-<100	2 (11.8)	2	8.6	1 (3.6)	1	2.6	0		
>=100	2 (13.3)	13	64.2	4 (11.4)	6	12.8	1 (5.6)	4	15.6
Abdominal pain upper									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<80	1 (3.2)	2	4.6	7 (9.6)	10	9.8	1 (4.2)	1	3.0
80-<90	2 (5.4)	3	6.1	1 (1.6)	1	1.1	0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			1 (2.9)	1	2.1	0		
Abdominal distension									
<80	1 (3.2)	1	2.3	2 (2.7)	3	3.0	2 (8.3)	3	9.0
80-<90	2 (5.4)	2	4.1	2 (3.2)	2	2.3	0		
90-<100	2 (11.8)	3	12.9	2 (7.1)	2	5.1	0		
>=100	2 (13.3)	2	9.9	1 (2.9)	1	2.1	0		
Eructation									
<80	0			0			0		
80-<90	2 (5.4)	2	4.1	1 (1.6)	1	1.1	0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	1 (6.7)	18	88.8	1 (2.9)	1	2.1	0		
Faeces soft									
<80	0			1 (1.4)	1	1.0	0		
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Flatulence									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	1 (6.7)	18	88.8	0			0		
Abdominal tenderness									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
>=100	0			0			0		
Faeces hard									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Abdominal pain lower									
<80	1 (3.2)	2	4.6	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			1 (5.6)	2	7.8
Epigastric discomfort									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	0			0		
Dental and gingival conditions									
<80	3 (9.7)	3	6.9	4 (5.5)	4	3.9	2 (8.3)	2	6.0
80-<90	3 (8.1)	3	6.1	4 (6.3)	5	5.7	1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			6 (17.1)	6	12.8	3 (16.7)	3	11.7
Dental caries									
<80	3 (9.7)	3	6.9	3 (4.1)	3	3.0	2 (8.3)	2	6.0
80-<90	1 (2.7)	1	2.0	2 (3.2)	3	3.4	1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			6 (17.1)	6	12.8	2 (11.1)	2	7.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Toothache									
<80	0			1 (1.4)	1	1.0	0		
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9
Tooth impacted									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Dental cyst									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Gastrointestinal conditions NEC									
<80	1 (3.2)	1	2.3	5 (6.8)	7	6.9	1 (4.2)	1	3.0
80-<90	1 (2.7)	1	2.0	2 (3.2)	2	2.3	0		
90-<100	2 (11.8)	2	8.6	1 (3.6)	1	2.6	0		
>=100	0			2 (5.7)	2	4.3	0		
Food poisoning									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			2 (5.7)	2	4.3	0		
Gastrointestinal disorder									
<80	0			3 (4.1)	5	4.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			0		
Gastric disorder									
<80	1 (3.2)	1	2.3	2 (2.7)	2	2.0	0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			0		
Barrett's oesophagus									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Gastrointestinal inflammatory conditions									
<80	1 (3.2)	1	2.3	4 (5.5)	4	3.9	1 (4.2)	1	3.0
80-<90	0			5 (7.9)	6	6.9	3 (8.3)	3	6.0
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	1 (5.6)	1	3.9
Enterocolitis									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	0			2 (3.2)	2	2.3	1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Gastritis									
<80	0			2 (2.7)	2	2.0	1 (4.2)	1	3.0
80-<90	0			1 (1.6)	1	1.1	1 (2.8)	1	2.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9
Chronic gastritis									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Colitis									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Enteritis									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Colitis ischaemic									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Benign neoplasms gastrointestinal									
<80	1 (3.2)	1	2.3	2 (2.7)	2	2.0	1 (4.2)	1	3.0
80-<90	1 (2.7)	1	2.0	4 (6.3)	5	5.7	0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			1 (5.6)	1	3.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Large intestine polyp									
<80	0			1 (1.4)	1	1.0	1 (4.2)	1	3.0
80-<90	1 (2.7)	1	2.0	3 (4.8)	3	3.4	0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			1 (5.6)	1	3.9
Gastric polyps									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			2 (3.2)	2	2.3	0		
90-<100	0			0			0		
>=100	0			0			0		
Rectal polyp									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Gastrointestinal haemorrhages NEC									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			1 (2.9)	1	2.1	0		
Anal haemorrhage									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Mallory-Weiss syndrome									
<80	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
80-<90	0				0				0			
90-<100	0				0				0			
>=100	0				1	(2.9)	1	2.1	0			
Oral soft tissue conditions												
<80	0				0				0			
80-<90	0				2	(3.2)	2	2.3	0			
90-<100	0				0				0			
>=100	0				1	(2.9)	1	2.1	0			
Stomatitis												
<80	0				0				0			
80-<90	0				1	(1.6)	1	1.1	0			
90-<100	0				0				0			
>=100	0				1	(2.9)	1	2.1	0			
Angular cheilitis												
<80	0				0				0			
80-<90	0				1	(1.6)	1	1.1	0			
90-<100	0				0				0			
>=100	0				0				0			
Anal and rectal conditions NEC												
<80	0				0				0			
80-<90	1	(2.7)	1	2.0	0				0			
90-<100	0				0				0			
>=100	1	(6.7)	1	4.9	1	(2.9)	1	2.1	0			
Anal fissure												
<80	0				0				0			
80-<90	1	(2.7)	1	2.0	0				0			
90-<100	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	0		
Gastrointestinal ulceration and perforation									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			1 (1.6)	2	2.3	0		
90-<100	0			0			0		
>=100	0			0			0		
Erosive duodenitis									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Gastritis erosive									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Diverticular disorders									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Diverticulum intestinal									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gastrointestinal vascular conditions									
<80	0			1 (1.4)	1	1.0	0		
80-<90	2 (5.4)	2	4.1	0			0		
90-<100	0			0			1 (4.3)	1	3.1
>=100	0			0			0		
Haemorrhoids									
<80	0			1 (1.4)	1	1.0	0		
80-<90	2 (5.4)	2	4.1	0			0		
90-<100	0			0			1 (4.3)	1	3.1
>=100	0			0			0		
Gastrointestinal stenosis and obstruction									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Intestinal obstruction									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Salivary gland conditions									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			0		
Parotid gland enlargement									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			0		
Infections and infestations									
<80	15 (48.4)	20	45.8	34 (46.6)	62	61.0	7 (29.2)	9	27.1
80-<90	14 (37.8)	19	38.8	21 (33.3)	40	45.7	16 (44.4)	26	51.7
90-<100	6 (35.3)	10	42.8	7 (25.0)	11	28.3	8 (34.8)	13	39.7
>=100	7 (46.7)	15	74.0	18 (51.4)	40	85.2	4 (22.2)	5	19.5
Infections - pathogen unspecified									
<80	15 (48.4)	19	43.5	30 (41.1)	55	54.1	7 (29.2)	9	27.1
80-<90	11 (29.7)	16	32.7	19 (30.2)	35	40.0	15 (41.7)	24	47.7
90-<100	6 (35.3)	9	38.6	6 (21.4)	9	23.1	8 (34.8)	13	39.7
>=100	7 (46.7)	14	69.1	16 (45.7)	33	70.3	4 (22.2)	5	19.5
Nasopharyngitis									
<80	9 (29.0)	10	22.9	19 (26.0)	25	24.6	4 (16.7)	5	15.1
80-<90	5 (13.5)	10	20.4	15 (23.8)	24	27.4	7 (19.4)	10	19.9
90-<100	6 (35.3)	6	25.7	5 (17.9)	6	15.4	4 (17.4)	5	15.3
>=100	4 (26.7)	10	49.4	14 (40.0)	26	55.4	3 (16.7)	4	15.6
Gastroenteritis									
<80	2 (6.5)	2	4.6	2 (2.7)	2	2.0	1 (4.2)	1	3.0
80-<90	3 (8.1)	3	6.1	3 (4.8)	5	5.7	0		
90-<100	1 (5.9)	2	8.6	2 (7.1)	2	5.1	0		
>=100	1 (6.7)	1	4.9	4 (11.4)	4	8.5	0		
Bronchitis									
<80	1 (3.2)	1	2.3	4 (5.5)	6	5.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	1 (6.7)	1	4.9	1 (2.9)	2	4.3	0		
Pharyngitis									
<80	2 (6.5)	2	4.6	2 (2.7)	3	3.0	1 (4.2)	1	3.0
80-<90	0			1 (1.6)	1	1.1	2 (5.6)	3	6.0
90-<100	0			0			1 (4.3)	1	3.1
>=100	1 (6.7)	1	4.9	0			0		
Cystitis									
<80	1 (3.2)	1	2.3	3 (4.1)	3	3.0	0		
80-<90	0			0			1 (2.8)	2	4.0
90-<100	0			0			0		
>=100	0			0			0		
Diverticulitis									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Rhinitis									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	0			1 (1.6)	1	1.1	2 (5.6)	2	4.0
90-<100	0			0			0		
>=100	0			0			0		
Tonsillitis									
<80	0			1 (1.4)	1	1.0	0		
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	1 (2.8)	1	2.0
90-<100	0			0			2 (8.7)	3	9.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	0			0			0		
Sinusitis									
<80	0			0			0		
80-<90	0			0			2 (5.6)	2	4.0
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	1 (5.6)	1	3.9
Conjunctivitis									
<80	0			2 (2.7)	3	3.0	1 (4.2)	1	3.0
80-<90	0			0			0		
90-<100	0			0			1 (4.3)	1	3.1
>=100	0			0			0		
Gingivitis									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Pyelonephritis acute									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Acute sinusitis									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Enteritis infectious									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Folliculitis									
<80	0			1 (1.4)	2	2.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Hordeolum									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			1 (4.3)	1	3.1
>=100	0			0			0		
Pelvic inflammatory disease									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Pyelonephritis									
<80	0			1 (1.4)	1	1.0	0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Urethritis									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
>=100	0			0			0		
Urinary tract infection									
<80	0			1	(1.4)	3 3.0	0		
80-<90	1	(2.7)	1 2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Periodontitis									
<80	1	(3.2)	1 2.3	0			1	(4.2)	1 3.0
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Pyoderma									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			1	(4.3)	2 6.1
>=100	0			0			0		
Upper respiratory tract infection									
<80	0			0			0		
80-<90	0			0			2	(5.6)	3 6.0
90-<100	0			0			0		
>=100	0			0			0		
Vaginal infection									
<80	0			0			0		
80-<90	0			0			1	(2.8)	1 2.0
90-<100	0			0			0		
>=100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Viral infectious disorders									
<80	0			4 (5.5)	4	3.9	0		
80-<90	3 (8.1)	3	6.1	4 (6.3)	5	5.7	1 (2.8)	1	2.0
90-<100	1 (5.9)	1	4.3	1 (3.6)	1	2.6	0		
>=100	1 (6.7)	1	4.9	4 (11.4)	4	8.5	0		
Influenza									
<80	0			3 (4.1)	3	3.0	0		
80-<90	1 (2.7)	1	2.0	3 (4.8)	3	3.4	1 (2.8)	1	2.0
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			2 (5.7)	2	4.3	0		
Herpes zoster									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			2 (5.7)	2	4.3	0		
Gastroenteritis viral									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	1 (6.7)	1	4.9	0			0		
Herpes simplex									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Infectious mononucleosis									
<80	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Bacterial infectious disorders									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			2 (5.7)	3	6.4	0		
Furuncle									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Cellulitis									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Erysipelas									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	2	4.3	0		
Alpha haemolytic streptococcal infection									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
>=100	0			0			0		
Helicobacter infection									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Fungal infectious disorders									
<80	0			2 (2.7)	2	2.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Tinea pedis									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Vulvovaginal candidiasis									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Musculoskeletal and connective tissue disorders									
<80	6 (19.4)	7	16.0	16 (21.9)	23	22.6	5 (20.8)	8	24.1
80-<90	10 (27.0)	11	22.5	12 (19.0)	14	16.0	7 (19.4)	11	21.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	3 (17.6)	10	42.8	8 (28.6)	8	20.6	5 (21.7)	7	21.4
>=100	5 (33.3)	6	29.6	7 (20.0)	7	14.9	7 (38.9)	8	31.2
Musculoskeletal and connective tissue disorders NEC									
<80	4 (12.9)	4	9.2	8 (11.0)	9	8.9	3 (12.5)	3	9.0
80-<90	3 (8.1)	3	6.1	7 (11.1)	7	8.0	3 (8.3)	4	8.0
90-<100	3 (17.6)	7	30.0	3 (10.7)	3	7.7	3 (13.0)	4	12.2
>=100	0			4 (11.4)	4	8.5	4 (22.2)	4	15.6
Back pain									
<80	3 (9.7)	3	6.9	7 (9.6)	8	7.9	3 (12.5)	3	9.0
80-<90	2 (5.4)	2	4.1	6 (9.5)	6	6.9	2 (5.6)	3	6.0
90-<100	3 (17.6)	7	30.0	3 (10.7)	3	7.7	2 (8.7)	3	9.2
>=100	0			3 (8.6)	3	6.4	2 (11.1)	2	7.8
Neck pain									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			1 (4.3)	1	3.1
>=100	0			1 (2.9)	1	2.1	0		
Musculoskeletal discomfort									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Pain in extremity									
<80	0			1 (1.4)	1	1.0	0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	0			0			2 (11.1)	2	7.8
Musculoskeletal pain									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Musculoskeletal stiffness									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Joint disorders									
<80	3 (9.7)	3	6.9	6 (8.2)	6	5.9	3 (12.5)	4	12.1
80-<90	6 (16.2)	6	12.3	2 (3.2)	2	2.3	3 (8.3)	6	11.9
90-<100	2 (11.8)	3	12.9	2 (7.1)	2	5.1	2 (8.7)	3	9.2
>=100	4 (26.7)	5	24.7	3 (8.6)	3	6.4	3 (16.7)	3	11.7
Arthralgia									
<80	3 (9.7)	3	6.9	2 (2.7)	2	2.0	2 (8.3)	3	9.0
80-<90	2 (5.4)	2	4.1	1 (1.6)	1	1.1	1 (2.8)	2	4.0
90-<100	2 (11.8)	3	12.9	1 (3.6)	1	2.6	1 (4.3)	2	6.1
>=100	2 (13.3)	2	9.9	1 (2.9)	1	2.1	2 (11.1)	2	7.8
Periarthritis									
<80	0			3 (4.1)	3	3.0	0		
80-<90	1 (2.7)	1	2.0	0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	0		
Osteoarthritis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<80	0			1 (1.4)	1	1.0	1 (4.2)	1	3.0
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			1 (3.6)	1	2.6	1 (4.3)	1	3.1
>=100	1 (6.7)	1	4.9	0			0		
Rotator cuff syndrome									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	0		
Spinal osteoarthritis									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9
Arthritis									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Articular calcification									
<80	0			0			0		
80-<90	0			0			1 (2.8)	2	4.0
90-<100	0			0			0		
>=100	0			0			0		
Muscle disorders									
<80	0			2 (2.7)	2	2.0	0		
80-<90	0			4 (6.3)	4	4.6	1 (2.8)	1	2.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			3 (10.7)	3	7.7	0		
>=100	1 (6.7)	1	4.9	0			0		
Muscle spasms									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			2 (7.1)	2	5.1	0		
>=100	0			0			0		
Myalgia									
<80	0			2 (2.7)	2	2.0	0		
80-<90	0			2 (3.2)	2	2.3	1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	0			0		
Rhabdomyolysis									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Fibromyalgia									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Tendon, ligament and cartilage disorders									
<80	0			3 (4.1)	4	3.9	0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	0			0			0		
Tendonitis									
<80	0			2 (2.7)	2	2.0	0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Trigger finger									
<80	0			1 (1.4)	2	2.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)									
<80	0			1 (1.4)	1	1.0	0		
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9
Intervertebral disc protrusion									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9
Spinal stenosis									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	0			0			0		
Synovial and bursal disorders									
<80	0			1 (1.4)	1	1.0	1 (4.2)	1	3.0
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Bursitis									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Synovitis									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Nervous system disorders									
<80	2 (6.5)	4	9.2	14 (19.2)	19	18.7	1 (4.2)	1	3.0
80-<90	2 (5.4)	2	4.1	13 (20.6)	23	26.3	3 (8.3)	3	6.0
90-<100	3 (17.6)	4	17.1	5 (17.9)	7	18.0	1 (4.3)	1	3.1
>=100	1 (6.7)	1	4.9	3 (8.6)	3	6.4	1 (5.6)	1	3.9
Neurological disorders NEC									
<80	2 (6.5)	4	9.2	10 (13.7)	13	12.8	1 (4.2)	1	3.0
80-<90	2 (5.4)	2	4.1	8 (12.7)	16	18.3	2 (5.6)	2	4.0
90-<100	1 (5.9)	1	4.3	3 (10.7)	3	7.7	0		
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Dizziness									
<80	2 (6.5)	4	9.2	7 (9.6)	9	8.9	0		
80-<90	1 (2.7)	1	2.0	4 (6.3)	7	8.0	0		
90-<100	0			2 (7.1)	2	5.1	0		
>=100	0			1 (2.9)	1	2.1	0		
Hypoaesthesia									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			2 (3.2)	3	3.4	0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	1 (6.7)	1	4.9	0			0		
Taste disorder									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Dizziness postural									
<80	0			0			0		
80-<90	0			1 (1.6)	2	2.3	0		
90-<100	0			0			0		
>=100	0			0			0		
Dysgeusia									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Neuralgia									
<80	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Neurological symptom									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Paraesthesia									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Dysaesthesia									
<80	0			1 (1.4)	2	2.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Somnolence									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Intercostal neuralgia									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=100	0			0			0		
Sensory loss									
<80	0			0			0		
80-<90	0			0			1	(2.8)	1 2.0
90-<100	0			0			0		
>=100	0			0			0		
Headaches									
<80	0			3	(4.1)	3 3.0	0		
80-<90	0			3	(4.8)	4 4.6	1	(2.8)	1 2.0
90-<100	2	(11.8)	2 8.6	3	(10.7)	4 10.3	1	(4.3)	1 3.1
>=100	0			1	(2.9)	1 2.1	1	(5.6)	1 3.9
Headache									
<80	0			3	(4.1)	3 3.0	0		
80-<90	0			3	(4.8)	4 4.6	1	(2.8)	1 2.0
90-<100	2	(11.8)	2 8.6	3	(10.7)	4 10.3	1	(4.3)	1 3.1
>=100	0			1	(2.9)	1 2.1	1	(5.6)	1 3.9
Spinal cord and nerve root disorders									
<80	0			1	(1.4)	1 1.0	0		
80-<90	0			1	(1.6)	1 1.1	0		
90-<100	1	(5.9)	1 4.3	0			0		
>=100	0			1	(2.9)	1 2.1	0		
Sciatica									
<80	0			1	(1.4)	1 1.0	0		
80-<90	0			1	(1.6)	1 1.1	0		
90-<100	1	(5.9)	1 4.3	0			0		
>=100	0			1	(2.9)	1 2.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Cranial nerve disorders (excl neoplasms)												
<80	0				0				0			
80-<90	0				1	(1.6)	1	1.1	0			
90-<100	0				0				0			
>=100	0				0				0			
Parosmia												
<80	0				0				0			
80-<90	0				1	(1.6)	1	1.1	0			
90-<100	0				0				0			
>=100	0				0				0			
Peripheral neuropathies												
<80	0				0				0			
80-<90	0				1	(1.6)	1	1.1	0			
90-<100	0				0				0			
>=100	0				0				0			
Carpal tunnel syndrome												
<80	0				0				0			
80-<90	0				1	(1.6)	1	1.1	0			
90-<100	0				0				0			
>=100	0				0				0			
Central nervous system vascular disorders												
<80	0				1	(1.4)	1	1.0	0			
80-<90	0				0				0			
90-<100	0				0				0			
>=100	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Lacunar infarction									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Neuromuscular disorders									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Autonomic nervous system imbalance									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Injury, poisoning and procedural complications									
<80	7 (22.6)	8	18.3	10 (13.7)	10	9.8	3 (12.5)	3	9.0
80-<90	3 (8.1)	3	6.1	5 (7.9)	5	5.7	4 (11.1)	5	9.9
90-<100	3 (17.6)	3	12.9	6 (21.4)	7	18.0	4 (17.4)	5	15.3
>=100	2 (13.3)	5	24.7	4 (11.4)	4	8.5	1 (5.6)	1	3.9
Injuries NEC									
<80	3 (9.7)	4	9.2	9 (12.3)	9	8.9	2 (8.3)	2	6.0
80-<90	2 (5.4)	2	4.1	3 (4.8)	3	3.4	3 (8.3)	4	8.0
90-<100	0			4 (14.3)	5	12.8	4 (17.4)	4	12.2
>=100	1 (6.7)	4	19.7	1 (2.9)	1	2.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Ligament sprain									
<80	2 (6.5)	3	6.9	0			1 (4.2)	1	3.0
80-<90	0			1 (1.6)	1	1.1	1 (2.8)	1	2.0
90-<100	0			1 (3.6)	1	2.6	0		
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	0		
Contusion									
<80	1 (3.2)	1	2.3	2 (2.7)	2	2.0	0		
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Arthropod sting									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Tendon rupture									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Post-traumatic neck syndrome									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			1 (3.6)	1	2.6	1 (4.3)	1	3.1
>=100	0			0			0		
Arthropod bite									
<80	0			1 (1.4)	1	1.0	1 (4.2)	1	3.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Epicondylitis									
<80	0			1	(1.4)	1 1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Limb injury									
<80	0			1	(1.4)	1 1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Subcutaneous haematoma									
<80	0			1	(1.4)	1 1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Tooth fracture									
<80	0			1	(1.4)	1 1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Limb crushing injury									
<80	0			0			0		
80-<90	1	(2.7)	1 2.0	0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=100	0			0			0		
Muscle contusion									
<80	0			0			0		
80-<90	0			0			1	(2.8)	1 2.0
90-<100	0			0			1	(4.3)	1 3.1
>=100	0			0			0		
Muscle strain									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	1	(6.7)	2 9.9	0			0		
Road traffic accident									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	1	(6.7)	1 4.9	0			0		
Skin laceration									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			1	(4.3)	1 3.1
>=100	0			0			0		
Subdural haematoma									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			1	(4.3)	1 3.1
>=100	0			0			0		
Bone and joint injuries									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<80	2 (6.5)	2	4.6	1 (1.4)	1	1.0	0		
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	1 (6.7)	1	4.9	2 (5.7)	2	4.3	1 (5.6)	1	3.9
Radius fracture									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	1 (5.6)	1	3.9
Rib fracture									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			1 (2.9)	1	2.1	0		
Ankle fracture									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Meniscus injury									
<80	0			1 (1.4)	1	1.0	0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Fracture									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
>=100	0			0			0		
Joint injury									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	0			0		
Medication errors and other product use errors and issues									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	2 (7.1)	2	5.1	0		
>=100	0			0			0		
Accidental overdose									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Product administration error									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	1 (3.6)	1	2.6	0		
>=100	0			0			0		
Injuries by physical agents									
<80	2 (6.5)	2	4.6	0			1 (4.2)	1	3.0
80-<90	0			1 (1.6)	1	1.1	1 (2.8)	1	2.0
90-<100	1 (5.9)	1	4.3	0			1 (4.3)	1	3.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	0			1 (2.9)	1	2.1	0		
Heat stroke									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			1 (2.9)	1	2.1	0		
Thermal burn									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			1 (4.3)	1	3.1
>=100	0			0			0		
Heat illness									
<80	1 (3.2)	1	2.3	0			1 (4.2)	1	3.0
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Respiratory, thoracic and mediastinal disorders									
<80	4 (12.9)	6	13.7	10 (13.7)	13	12.8	4 (16.7)	4	12.1
80-<90	3 (8.1)	4	8.2	7 (11.1)	7	8.0	5 (13.9)	7	13.9
90-<100	1 (5.9)	1	4.3	4 (14.3)	4	10.3	4 (17.4)	8	24.4
>=100	2 (13.3)	2	9.9	3 (8.6)	3	6.4	0		
Respiratory tract signs and symptoms									
<80	2 (6.5)	3	6.9	8 (11.0)	10	9.8	3 (12.5)	3	9.0
80-<90	3 (8.1)	3	6.1	4 (6.3)	4	4.6	4 (11.1)	5	9.9
90-<100	0			3 (10.7)	3	7.7	4 (17.4)	7	21.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	1 (6.7)	1	4.9	0			0		
Upper respiratory tract inflammation									
<80	2 (6.5)	3	6.9	6 (8.2)	8	7.9	2 (8.3)	2	6.0
80-<90	2 (5.4)	2	4.1	2 (3.2)	2	2.3	3 (8.3)	4	8.0
90-<100	0			3 (10.7)	3	7.7	4 (17.4)	7	21.4
>=100	1 (6.7)	1	4.9	0			0		
Oropharyngeal pain									
<80	0			2 (2.7)	2	2.0	1 (4.2)	1	3.0
80-<90	1 (2.7)	1	2.0	0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Hiccups									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Rhinorrhoea									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Upper respiratory tract disorders (excl infections)									
<80	2 (6.5)	2	4.6	2 (2.7)	2	2.0	0		
80-<90	0			3 (4.8)	3	3.4	1 (2.8)	2	4.0
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			1 (2.9)	1	2.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Rhinitis allergic									
<80	1 (3.2)	1	2.3	2 (2.7)	2	2.0	0		
80-<90	0			3 (4.8)	3	3.4	1 (2.8)	2	4.0
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Epistaxis									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Vasomotor rhinitis									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Respiratory disorders NEC									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	1 (4.2)	1	3.0
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Cough									
<80	1 (3.2)	1	2.3	0			1 (4.2)	1	3.0
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Dyspnoea									
<80	0			1 (1.4)	1	1.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Bronchial disorders (excl neoplasms)									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	1 (5.9)	1	4.3	0			1 (4.3)	1	3.1
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	0		
Asthma									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			1 (2.9)	1	2.1	0		
Cough variant asthma									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			1 (4.3)	1	3.1
>=100	1 (6.7)	1	4.9	0			0		
Metabolism and nutrition disorders									
<80	1 (3.2)	1	2.3	4 (5.5)	5	4.9	2 (8.3)	3	9.0
80-<90	2 (5.4)	2	4.1	11 (17.5)	11	12.6	2 (5.6)	2	4.0
90-<100	3 (17.6)	3	12.9	2 (7.1)	2	5.1	3 (13.0)	5	15.3
>=100	0			6 (17.1)	6	12.8	1 (5.6)	1	3.9
Appetite and general nutritional disorders									
<80	1 (3.2)	1	2.3	2 (2.7)	2	2.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	2 (5.4)	2	4.1	6 (9.5)	6	6.9	0		
90-<100	2 (11.8)	2	8.6	1 (3.6)	1	2.6	0		
>=100	0			4 (11.4)	4	8.5	0		
Decreased appetite									
<80	1 (3.2)	1	2.3	2 (2.7)	2	2.0	0		
80-<90	2 (5.4)	2	4.1	6 (9.5)	6	6.9	0		
90-<100	2 (11.8)	2	8.6	1 (3.6)	1	2.6	0		
>=100	0			4 (11.4)	4	8.5	0		
Purine and pyrimidine metabolism disorders									
<80	0			0			0		
80-<90	0			2 (3.2)	2	2.3	1 (2.8)	1	2.0
90-<100	1 (5.9)	1	4.3	1 (3.6)	1	2.6	3 (13.0)	4	12.2
>=100	0			1 (2.9)	1	2.1	0		
Gout									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	1 (5.9)	1	4.3	1 (3.6)	1	2.6	1 (4.3)	2	6.1
>=100	0			0			0		
Hyperuricaemia									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	1 (2.8)	1	2.0
90-<100	0			0			2 (8.7)	2	6.1
>=100	0			1 (2.9)	1	2.1	0		
Lipid metabolism disorders									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			1 (4.3)	1	3.1
>=100	0			1 (2.9)	1	2.1	1 (5.6)	1	3.9
Dyslipidaemia									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			1 (4.3)	1	3.1
>=100	0			1 (2.9)	1	2.1	1 (5.6)	1	3.9
Glucose metabolism disorders (incl diabetes mellitus)									
<80	0			2 (2.7)	3	3.0	2 (8.3)	3	9.0
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Diabetes mellitus									
<80	0			1 (1.4)	1	1.0	1 (4.2)	1	3.0
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Type 2 diabetes mellitus									
<80	0			1 (1.4)	2	2.0	0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Glucose tolerance impaired									
<80	0			0			1 (4.2)	2	6.0
80-<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	0			0			0		
Electrolyte and fluid balance conditions									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Dehydration									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Metabolism disorders NEC									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Hypercreatininaemia									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Skin and subcutaneous tissue disorders									
<80	4 (12.9)	8	18.3	12 (16.4)	15	14.8	3 (12.5)	3	9.0
80-<90	5 (13.5)	8	16.3	4 (6.3)	5	5.7	4 (11.1)	5	9.9
90-<100	2 (11.8)	2	8.6	2 (7.1)	2	5.1	2 (8.7)	2	6.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	2 (13.3)	4	19.7	6 (17.1)	8	17.0	2 (11.1)	4	15.6
Epidermal and dermal conditions									
<80	3 (9.7)	5	11.5	9 (12.3)	9	8.9	3 (12.5)	3	9.0
80-<90	4 (10.8)	5	10.2	2 (3.2)	3	3.4	2 (5.6)	3	6.0
90-<100	2 (11.8)	2	8.6	1 (3.6)	1	2.6	1 (4.3)	1	3.1
>=100	1 (6.7)	1	4.9	5 (14.3)	6	12.8	2 (11.1)	3	11.7
Pruritus									
<80	0			2 (2.7)	2	2.0	1 (4.2)	1	3.0
80-<90	0			0			1 (2.8)	2	4.0
90-<100	0			1 (3.6)	1	2.6	0		
>=100	1 (6.7)	1	4.9	0			0		
Eczema									
<80	2 (6.5)	2	4.6	3 (4.1)	3	3.0	1 (4.2)	1	3.0
80-<90	2 (5.4)	2	4.1	1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9
Dermatitis									
<80	0			0			0		
80-<90	0			1 (1.6)	2	2.3	0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Dermatitis atopic									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	2	4.3	0		
Dyshidrotic eczema									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Rash									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Stasis dermatitis									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Eczema asteatotic									
<80	0			2 (2.7)	2	2.0	0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Dermatitis contact									
<80	0			1 (1.4)	1	1.0	1 (4.2)	1	3.0
80-<90	0			0			1 (2.8)	1	2.0
90-<100	1 (5.9)	1	4.3	0			1 (4.3)	1	3.1
>=100	0			0			0		
Erythema									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			1 (5.6)	1	3.9
Drug eruption									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Dry skin									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Pain of skin									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Rash pruritic									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Seborrhoeic dermatitis									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Xanthelasma									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Skin appendage conditions									
<80	1 (3.2)	1	2.3	3 (4.1)	3	3.0	0		
80-<90	2 (5.4)	2	4.1	2 (3.2)	2	2.3	1 (2.8)	1	2.0
90-<100	0			1 (3.6)	1	2.6	0		
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	1 (5.6)	1	3.9
Alopecia									
<80	1 (3.2)	1	2.3	0			0		
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Alopecia areata									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Ingrowing nail									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Acne									
<80	0			1 (1.4)	1	1.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Miliaria									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	0			1 (5.6)	1	3.9
Cornification and dystrophic skin disorders									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	0		
Hyperkeratosis									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	0		
Xeroderma									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Angioedema and urticaria									
<80	1 (3.2)	2	4.6	2 (2.7)	2	2.0	0		
80-<90	1 (2.7)	1	2.0	0			1 (2.8)	1	2.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			1 (4.3)	1	3.1
>=100	1 (6.7)	1	4.9	0			0		
Urticaria									
<80	1 (3.2)	2	4.6	2 (2.7)	2	2.0	0		
80-<90	1 (2.7)	1	2.0	0			1 (2.8)	1	2.0
90-<100	0			0			1 (4.3)	1	3.1
>=100	1 (6.7)	1	4.9	0			0		
Eye disorders									
<80	2 (6.5)	2	4.6	7 (9.6)	7	6.9	3 (12.5)	3	9.0
80-<90	1 (2.7)	2	4.1	6 (9.5)	7	8.0	3 (8.3)	4	8.0
90-<100	3 (17.6)	3	12.9	2 (7.1)	3	7.7	1 (4.3)	1	3.1
>=100	0			2 (5.7)	2	4.3	0		
Retina, choroid and vitreous haemorrhages and vascular disorders									
<80	0			1 (1.4)	1	1.0	1 (4.2)	1	3.0
80-<90	1 (2.7)	2	4.1	3 (4.8)	3	3.4	1 (2.8)	1	2.0
90-<100	1 (5.9)	1	4.3	1 (3.6)	1	2.6	0		
>=100	0			0			0		
Diabetic retinopathy									
<80	0			0			1 (4.2)	1	3.0
80-<90	1 (2.7)	2	4.1	3 (4.8)	3	3.4	1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Retinal exudates									
<80	0			0			0		
80-<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Retinal haemorrhage									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Retinopathy									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			0		
Vision disorders									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			2 (5.7)	2	4.3	0		
Optic nerve disorder									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Presbyopia									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Amblyopia									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Visual acuity reduced									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Anterior eye structural change, deposit and degeneration									
<80	0			3 (4.1)	3	3.0	0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Cataract									
<80	0			3 (4.1)	3	3.0	0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Eye disorders NEC									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	1 (3.6)	2	5.1	0		
>=100	0			0			0		
Lacrimal disorder									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Lacrimation increased									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Dry eye									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			0		
Ocular infections, irritations and inflammations									
<80	0			1 (1.4)	1	1.0	1 (4.2)	1	3.0
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			0		
Ocular hyperaemia									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Conjunctivitis allergic									
<80	0			1 (1.4)	1	1.0	1 (4.2)	1	3.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
80-<90	0				0				0			
90-<100	1	(5.9)	1	4.3	0				0			
>=100	0				0				0			
Glaucoma and ocular hypertension												
<80	0				0				0			
80-<90	0				1	(1.6)	1	1.1	0			
90-<100	0				0				1	(4.3)	1	3.1
>=100	0				0				0			
Glaucoma												
<80	0				0				0			
80-<90	0				1	(1.6)	1	1.1	0			
90-<100	0				0				0			
>=100	0				0				0			
Open angle glaucoma												
<80	0				0				0			
80-<90	0				0				0			
90-<100	0				0				1	(4.3)	1	3.1
>=100	0				0				0			
Ocular haemorrhages and vascular disorders NEC												
<80	0				0				0			
80-<90	0				1	(1.6)	1	1.1	1	(2.8)	1	2.0
90-<100	0				0				0			
>=100	0				0				0			
Optic disc haemorrhage												
<80	0				0				0			
80-<90	0				1	(1.6)	1	1.1	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
>=100	0			0			0		
Conjunctival haemorrhage									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Ocular structural change, deposit and degeneration NEC									
<80	2 (6.5)	2	4.6	1 (1.4)	1	1.0	0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Retinal tear									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Macular fibrosis									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Rhegmatogenous retinal detachment									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	0			0			0		
General disorders and administration site conditions									
<80	1 (3.2)	3	6.9	4 (5.5)	16	15.7	0		
80-<90	1 (2.7)	1	2.0	7 (11.1)	11	12.6	1 (2.8)	1	2.0
90-<100	1 (5.9)	1	4.3	1 (3.6)	1	2.6	1 (4.3)	1	3.1
>=100	0			4 (11.4)	7	14.9	0		
General system disorders NEC									
<80	1 (3.2)	3	6.9	3 (4.1)	4	3.9	0		
80-<90	1 (2.7)	1	2.0	5 (7.9)	9	10.3	1 (2.8)	1	2.0
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			2 (5.7)	4	8.5	0		
Malaise									
<80	0			1 (1.4)	2	2.0	0		
80-<90	1 (2.7)	1	2.0	3 (4.8)	5	5.7	0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Fatigue									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			1 (2.9)	1	2.1	0		
Feeling abnormal									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
>=100	0			1	(2.9)	1	2.1	0			
Thirst											
<80	0			0				0			
80-<90	0			0				0			
90-<100	0			0				0			
>=100	0			1	(2.9)	1	2.1	0			
Oedema peripheral											
<80	0			0				0			
80-<90	0			1	(1.6)	1	1.1	0			
90-<100	0			0				0			
>=100	0			0				0			
Pain											
<80	0			0				0			
80-<90	0			1	(1.6)	1	1.1	0			
90-<100	0			0				0			
>=100	0			0				0			
Influenza like illness											
<80	0			1	(1.4)	1	1.0	0			
80-<90	0			0				0			
90-<100	0			0				0			
>=100	0			0				0			
Non-cardiac chest pain											
<80	0			1	(1.4)	1	1.0	0			
80-<90	0			0				0			
90-<100	0			0				0			
>=100	0			0				0			
Hangover											

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<80	1 (3.2)	3	6.9	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Hunger									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Administration site reactions									
<80	0			1 (1.4)	12	11.8	0		
80-<90	0			2 (3.2)	2	2.3	0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Injection site erythema									
<80	0			1 (1.4)	12	11.8	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Injection site dermatitis									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Injection site discomfort									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			0			0		
>=100	0			0			0		
Body temperature conditions									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			1 (4.3)	1	3.1
>=100	0			2 (5.7)	2	4.3	0		
Pyrexia									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			1 (4.3)	1	3.1
>=100	0			2 (5.7)	2	4.3	0		
Investigations									
<80	5 (16.1)	7	16.0	8 (11.0)	9	8.9	1 (4.2)	2	6.0
80-<90	6 (16.2)	7	14.3	4 (6.3)	6	6.9	6 (16.7)	7	13.9
90-<100	1 (5.9)	1	4.3	2 (7.1)	3	7.7	0		
>=100	1 (6.7)	1	4.9	2 (5.7)	2	4.3	2 (11.1)	2	7.8
Enzyme investigations NEC									
<80	1 (3.2)	1	2.3	3 (4.1)	4	3.9	0		
80-<90	2 (5.4)	2	4.1	1 (1.6)	1	1.1	2 (5.6)	2	4.0
90-<100	1 (5.9)	1	4.3	1 (3.6)	1	2.6	0		
>=100	0			1 (2.9)	1	2.1	0		
Blood creatine phosphokinase increased									
<80	1 (3.2)	1	2.3	3 (4.1)	4	3.9	0		
80-<90	2 (5.4)	2	4.1	1 (1.6)	1	1.1	2 (5.6)	2	4.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	1 (5.9)	1	4.3	1 (3.6)	1	2.6	0		
>=100	0			1 (2.9)	1	2.1	0		
Gastrointestinal investigations									
<80	1 (3.2)	1	2.3	2 (2.7)	2	2.0	0		
80-<90	3 (8.1)	3	6.1	1 (1.6)	2	2.3	0		
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	0		
Lipase increased									
<80	0			2 (2.7)	2	2.0	0		
80-<90	2 (5.4)	2	4.1	1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	0		
Amylase increased									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Occult blood positive									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Cardiac and vascular investigations (excl enzyme tests)									
<80	0			1 (1.4)	1	1.0	0		
80-<90	2 (5.4)	2	4.1	1 (1.6)	1	1.1	0		
90-<100	0			1 (3.6)	1	2.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	0			0			0		
Blood pressure decreased									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Electrocardiogram QRS complex prolonged									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Electrocardiogram QT prolonged									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Hepatobiliary investigations									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			1 (1.6)	1	1.1	3 (8.3)	3	6.0
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			1 (5.6)	1	3.9
Aspartate aminotransferase increased									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Liver function test increased									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			1 (1.6)	1	1.1	1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Alanine aminotransferase increased									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9
Blood bilirubin increased									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Haematology investigations (incl blood groups)									
<80	1 (3.2)	2	4.6	0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Haemoglobin decreased									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Lymphocyte count decreased									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
White blood cell count increased									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Endocrine investigations (incl sex hormones)									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Blood thyroid stimulating hormone decreased									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Physical examination and organ system status topics									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Weight decreased									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Lipid analyses									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Blood triglycerides increased									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Metabolic, nutritional and blood gas investigations									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Blood uric acid increased									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Glycosylated haemoglobin increased									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Protein and chemistry analyses NEC									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9
C-reactive protein increased									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9
Water, electrolyte and mineral investigations									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Blood potassium increased									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Vascular disorders									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<80	1 (3.2)	1	2.3	6 (8.2)	6	5.9	0		
80-<90	0			2 (3.2)	2	2.3	0		
90-<100	1 (5.9)	1	4.3	2 (7.1)	2	5.1	4 (17.4)	4	12.2
>=100	0			1 (2.9)	1	2.1	0		
Decreased and nonspecific blood pressure disorders and shock									
<80	0			2 (2.7)	2	2.0	0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			2 (7.1)	2	5.1	0		
>=100	0			0			0		
Orthostatic hypotension									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			2 (7.1)	2	5.1	0		
>=100	0			0			0		
Hypotension									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Vascular hypertensive disorders									
<80	0			3 (4.1)	3	3.0	0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			3 (13.0)	3	9.2
>=100	0			1 (2.9)	1	2.1	0		
Hypertension									
<80	0			3 (4.1)	3	3.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			3 (13.0)	3	9.2
>=100	0			1 (2.9)	1	2.1	0		
Arteriosclerosis, stenosis, vascular insufficiency and necrosis									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			1 (4.3)	1	3.1
>=100	0			0			0		
Arteriosclerosis									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			1 (4.3)	1	3.1
>=100	0			0			0		
Embolism and thrombosis									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Venous thrombosis limb									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Reproductive system and breast disorders									
<80	1 (3.2)	1	2.3	3 (4.1)	3	3.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	2 (5.4)	3	6.1	4 (6.3)	5	5.7	0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			1 (2.9)	1	2.1	0		
Menstrual cycle and uterine bleeding disorders									
<80	0			2 (2.7)	2	2.0	0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Dysmenorrhoea									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Menstrual disorder									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Menstruation irregular									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Prostatic disorders (excl infections and inflammations)									
<80	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Benign prostatic hyperplasia									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	1 (1.6)	1	1.1	0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Male reproductive tract infections and inflammations									
<80	0			0			0		
80-<90	0			1 (1.6)	2	2.3	0		
90-<100	0			0			0		
>=100	0			0			0		
Prostatitis									
<80	0			0			0		
80-<90	0			1 (1.6)	2	2.3	0		
90-<100	0			0			0		
>=100	0			0			0		
Menopause related conditions									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Menopausal symptoms									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
90-<100	0				0				0			
>=100	0				0				0			
Breast disorders												
<80	0				1	(1.4)	1	1.0	0			
80-<90	0				0				0			
90-<100	0				0				0			
>=100	0				0				0			
Breast calcifications												
<80	0				1	(1.4)	1	1.0	0			
80-<90	0				0				0			
90-<100	0				0				0			
>=100	0				0				0			
Uterine, pelvic and broad ligament disorders												
<80	1	(3.2)	1	2.3	0				0			
80-<90	1	(2.7)	2	4.1	0				0			
90-<100	0				0				0			
>=100	0				0				0			
Endometrial hyperplasia												
<80	0				0				0			
80-<90	1	(2.7)	1	2.0	0				0			
90-<100	0				0				0			
>=100	0				0				0			
Endometriosis												
<80	0				0				0			
80-<90	1	(2.7)	1	2.0	0				0			
90-<100	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	0			0			0		
Uterine haemorrhage									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Renal and urinary disorders									
<80	1 (3.2)	1	2.3	2 (2.7)	2	2.0	0		
80-<90	2 (5.4)	2	4.1	1 (1.6)	1	1.1	4 (11.1)	6	11.9
90-<100	1 (5.9)	2	8.6	1 (3.6)	1	2.6	1 (4.3)	1	3.1
>=100	1 (6.7)	1	4.9	1 (2.9)	1	2.1	0		
Renal disorders (excl nephropathies)									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	1 (4.3)	1	3.1
>=100	0			0			0		
Azotaemia									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Renal cyst									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			1 (4.3)	1	3.1
>=100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Urolithiases									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	2 (5.4)	2	4.1	1 (1.6)	1	1.1	3 (8.3)	5	9.9
90-<100	0			0			0		
>=100	0			0			0		
Ureterolithiasis									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	0			1 (1.6)	1	1.1	2 (5.6)	4	8.0
90-<100	0			0			0		
>=100	0			0			0		
Calculus urinary									
<80	0			0			0		
80-<90	2 (5.4)	2	4.1	0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Urinary tract signs and symptoms									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	2	8.6	0			0		
>=100	0			1 (2.9)	1	2.1	0		
Hyperuricosuria									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Nocturia									
<80	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			0		
Proteinuria									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			0		
Nephropathies									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	0			0		
Diabetic nephropathy									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Nephropathy toxic									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	1 (6.7)	1	4.9	0			0		
Cardiac disorders									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	1 (4.2)	1	3.0
80-<90	0			1 (1.6)	1	1.1	1 (2.8)	1	2.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	1 (5.9)	1	4.3	1 (3.6)	1	2.6	0		
>=100	0			1 (2.9)	1	2.1	1 (5.6)	1	3.9
Cardiac arrhythmias									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			1 (1.6)	1	1.1	1 (2.8)	1	2.0
90-<100	1 (5.9)	1	4.3	1 (3.6)	1	2.6	0		
>=100	0			0			0		
Ventricular extrasystoles									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	1 (3.6)	1	2.6	0		
>=100	0			0			0		
Tachycardia									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Arrhythmia									
<80	0			0			1 (4.2)	1	3.0
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Atrial fibrillation									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Coronary artery disorders									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Acute myocardial infarction									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Cardiac disorders, signs and symptoms NEC									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9
Palpitations									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9
Psychiatric disorders									
<80	0			2 (2.7)	2	2.0	0		
80-<90	2 (5.4)	2	4.1	4 (6.3)	4	4.6	1 (2.8)	1	2.0
90-<100	1 (5.9)	1	4.3	0			0		
>=100	1 (6.7)	1	4.9	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Sleep disorders and disturbances									
<80	0			1 (1.4)	1	1.0	0		
80-<90	1 (2.7)	1	2.0	3 (4.8)	3	3.4	0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	1 (6.7)	1	4.9	0			0		
Insomnia									
<80	0			1 (1.4)	1	1.0	0		
80-<90	1 (2.7)	1	2.0	3 (4.8)	3	3.4	0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	1 (6.7)	1	4.9	0			0		
Mood disorders and disturbances NEC									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Emotional disorder									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Listless									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Depressed mood disorders and disturbances									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<80	0			1	(1.4)	1 1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Depression									
<80	0			1	(1.4)	1 1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Adjustment disorders (incl subtypes)									
<80	0			0			0		
80-<90	1	(2.7)	1 2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Adjustment disorder									
<80	0			0			0		
80-<90	1	(2.7)	1 2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Hepatobiliary disorders									
<80	1	(3.2)	1 2.3	1	(1.4)	1 1.0	0		
80-<90	1	(2.7)	1 2.0	3	(4.8)	3 3.4	0		
90-<100	0			0			0		
>=100	0			1	(2.9)	1 2.1	1	(5.6)	1 3.9
Gallbladder disorders									
<80	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
80-<90	1 (2.7)	1	2.0	2 (3.2)	2	2.3	0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Cholelithiasis									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			1 (2.9)	1	2.1	0		
Gallbladder polyp									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Hyperplastic cholecystopathy									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Hepatic and hepatobiliary disorders									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			1 (5.6)	1	3.9
Hepatic cyst									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=100	0			0			0		
Hepatic function abnormal									
<80	0			1	(1.4)	1 1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Alcoholic liver disease									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			1	(5.6)	1 3.9
Hepatic steatosis									
<80	1	(3.2)	1 2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Congenital, familial and genetic disorders									
<80	0			1	(1.4)	1 1.0	0		
80-<90	0			0			0		
90-<100	0			1	(3.6)	1 2.6	0		
>=100	0			0			0		
Skin and subcutaneous tissue disorders congenital									
<80	0			0			0		
80-<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Birth mark									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Gastrointestinal tract disorders congenital									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Diverticulitis Meckel's									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Ear and labyrinth disorders									
<80	3 (9.7)	3	6.9	1 (1.4)	1	1.0	0		
80-<90	0			2 (3.2)	2	2.3	1 (2.8)	1	2.0
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			0		
Hearing disorders									
<80	0			0			0		
80-<90	0			2 (3.2)	2	2.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
>=100	0			0			0		
Deafness									
<80	0			0			0		
80-<90	0			1	(1.6)	1 1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Deafness neurosensory									
<80	0			0			0		
80-<90	0			1	(1.6)	1 1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Inner ear and VIIIth cranial nerve disorders									
<80	3	(9.7)	3 6.9	1	(1.4)	1 1.0	0		
80-<90	0			0			1	(2.8)	1 2.0
90-<100	1	(5.9)	1 4.3	0			0		
>=100	0			0			0		
Vertigo									
<80	2	(6.5)	2 4.6	1	(1.4)	1 1.0	0		
80-<90	0			0			1	(2.8)	1 2.0
90-<100	1	(5.9)	1 4.3	0			0		
>=100	0			0			0		
Tinnitus									
<80	1	(3.2)	1 2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	0			0			0		
Immune system disorders									
<80	0			0			0		
80-<90	2 (5.4)	2	4.1	0			1 (2.8)	1	2.0
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Allergic conditions									
<80	0			0			0		
80-<90	2 (5.4)	2	4.1	0			1 (2.8)	1	2.0
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Seasonal allergy									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	0			1 (2.8)	1	2.0
90-<100	0			1 (3.6)	1	2.6	0		
>=100	0			0			0		
Food allergy									
<80	0			0			0		
80-<90	1 (2.7)	1	2.0	0			0		
90-<100	0			0			0		
>=100	0			0			0		
Blood and lymphatic system disorders									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			2 (3.2)	2	2.3	1 (2.8)	1	2.0
90-<100	1 (5.9)	1	4.3	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	0			0			0		
Anaemias nonhaemolytic and marrow depression									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			2 (3.2)	2	2.3	1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Iron deficiency anaemia									
<80	1 (3.2)	1	2.3	0			0		
80-<90	0			2 (3.2)	2	2.3	0		
90-<100	0			0			0		
>=100	0			0			0		
Anaemia									
<80	0			0			0		
80-<90	0			0			1 (2.8)	1	2.0
90-<100	0			0			0		
>=100	0			0			0		
Spleen, lymphatic and reticuloendothelial system disorders									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			0		
Lymphadenitis									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1 (5.9)	1	4.3	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=100	0			0			0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)									
<80	1 (3.2)	1	2.3	1 (1.4)	1	1.0	1 (4.2)	1	3.0
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	1 (5.9)	1	4.3	0			0		
>=100	0			0			0		
Reproductive neoplasms female benign									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Uterine leiomyoma									
<80	0			0			0		
80-<90	0			1 (1.6)	1	1.1	0		
90-<100	0			0			0		
>=100	0			0			0		
Gastrointestinal neoplasms benign									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Intraductal papillary mucinous neoplasm									
<80	0			1 (1.4)	1	1.0	0		
80-<90	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
90-<100	0			0			0		
>=100	0			0			0		
Hepatobiliary neoplasms malignant and unspecified									
<80	1	(3.2)	1 2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Bile duct adenocarcinoma									
<80	1	(3.2)	1 2.3	0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Renal and urinary tract neoplasms malignant and unspecified									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1	(5.9)	1 4.3	0			0		
>=100	0			0			0		
Clear cell renal cell carcinoma									
<80	0			0			0		
80-<90	0			0			0		
90-<100	1	(5.9)	1 4.3	0			0		
>=100	0			0			0		
Respiratory and mediastinal neoplasms malignant and unspecified									
<80	0			0			1	(4.2)	1 3.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Lung neoplasm malignant									
<80	0			0			1	(4.2)	1 3.0
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			0			0		
Surgical and medical procedures									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1	(2.9)	1 2.1	0		
Gastrointestinal therapeutic procedures									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1	(2.9)	1 2.1	0		
Large intestinal polypectomy									
<80	0			0			0		
80-<90	0			0			0		
90-<100	0			0			0		
>=100	0			1	(2.9)	1 2.1	0		
Endocrine disorders									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

Adverse events by body weight at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 6

	Sema 1.7 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
<80	0				1	(1.4)	1	1.0	0			
80-<90	0				0				0			
90-<100	0				0				0			
>=100	0				0				0			
Thyroid gland disorders												
<80	0				1	(1.4)	1	1.0	0			
80-<90	0				0				0			
90-<100	0				0				0			
>=100	0				0				0			
Hyperthyroidism												
<80	0				1	(1.4)	1	1.0	0			
80-<90	0				0				0			
90-<100	0				0				0			
>=100	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 23.1

19 Adverse events by BMI at baseline - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE		
<30	81	106.8			36	47.8		
30-<35	436	576.9			207	269.8		
35-<40	406	525.5			208	257.0		
>=40	383	496.9			204	255.0		
Subjects with events	N	(%)	E	R	N	(%)	E	R
Events								
<30	70	(86.4)	439	410.9	30	(83.3)	124	259.3
30-<35	392	(89.9)	3079	533.7	170	(82.1)	1001	371.1
35-<40	372	(91.6)	3087	587.4	187	(89.9)	1073	417.5
>=40	337	(88.0)	3053	614.4	179	(87.7)	1104	433.0
Serious								
Yes								
<30	6	(7.4)	8	7.5	1	(2.8)	1	2.1
30-<35	41	(9.4)	50	8.7	11	(5.3)	14	5.2
35-<40	37	(9.1)	50	9.5	16	(7.7)	18	7.0
>=40	44	(11.5)	56	11.3	14	(6.9)	20	7.8
No								
<30	70	(86.4)	431	403.4	30	(83.3)	123	257.2
30-<35	392	(89.9)	3029	525.1	170	(82.1)	987	365.9
35-<40	370	(91.1)	3037	577.9	183	(88.0)	1055	410.5
>=40	337	(88.0)	2997	603.2	177	(86.8)	1084	425.2

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by BMI at baseline - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Severity								
Severe								
<30	3	(3.7)	13	12.2	3	(8.3)	3	6.3
30-<35	43	(9.9)	67	11.6	9	(4.3)	10	3.7
35-<40	43	(10.6)	77	14.7	18	(8.7)	24	9.3
>=40	54	(14.1)	85	17.1	14	(6.9)	31	12.2
Moderate								
<30	31	(38.3)	98	91.7	14	(38.9)	37	77.4
30-<35	248	(56.9)	850	147.3	86	(41.5)	233	86.4
35-<40	223	(54.9)	775	147.5	114	(54.8)	332	129.2
>=40	221	(57.7)	889	178.9	97	(47.5)	261	102.4
Mild								
<30	66	(81.5)	328	307.0	28	(77.8)	84	175.6
30-<35	356	(81.7)	2162	374.8	156	(75.4)	758	281.0
35-<40	344	(84.7)	2235	425.3	159	(76.4)	717	279.0
>=40	313	(81.7)	2079	418.4	164	(80.4)	812	318.5
Relationship to trial product								
Missing								
<30	2	(2.5)	2	1.9	0			
30-<35	2	(0.5)	2	0.3	2	(1.0)	3	1.1
35-<40	8	(2.0)	14	2.7	1	(0.5)	1	0.4
>=40	12	(3.1)	12	2.4	4	(2.0)	4	1.6
Probable								
<30	29	(35.8)	89	83.3	5	(13.9)	11	23.0
30-<35	189	(43.3)	593	102.8	46	(22.2)	118	43.7
35-<40	186	(45.8)	753	143.3	48	(23.1)	107	41.6
>=40	167	(43.6)	713	143.5	48	(23.5)	94	36.9

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by BMI at baseline - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Relationship to trial product								
Possible								
<30	36	(44.4)	122	114.2	9	(25.0)	15	31.4
30-<35	252	(57.8)	937	162.4	67	(32.4)	155	57.5
35-<40	218	(53.7)	819	155.9	83	(39.9)	216	84.0
>=40	220	(57.4)	822	165.4	64	(31.4)	169	66.3
Unlikely								
<30	64	(79.0)	226	211.5	25	(69.4)	98	204.9
30-<35	337	(77.3)	1547	268.2	162	(78.3)	725	268.7
35-<40	331	(81.5)	1501	285.6	176	(84.6)	749	291.4
>=40	300	(78.3)	1506	303.1	173	(84.8)	837	328.3
Outcome								
Fatal								
<30	0				0			
30-<35	0				0			
35-<40	0				1	(0.5)	1	0.4
>=40	0				0			
Recovered								
<30	67	(82.7)	396	370.7	29	(80.6)	107	223.7
30-<35	383	(87.8)	2695	467.2	165	(79.7)	838	310.6
35-<40	361	(88.9)	2696	513.0	177	(85.1)	866	337.0
>=40	329	(85.9)	2652	533.7	174	(85.3)	899	352.6
Recovering								
<30	6	(7.4)	6	5.6	0			
30-<35	19	(4.4)	28	4.9	12	(5.8)	18	6.7
35-<40	15	(3.7)	32	6.1	6	(2.9)	11	4.3
>=40	19	(5.0)	25	5.0	7	(3.4)	8	3.1

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by BMI at baseline - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Outcome								
Recovered With Sequelae								
<30	0				1	(2.8)	1	2.1
30-<35	3	(0.7)	6	1.0	1	(0.5)	1	0.4
35-<40	4	(1.0)	4	0.8	1	(0.5)	2	0.8
>=40	4	(1.0)	9	1.8	1	(0.5)	1	0.4
Not Recovered								
<30	22	(27.2)	37	34.6	12	(33.3)	16	33.5
30-<35	167	(38.3)	348	60.3	79	(38.2)	144	53.4
35-<40	162	(39.9)	355	67.6	92	(44.2)	192	74.7
>=40	162	(42.3)	366	73.7	82	(40.2)	196	76.9
Unknown								
<30	0				0			
30-<35	1	(0.2)	2	0.3	0			
35-<40	0				1	(0.5)	1	0.4
>=40	1	(0.3)	1	0.2	0			
Leading to								
Permanent treatment discontinuation								
<30	9	(11.1)	11	10.3	1	(2.8)	1	2.1
30-<35	31	(7.1)	39	6.8	6	(2.9)	8	3.0
35-<40	29	(7.1)	40	7.6	6	(2.9)	7	2.7
>=40	23	(6.0)	33	6.6	7	(3.4)	7	2.7
Temporary interruption of trial product								
<30	11	(13.6)	21	19.7	0			
30-<35	39	(8.9)	77	13.3	8	(3.9)	12	4.4
35-<40	41	(10.1)	101	19.2	11	(5.3)	21	8.2
>=40	35	(9.1)	66	13.3	7	(3.4)	11	4.3

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by BMI at baseline - overview - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Leading to								
Dose reduction of trial product								
<30	12	(14.8)	21	19.7	0			
30-<35	53	(12.2)	94	16.3	2	(1.0)	3	1.1
35-<40	34	(8.4)	71	13.5	2	(1.0)	6	2.3
>=40	25	(6.5)	39	7.8	0			

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

20 Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects and exposure	N		PYE		N		PYE	
<30	81		106.8		36		47.8	
30-<35	436		576.9		207		269.8	
35-<40	406		525.5		208		257.0	
>=40	383		496.9		204		255.0	
Subjects with events	N	(%)	E	R	N	(%)	E	R
Adverse events								
<30	70	(86.4)	439	410.9	30	(83.3)	124	259.3
30-<35	392	(89.9)	3079	533.7	170	(82.1)	1001	371.1
35-<40	372	(91.6)	3087	587.4	187	(89.9)	1073	417.5
>=40	337	(88.0)	3053	614.4	179	(87.7)	1104	433.0
Gastrointestinal disorders								
<30	51	(63.0)	207	193.8	13	(36.1)	27	56.5
30-<35	316	(72.5)	1340	232.3	92	(44.4)	200	74.1
35-<40	310	(76.4)	1350	256.9	104	(50.0)	260	101.2
>=40	292	(76.2)	1412	284.2	105	(51.5)	252	98.8
Gastrointestinal signs and symptoms								
<30	44	(54.3)	122	114.2	6	(16.7)	11	23.0
30-<35	261	(59.9)	831	144.0	57	(27.5)	111	41.1
35-<40	265	(65.3)	855	162.7	67	(32.2)	135	52.5
>=40	254	(66.3)	906	182.3	71	(34.8)	138	54.1
Nausea								
<30	30	(37.0)	45	42.1	3	(8.3)	5	10.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	189 (43.3)	353	61.2	31 (15.0)	36	13.3
35-<40	181 (44.6)	350	66.6	37 (17.8)	50	19.5
>=40	177 (46.2)	320	64.4	43 (21.1)	55	21.6
Vomiting						
<30	17 (21.0)	31	29.0	0		
30-<35	98 (22.5)	180	31.2	10 (4.8)	12	4.4
35-<40	99 (24.4)	202	38.4	17 (8.2)	19	7.4
>=40	110 (28.7)	223	44.9	16 (7.8)	21	8.2
Dyspepsia						
<30	9 (11.1)	12	11.2	1 (2.8)	2	4.2
30-<35	39 (8.9)	51	8.8	11 (5.3)	13	4.8
35-<40	43 (10.6)	52	9.9	5 (2.4)	6	2.3
>=40	44 (11.5)	64	12.9	6 (2.9)	9	3.5
Abdominal pain						
<30	5 (6.2)	10	9.4	1 (2.8)	1	2.1
30-<35	41 (9.4)	59	10.2	12 (5.8)	14	5.2
35-<40	44 (10.8)	51	9.7	11 (5.3)	12	4.7
>=40	40 (10.4)	55	11.1	12 (5.9)	14	5.5
Abdominal pain upper						
<30	6 (7.4)	7	6.6	0		
30-<35	41 (9.4)	53	9.2	12 (5.8)	14	5.2
35-<40	38 (9.4)	62	11.8	14 (6.7)	14	5.4
>=40	40 (10.4)	54	10.9	9 (4.4)	9	3.5
Abdominal distension						
<30	7 (8.6)	7	6.6	1 (2.8)	1	2.1
30-<35	24 (5.5)	31	5.4	8 (3.9)	10	3.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	30 (7.4)	37	7.0	10 (4.8)	14	5.4
>=40	35 (9.1)	60	12.1	12 (5.9)	17	6.7
Eructation						
<30	1 (1.2)	1	0.9	0		
30-<35	38 (8.7)	47	8.1	1 (0.5)	1	0.4
35-<40	32 (7.9)	43	8.2	2 (1.0)	2	0.8
>=40	41 (10.7)	48	9.7	0		
Abdominal discomfort						
<30	6 (7.4)	7	6.6	1 (2.8)	1	2.1
30-<35	18 (4.1)	24	4.2	3 (1.4)	3	1.1
35-<40	13 (3.2)	16	3.0	2 (1.0)	2	0.8
>=40	19 (5.0)	32	6.4	3 (1.5)	3	1.2
Flatulence						
<30	0			1 (2.8)	1	2.1
30-<35	12 (2.8)	16	2.8	6 (2.9)	6	2.2
35-<40	24 (5.9)	29	5.5	9 (4.3)	9	3.5
>=40	29 (7.6)	39	7.8	5 (2.5)	6	2.4
Abdominal pain lower						
<30	1 (1.2)	1	0.9	0		
30-<35	5 (1.1)	5	0.9	1 (0.5)	1	0.4
35-<40	3 (0.7)	3	0.6	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	2 (1.0)	2	0.8
Abnormal faeces						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	0			0		
Epigastric discomfort						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		
>=40	1 (0.3)	1	0.2	0		
Faeces soft						
<30	0			0		
30-<35	1 (0.2)	2	0.3	1 (0.5)	1	0.4
35-<40	0			4 (1.9)	4	1.6
>=40	2 (0.5)	2	0.4	0		
Regurgitation						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	1 (0.3)	2	0.4	0		
Gastrointestinal pain						
<30	0			0		
30-<35	3 (0.7)	4	0.7	0		
35-<40	0			0		
>=40	0			0		
Gastrointestinal sounds abnormal						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Retching						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Breath odour						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	3	0.6	1 (0.5)	1	0.4
>=40	0			0		
Dysphagia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Faeces discoloured						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	0			2 (1.0)	2	0.8
Abdominal tenderness						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Aerophagia						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Oesophageal pain								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Faeces hard								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Gastrointestinal motility and defaecation conditions								
<30	33	(40.7)	66	61.8	5	(13.9)	9	18.8
30-<35	188	(43.1)	383	66.4	45	(21.7)	59	21.9
35-<40	208	(51.2)	406	77.3	60	(28.8)	94	36.6
>=40	197	(51.4)	416	83.7	56	(27.5)	77	30.2
Diarrhoea								
<30	17	(21.0)	41	38.4	1	(2.8)	1	2.1
30-<35	125	(28.7)	218	37.8	26	(12.6)	33	12.2
35-<40	133	(32.8)	239	45.5	38	(18.3)	50	19.5
>=40	137	(35.8)	268	53.9	39	(19.1)	54	21.2
Constipation								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	17 (21.0)	20	18.7	3 (8.3)	6	12.5
30-<35	94 (21.6)	126	21.8	18 (8.7)	20	7.4
35-<40	103 (25.4)	131	24.9	21 (10.1)	27	10.5
>=40	92 (24.0)	113	22.7	20 (9.8)	20	7.8
Gastrooesophageal reflux disease						
<30	5 (6.2)	5	4.7	0		
30-<35	25 (5.7)	31	5.4	5 (2.4)	5	1.9
35-<40	28 (6.9)	29	5.5	13 (6.3)	14	5.4
>=40	24 (6.3)	27	5.4	2 (1.0)	2	0.8
Irritable bowel syndrome						
<30	0			1 (2.8)	2	4.2
30-<35	1 (0.2)	2	0.3	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	4 (1.0)	4	0.8	0		
Frequent bowel movements						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	0		
Dyschezia						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			0		
Impaired gastric emptying						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Change of bowel habit						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Oesophageal achalasia						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Bowel movement irregularity						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Defaecation urgency						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Gastrointestinal hypermotility						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
35-<40	0				0			
>=40	0				0			
Gastrointestinal motility disorder								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Infrequent bowel movements								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Gastrointestinal inflammatory conditions								
<30	5	(6.2)	7	6.6	1	(2.8)	1	2.1
30-<35	28	(6.4)	42	7.3	2	(1.0)	2	0.7
35-<40	21	(5.2)	25	4.8	7	(3.4)	7	2.7
>=40	17	(4.4)	20	4.0	2	(1.0)	3	1.2
Gastritis								
<30	3	(3.7)	4	3.7	1	(2.8)	1	2.1
30-<35	21	(4.8)	32	5.5	1	(0.5)	1	0.4
35-<40	14	(3.4)	18	3.4	2	(1.0)	2	0.8
>=40	12	(3.1)	13	2.6	2	(1.0)	3	1.2
Colitis								
<30	0				0			
30-<35	2	(0.5)	4	0.7	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	0		
Duodenitis						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Colitis ischaemic						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Crohn's disease						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Reflux gastritis						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Gastrointestinal inflammation						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	1 (0.3)	1	0.2	0		
Enteritis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Chronic gastritis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Oesophagitis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Gastroenteritis eosinophilic						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Eosinophilic oesophagitis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Epiploic appendagitis						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Inflammatory bowel disease						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Gastrointestinal conditions NEC						
<30	2 (2.5)	3	2.8	0		
30-<35	18 (4.1)	24	4.2	6 (2.9)	8	3.0
35-<40	16 (3.9)	24	4.6	4 (1.9)	4	1.6
>=40	12 (3.1)	16	3.2	2 (1.0)	4	1.6
Hyperchlorhydria						
<30	1 (1.2)	2	1.9	0		
30-<35	8 (1.8)	13	2.3	2 (1.0)	4	1.5
35-<40	6 (1.5)	14	2.7	0		
>=40	5 (1.3)	8	1.6	1 (0.5)	1	0.4
Food poisoning						
<30	1 (1.2)	1	0.9	0		
30-<35	7 (1.6)	7	1.2	2 (1.0)	2	0.7
35-<40	5 (1.2)	5	1.0	1 (0.5)	1	0.4
>=40	5 (1.3)	5	1.0	1 (0.5)	3	1.2
Gastrointestinal disorder						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	2 (0.5)	3	0.5	2 (1.0)	2	0.7
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	1 (0.3)	2	0.4	0		
Anal fistula						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	0			0		
Barrett's oesophagus						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Functional gastrointestinal disorder						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Gastric mucosal hypertrophy						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Gastrointestinal vascular conditions						
<30	3 (3.7)	3	2.8	1 (2.8)	1	2.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	11 (2.5)	12	2.1	2 (1.0)	2	0.7
35-<40	9 (2.2)	10	1.9	1 (0.5)	1	0.4
>=40	5 (1.3)	5	1.0	1 (0.5)	1	0.4
Haemorrhoids						
<30	3 (3.7)	3	2.8	1 (2.8)	1	2.1
30-<35	10 (2.3)	10	1.7	1 (0.5)	1	0.4
35-<40	9 (2.2)	10	1.9	0		
>=40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
Haemorrhoids thrombosed						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Haemorrhoidal haemorrhage						
<30	0			0		
30-<35	1 (0.2)	2	0.3	1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Dental and gingival conditions						
<30	0			2 (5.6)	2	4.2
30-<35	6 (1.4)	7	1.2	8 (3.9)	10	3.7
35-<40	6 (1.5)	7	1.3	7 (3.4)	7	2.7
>=40	15 (3.9)	18	3.6	12 (5.9)	13	5.1
Toothache						
<30	0			0		
30-<35	2 (0.5)	2	0.3	6 (2.9)	7	2.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	4 (1.0)	5	1.0	3 (1.4)	3	1.2
>=40	11 (2.9)	13	2.6	8 (3.9)	8	3.1
Dental caries						
<30	0			1 (2.8)	1	2.1
30-<35	2 (0.5)	3	0.5	2 (1.0)	2	0.7
35-<40	1 (0.2)	1	0.2	4 (1.9)	4	1.6
>=40	1 (0.3)	1	0.2	3 (1.5)	3	1.2
Gingival disorder						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Noninfective gingivitis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Tooth impacted						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Tooth loss						
<30	0			0		
30-<35	0			0		
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	1 (0.3)	1	0.2	0		
Gingival bleeding						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Gingival pain						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Periodontal disease						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Dental necrosis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Dental pulp disorder						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	0			0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Tooth disorder						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Salivary gland conditions						
<30	0			0		
30-<35	14 (3.2)	14	2.4	1 (0.5)	1	0.4
35-<40	9 (2.2)	9	1.7	1 (0.5)	1	0.4
>=40	4 (1.0)	4	0.8	6 (2.9)	7	2.7
Dry mouth						
<30	0			0		
30-<35	14 (3.2)	14	2.4	1 (0.5)	1	0.4
35-<40	8 (2.0)	8	1.5	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	5 (2.5)	6	2.4
Salivary gland cyst						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Salivary gland calculus						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Salivary gland enlargement						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Gastrointestinal haemorrhages NEC						
<30	0			0		
30-<35	9 (2.1)	9	1.6	2 (1.0)	2	0.7
35-<40	2 (0.5)	2	0.4	3 (1.4)	4	1.6
>=40	4 (1.0)	5	1.0	1 (0.5)	1	0.4
Rectal haemorrhage						
<30	0			0		
30-<35	3 (0.7)	3	0.5	0		
35-<40	2 (0.5)	2	0.4	0		
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Haematochezia						
<30	0			0		
30-<35	5 (1.1)	5	0.9	1 (0.5)	1	0.4
35-<40	0			2 (1.0)	3	1.2
>=40	2 (0.5)	2	0.4	0		
Haematemesis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Lower gastrointestinal haemorrhage						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Melaena						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Upper gastrointestinal haemorrhage						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Oral soft tissue conditions						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	5 (1.3)	6	1.2	4 (2.0)	4	1.6
Mouth ulceration						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			2 (1.0)	2	0.8
Lip swelling						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Aphthous ulcer								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Cheilitis								
<30	0				0			
30-<35	0				0			
35-<40	0				1	(0.5)	1	0.4
>=40	1	(0.3)	1	0.2	1	(0.5)	1	0.4
Lip disorder								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Odynophagia								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Stomatitis								
<30	0				0			
30-<35	0				0			
35-<40	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	1 (0.3)	1	0.2	0		
Paraesthesia oral						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Oral mucosal eruption						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Diverticular disorders						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	4 (0.9)	4	0.7	1 (0.5)	1	0.4
35-<40	0			2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Diverticulum						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	4 (0.9)	4	0.7	1 (0.5)	1	0.4
35-<40	0			2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Benign neoplasms gastrointestinal						
<30	0			1 (2.8)	1	2.1
30-<35	6 (1.4)	6	1.0	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	2 (1.0)	2	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Large intestine polyp						
<30	0			1 (2.8)	1	2.1
30-<35	5 (1.1)	5	0.9	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Gastric polyps						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Abdominal hernias and other abdominal wall conditions						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	4 (1.0)	4	0.8	2 (1.0)	2	0.8
>=40	4 (1.0)	5	1.0	1 (0.5)	1	0.4
Hiatus hernia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	2 (0.5)	3	0.6	0		
Abdominal hernia						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Umbilical hernia						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Gastrointestinal ulceration and perforation						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	2 (0.5)	2	0.4	0		
Large intestine perforation						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Duodenal ulcer						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Gastric ulcer						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Oesophageal ulcer						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Peptic ulcer						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Anal and rectal conditions NEC						
<30	0			0		
30-<35	3 (0.7)	3	0.5	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	3 (0.8)	5	1.0	0		
Anal fissure						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Proctalgia						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	3	0.6	0		
Rectal fissure						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Anal pruritus						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Anorectal discomfort						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Gastrointestinal stenosis and obstruction						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Ileus						
<30	1 (1.2)	1	0.9	0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Volvulus						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Oesophageal stenosis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Intestinal obstruction						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Peritoneal and retroperitoneal conditions						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Pneumoperitoneum						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Tongue conditions						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	1	(1.2)	1	0.9	0			
30-<35	0				0			
35-<40	0				0			
>=40	0				0			
Glossodynia								
<30	1	(1.2)	1	0.9	0			
30-<35	0				0			
35-<40	0				0			
>=40	0				0			
Exocrine pancreas conditions								
<30	0				0			
30-<35	0				0			
35-<40	2	(0.5)	2	0.4	0			
>=40	0				0			
Pancreatitis acute								
<30	0				0			
30-<35	0				0			
35-<40	2	(0.5)	2	0.4	0			
>=40	0				0			
Malabsorption conditions								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Coeliac disease								
<30	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Infections and infestations						
<30	38 (46.9)	75	70.2	16 (44.4)	38	79.5
30-<35	230 (52.8)	504	87.4	115 (55.6)	257	95.3
35-<40	230 (56.7)	508	96.7	124 (59.6)	240	93.4
>=40	216 (56.4)	528	106.3	117 (57.4)	267	104.7
Infections - pathogen unspecified						
<30	34 (42.0)	61	57.1	15 (41.7)	28	58.5
30-<35	200 (45.9)	386	66.9	100 (48.3)	198	73.4
35-<40	200 (49.3)	385	73.3	101 (48.6)	184	71.6
>=40	192 (50.1)	415	83.5	98 (48.0)	200	78.4
Nasopharyngitis						
<30	17 (21.0)	26	24.3	6 (16.7)	11	23.0
30-<35	87 (20.0)	151	26.2	44 (21.3)	73	27.1
35-<40	78 (19.2)	118	22.5	49 (23.6)	71	27.6
>=40	99 (25.8)	185	37.2	34 (16.7)	61	23.9
Upper respiratory tract infection						
<30	1 (1.2)	2	1.9	3 (8.3)	3	6.3
30-<35	34 (7.8)	43	7.5	25 (12.1)	35	13.0
35-<40	47 (11.6)	67	12.7	21 (10.1)	28	10.9
>=40	32 (8.4)	46	9.3	31 (15.2)	50	19.6
Gastroenteritis						
<30	5 (6.2)	5	4.7	2 (5.6)	3	6.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	34 (7.8)	39	6.8	10 (4.8)	12	4.4
35-<40	25 (6.2)	31	5.9	7 (3.4)	10	3.9
>=40	21 (5.5)	29	5.8	11 (5.4)	13	5.1
Urinary tract infection						
<30	4 (4.9)	4	3.7	2 (5.6)	2	4.2
30-<35	18 (4.1)	19	3.3	8 (3.9)	11	4.1
35-<40	24 (5.9)	34	6.5	9 (4.3)	12	4.7
>=40	22 (5.7)	26	5.2	9 (4.4)	9	3.5
Sinusitis						
<30	1 (1.2)	1	0.9	2 (5.6)	3	6.3
30-<35	27 (6.2)	32	5.5	7 (3.4)	7	2.6
35-<40	14 (3.4)	16	3.0	16 (7.7)	18	7.0
>=40	29 (7.6)	35	7.0	11 (5.4)	12	4.7
Bronchitis						
<30	4 (4.9)	4	3.7	1 (2.8)	1	2.1
30-<35	16 (3.7)	16	2.8	10 (4.8)	13	4.8
35-<40	14 (3.4)	18	3.4	10 (4.8)	10	3.9
>=40	13 (3.4)	14	2.8	4 (2.0)	4	1.6
Pharyngitis						
<30	3 (3.7)	3	2.8	1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	3 (1.4)	3	1.1
35-<40	4 (1.0)	4	0.8	2 (1.0)	2	0.8
>=40	5 (1.3)	5	1.0	3 (1.5)	3	1.2
Tonsillitis						
<30	2 (2.5)	4	3.7	0		
30-<35	4 (0.9)	4	0.7	4 (1.9)	6	2.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	4 (1.0)	5	1.0	2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	4 (2.0)	4	1.6
Rhinitis						
<30	0			2 (5.6)	3	6.3
30-<35	6 (1.4)	9	1.6	2 (1.0)	3	1.1
35-<40	9 (2.2)	12	2.3	2 (1.0)	4	1.6
>=40	4 (1.0)	4	0.8	3 (1.5)	4	1.6
Cystitis						
<30	0			0		
30-<35	7 (1.6)	8	1.4	2 (1.0)	2	0.7
35-<40	7 (1.7)	8	1.5	0		
>=40	5 (1.3)	5	1.0	1 (0.5)	1	0.4
Laryngitis						
<30	1 (1.2)	1	0.9	0		
30-<35	3 (0.7)	3	0.5	2 (1.0)	3	1.1
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	6 (1.6)	6	1.2	1 (0.5)	1	0.4
Acute sinusitis						
<30	1 (1.2)	1	0.9	0		
30-<35	4 (0.9)	4	0.7	4 (1.9)	5	1.9
35-<40	4 (1.0)	5	1.0	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	3 (1.5)	3	1.2
Ear infection						
<30	1 (1.2)	1	0.9	0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	3 (0.7)	5	1.0	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	3 (0.8)	3	0.6	1 (0.5)	1	0.4
Tooth infection						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	3 (0.7)	4	0.8	2 (1.0)	2	0.8
>=40	6 (1.6)	6	1.2	3 (1.5)	3	1.2
Pneumonia						
<30	0			0		
30-<35	3 (0.7)	5	0.9	1 (0.5)	1	0.4
35-<40	5 (1.2)	6	1.1	4 (1.9)	4	1.6
>=40	3 (0.8)	3	0.6	3 (1.5)	3	1.2
Vaginal infection						
<30	0			0		
30-<35	4 (0.9)	5	0.9	0		
35-<40	4 (1.0)	5	1.0	0		
>=40	3 (0.8)	3	0.6	0		
Otitis media						
<30	1 (1.2)	1	0.9	0		
30-<35	3 (0.7)	3	0.5	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	0		
>=40	0			1 (0.5)	1	0.4
Lower respiratory tract infection						
<30	0			0		
30-<35	2 (0.5)	3	0.5	3 (1.4)	4	1.5
35-<40	1 (0.2)	1	0.2	4 (1.9)	4	1.6
>=40	6 (1.6)	6	1.2	5 (2.5)	8	3.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Pulpitis dental						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	2 (0.5)	2	0.4	0		
Tooth abscess						
<30	0			1 (2.8)	1	2.1
30-<35	3 (0.7)	3	0.5	2 (1.0)	2	0.7
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	4 (2.0)	5	2.0
Breast abscess						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Hordeolum						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Conjunctivitis						
<30	0			0		
30-<35	3 (0.7)	3	0.5	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	3 (0.8)	3	0.6	2 (1.0)	2	0.8
Gingivitis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Abdominal abscess						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Haematoma infection						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Peritonitis						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Sepsis syndrome						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Appendicitis						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	3 (0.7)	3	0.6	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Gastrointestinal infection						
<30	0			0		
30-<35	2 (0.5)	3	0.5	1 (0.5)	1	0.4
35-<40	2 (0.5)	3	0.6	2 (1.0)	2	0.8
>=40	1 (0.3)	1	0.2	0		
Eye infection						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	3 (0.7)	3	0.6	0		
>=40	0			0		
Folliculitis						
<30	0			0		
30-<35	3 (0.7)	3	0.5	0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			1 (0.5)	1	0.4
Pyelonephritis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	3 (0.8)	3	0.6	0		
Subcutaneous abscess						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	0		
Chronic sinusitis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	0		
Infected bite						
<30	0			0		
30-<35	1 (0.2)	1	0.2	2 (1.0)	2	0.7
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Kidney infection						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Pharyngotonsillitis						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			1 (0.5)	2	0.8
>=40	1 (0.3)	1	0.2	0		
Otitis externa						
<30	0			0		
30-<35	0			0		
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	2 (0.5)	2	0.4	0		
Periodontitis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Abdominal wall abscess						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Omphalitis						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Localised infection						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	0		
>=40	0			1 (0.5)	1	0.4
Abscess						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Atypical pneumonia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Diarrhoea infectious						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	2	0.7
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Infection						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Postoperative wound infection						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Bartholinitis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Diverticulitis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Endometritis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Groin abscess						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Oral infection						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Purulence						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Respiratory tract infection						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Abscess limb						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Carbuncle						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Epididymitis						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Mastitis						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Nail infection						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Paronychia						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Perirectal abscess						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	2	0.4	0		
>=40	0			0		
Prostate infection						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Skin infection						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Appendicitis perforated						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=40	0				0			
Device related infection								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Eyelid infection								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Fracture infection								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Large intestine infection								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Oophoritis								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Osteomyelitis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Parasitic gastroenteritis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Parotitis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Salpingitis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Arthritis infective						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Cervicitis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Empyema						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Gastric infection						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Infected dermal cyst						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Lymphangitis						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Neutropenic sepsis						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Otitis media acute						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Peritonsillar abscess						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Peritonsillitis						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Root canal infection						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Septic shock						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Tracheitis						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Wound infection						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Viral infectious disorders						
<30	11 (13.6)	12	11.2	4 (11.1)	6	12.5
30-<35	64 (14.7)	83	14.4	29 (14.0)	43	15.9
35-<40	64 (15.8)	83	15.8	34 (16.3)	41	16.0
>=40	55 (14.4)	70	14.1	36 (17.6)	46	18.0
Influenza						
<30	6 (7.4)	7	6.6	3 (8.3)	4	8.4
30-<35	39 (8.9)	46	8.0	20 (9.7)	27	10.0
35-<40	24 (5.9)	34	6.5	17 (8.2)	20	7.8
>=40	20 (5.2)	25	5.0	23 (11.3)	28	11.0
Gastroenteritis viral						
<30	1 (1.2)	1	0.9	0		
30-<35	9 (2.1)	10	1.7	5 (2.4)	5	1.9
35-<40	19 (4.7)	19	3.6	6 (2.9)	7	2.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	13 (3.4)	14	2.8	3 (1.5)	3	1.2
Herpes zoster						
<30	1 (1.2)	1	0.9	0		
30-<35	4 (0.9)	5	0.9	5 (2.4)	5	1.9
35-<40	4 (1.0)	4	0.8	2 (1.0)	2	0.8
>=40	3 (0.8)	3	0.6	4 (2.0)	4	1.6
Viral infection						
<30	0			1 (2.8)	1	2.1
30-<35	5 (1.1)	9	1.6	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	7 (1.8)	9	1.8	4 (2.0)	4	1.6
Gastrointestinal viral infection						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	4 (1.0)	4	0.8	0		
>=40	3 (0.8)	4	0.8	1 (0.5)	1	0.4
Herpes simplex						
<30	1 (1.2)	1	0.9	0		
30-<35	0			1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Viral upper respiratory tract infection						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	2	0.7
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	3 (0.8)	3	0.6	2 (1.0)	2	0.8
Dengue fever						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Gastroenteritis norovirus						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	3 (0.7)	4	0.8	0		
>=40	1 (0.3)	1	0.2	0		
Ear infection viral						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	3 (0.7)	3	0.6	0		
>=40	0			0		
Oral herpes						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	2 (0.5)	3	0.6	1 (0.5)	1	0.4
Viral pharyngitis						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Herpes virus infection						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Respiratory tract infection viral						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Gastroenteritis astroviral						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Papilloma viral infection						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Varicella						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Vestibular neuronitis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Cytomegalovirus infection						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Hepatitis E						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Infectious mononucleosis						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Oral viral infection						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Parainfluenzae virus infection						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Chronic hepatitis B								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Genital herpes zoster								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Respiratory syncytial virus infection								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Viral sinusitis								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				1	(0.5)	1	0.4
>=40	0				0			
Bronchitis viral								
<30	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	0			2 (1.0)	2	0.8
>=40	0			0		
Conjunctivitis viral						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Hand-foot-and-mouth disease						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Meningitis viral						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Viral rhinitis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Bacterial infectious disorders						
<30	2 (2.5)	2	1.9	1 (2.8)	1	2.1
30-<35	13 (3.0)	14	2.4	8 (3.9)	11	4.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	22 (5.4)	26	4.9	9 (4.3)	9	3.5
>=40	20 (5.2)	21	4.2	9 (4.4)	10	3.9
Pharyngitis streptococcal						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	2 (1.0)	2	0.7
35-<40	6 (1.5)	6	1.1	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	3 (1.5)	3	1.2
Cellulitis						
<30	0			0		
30-<35	5 (1.1)	5	0.9	2 (1.0)	3	1.1
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	3 (1.5)	3	1.2
Erysipelas						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Helicobacter infection						
<30	0			0		
30-<35	0			0		
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Ear infection bacterial						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Bacterial vaginosis						
<30	0			0		
30-<35	0			0		
35-<40	3 (0.7)	6	1.1	2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	0		
Furuncle						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	2	0.4	0		
>=40	1 (0.3)	1	0.2	0		
Staphylococcal infection						
<30	0			0		
30-<35	1 (0.2)	1	0.2	2 (1.0)	2	0.7
35-<40	2 (0.5)	2	0.4	0		
>=40	0			0		
Helicobacter gastritis						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Bacterial colitis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Bacterial vulvovaginitis								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Genital infection bacterial								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Sinusitis bacterial								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Skin bacterial infection								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Tonsillitis bacterial								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Lyme disease								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Typhoid fever								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	1	(0.5)	1	0.4
>=40	0				0			
Pharyngitis bacterial								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Salmonellosis								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Syphilis								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Bacteriuria								
<30	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Gastric ulcer helicobacter						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Listeriosis						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Staphylococcal sepsis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Streptococcal urinary tract infection						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Upper respiratory tract infection bacterial						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Fungal infectious disorders						
<30	0			2 (5.6)	3	6.3
30-<35	18 (4.1)	21	3.6	5 (2.4)	5	1.9
35-<40	9 (2.2)	12	2.3	5 (2.4)	5	1.9
>=40	18 (4.7)	20	4.0	10 (4.9)	11	4.3
Vulvovaginal mycotic infection						
<30	0			0		
30-<35	4 (0.9)	4	0.7	1 (0.5)	1	0.4
35-<40	2 (0.5)	3	0.6	0		
>=40	5 (1.3)	6	1.2	1 (0.5)	1	0.4
Fungal infection						
<30	0			0		
30-<35	4 (0.9)	4	0.7	2 (1.0)	2	0.7
35-<40	2 (0.5)	3	0.6	2 (1.0)	2	0.8
>=40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
Tinea pedis						
<30	0			0		
30-<35	3 (0.7)	3	0.5	0		
35-<40	0			0		
>=40	3 (0.8)	3	0.6	1 (0.5)	1	0.4
Vulvovaginal candidiasis						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	3 (0.7)	5	0.9	1 (0.5)	1	0.4
35-<40	1 (0.2)	2	0.4	0		
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Skin candida						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Onychomycosis						
<30	0			1 (2.8)	2	4.2
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Dermatophytosis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Fungal skin infection						
<30	0			1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Body tinea						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Tinea capitis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Candida infection						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
Dermatophytosis of nail						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Tinea cruris						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Tinea infection						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	0			0		
Oral candidiasis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Otitis externa fungal						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Protozoal infectious disorders						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Trichomoniasis						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Toxoplasmosis						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Chlamydial infectious disorders								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Chlamydial infection								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Ectoparasitic disorders								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Acarodermatitis								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Nervous system disorders								
<30	17	(21.0)	23	21.5	2	(5.6)	3	6.3
30-<35	135	(31.0)	294	51.0	42	(20.3)	66	24.5
35-<40	123	(30.3)	222	42.2	50	(24.0)	85	33.1
>=40	116	(30.3)	219	44.1	47	(23.0)	68	26.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Headaches						
<30	10 (12.3)	15	14.0	1 (2.8)	1	2.1
30-<35	76 (17.4)	178	30.9	29 (14.0)	37	13.7
35-<40	68 (16.7)	129	24.5	30 (14.4)	40	15.6
>=40	75 (19.6)	129	26.0	29 (14.2)	40	15.7
Headache						
<30	7 (8.6)	12	11.2	1 (2.8)	1	2.1
30-<35	72 (16.5)	161	27.9	24 (11.6)	30	11.1
35-<40	58 (14.3)	104	19.8	30 (14.4)	39	15.2
>=40	61 (15.9)	110	22.1	25 (12.3)	34	13.3
Migraine						
<30	2 (2.5)	2	1.9	0		
30-<35	4 (0.9)	12	2.1	5 (2.4)	5	1.9
35-<40	12 (3.0)	22	4.2	1 (0.5)	1	0.4
>=40	14 (3.7)	16	3.2	3 (1.5)	5	2.0
Tension headache						
<30	1 (1.2)	1	0.9	0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Sinus headache						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	2 (0.5)	2	0.4	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Migraine with aura						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Occipital neuralgia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Neurological disorders NEC						
<30	6 (7.4)	6	5.6	1 (2.8)	2	4.2
30-<35	70 (16.1)	94	16.3	15 (7.2)	23	8.5
35-<40	56 (13.8)	76	14.5	17 (8.2)	27	10.5
>=40	49 (12.8)	72	14.5	14 (6.9)	16	6.3
Dizziness						
<30	2 (2.5)	2	1.9	1 (2.8)	2	4.2
30-<35	35 (8.0)	47	8.1	6 (2.9)	7	2.6
35-<40	31 (7.6)	41	7.8	9 (4.3)	17	6.6
>=40	30 (7.8)	40	8.1	7 (3.4)	9	3.5
Dysgeusia						
<30	0			0		
30-<35	5 (1.1)	7	1.2	1 (0.5)	8	3.0
35-<40	5 (1.2)	6	1.1	1 (0.5)	1	0.4
>=40	8 (2.1)	11	2.2	2 (1.0)	2	0.8
Paraesthesia						
<30	1 (1.2)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	5 (1.1)	7	1.2	3 (1.4)	3	1.1
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	5 (1.3)	7	1.4	1 (0.5)	1	0.4
Lethargy						
<30	1 (1.2)	1	0.9	0		
30-<35	2 (0.5)	2	0.3	2 (1.0)	2	0.7
35-<40	1 (0.2)	1	0.2	0		
>=40	3 (0.8)	3	0.6	1 (0.5)	1	0.4
Syncope						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	7 (1.7)	7	1.3	2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	0		
Hypoaesthesia						
<30	1 (1.2)	1	0.9	0		
30-<35	3 (0.7)	3	0.5	0		
35-<40	1 (0.2)	1	0.2	2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	0		
Taste disorder						
<30	0			0		
30-<35	3 (0.7)	3	0.5	0		
35-<40	4 (1.0)	6	1.1	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	0		
Somnolence						
<30	0			0		
30-<35	4 (0.9)	5	0.9	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	2 (0.5)	3	0.6	0		
>=40	1 (0.3)	1	0.2	0		
Burning sensation						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Neuralgia						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Hyperaesthesia						
<30	0			0		
30-<35	4 (0.9)	6	1.0	0		
35-<40	0			0		
>=40	0			0		
Dizziness postural						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Allodynia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	1 (0.3)	1	0.2	0		
Balance disorder						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Presyncope						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Dysarthria						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Loss of consciousness						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Ageusia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Aphasia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Restless legs syndrome						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	2	0.4	0		
>=40	0			1 (0.5)	1	0.4
Dysaesthesia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Hyporeflexia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			2 (1.0)	2	0.8
>=40	0			0		
Sensory disturbance						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Vertigo CNS origin						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Sensory loss								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	0				1	(0.5)	1	0.4
Spinal cord and nerve root disorders								
<30	1	(1.2)	1	0.9	0			
30-<35	10	(2.3)	10	1.7	2	(1.0)	2	0.7
35-<40	5	(1.2)	6	1.1	9	(4.3)	9	3.5
>=40	4	(1.0)	5	1.0	3	(1.5)	3	1.2
Sciatica								
<30	0				0			
30-<35	7	(1.6)	7	1.2	0			
35-<40	4	(1.0)	5	1.0	5	(2.4)	5	1.9
>=40	3	(0.8)	4	0.8	3	(1.5)	3	1.2
Cervicobrachial syndrome								
<30	1	(1.2)	1	0.9	0			
30-<35	1	(0.2)	1	0.2	2	(1.0)	2	0.7
35-<40	0				2	(1.0)	2	0.8
>=40	0				0			
Lumbar radiculopathy								
<30	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Lumbosacral radiculopathy						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Cervical radiculopathy						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Spinal cord compression						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Peripheral neuropathies						
<30	0			0		
30-<35	3 (0.7)	4	0.7	1 (0.5)	1	0.4
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	5 (1.3)	5	1.0	6 (2.9)	7	2.7
Neuropathy peripheral						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	2 (0.5)	2	0.4	0		
>=40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
Carpal tunnel syndrome						
<30	0			0		
30-<35	2 (0.5)	3	0.5	1 (0.5)	1	0.4
35-<40	0			1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Nerve compression						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Peripheral sensory neuropathy						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Peroneal nerve palsy						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Radial nerve compression						
<30	0			0		
30-<35	0			0		
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	0			1 (0.5)	1	0.4
Cranial nerve disorders (excl neoplasms)						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Cranial nerve disorder						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Anosmia						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Parosmia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Movement disorders (incl parkinsonism)						
<30	0			0		
30-<35	3 (0.7)	3	0.5	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	1 (0.5)	2	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	1 (0.3)	1	0.2	0		
Tremor						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	1 (0.5)	2	0.8
>=40	1 (0.3)	1	0.2	0		
Essential tremor						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Mental impairment disorders						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	2	0.7
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	1 (0.3)	1	0.2	0		
Memory impairment						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Amnesia						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Disturbance in attention						
<30	0			0		
30-<35	0			1 (0.5)	2	0.7
35-<40	1 (0.2)	1	0.2	2 (1.0)	2	0.8
>=40	0			0		
Dementia Alzheimer's type						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Sleep disturbances (incl subtypes)						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			1 (0.5)	1	0.4
Poor quality sleep						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			1 (0.5)	1	0.4
Central nervous system vascular disorders						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Cerebral infarction						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Ischaemic stroke						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Increased intracranial pressure and hydrocephalus						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	2	0.4	0		
Idiopathic intracranial hypertension						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	2	0.4	0		
Neuromuscular disorders						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Autonomic nervous system imbalance						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Neurological disorders of the eye						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Visual field defect						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Demyelinating disorders						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Multiple sclerosis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Seizures (incl subtypes)						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	0				0			
35-<40	0				2	(1.0)	2	0.8
>=40	0				0			
Partial seizures								
<30	0				0			
30-<35	0				0			
35-<40	0				1	(0.5)	1	0.4
>=40	0				0			
Psychogenic seizure								
<30	0				0			
30-<35	0				0			
35-<40	0				1	(0.5)	1	0.4
>=40	0				0			
Musculoskeletal and connective tissue disorders								
<30	9	(11.1)	14	13.1	6	(16.7)	8	16.7
30-<35	106	(24.3)	168	29.1	61	(29.5)	97	36.0
35-<40	119	(29.3)	204	38.8	57	(27.4)	100	38.9
>=40	104	(27.2)	172	34.6	62	(30.4)	99	38.8
Musculoskeletal and connective tissue disorders NEC								
<30	7	(8.6)	8	7.5	3	(8.3)	4	8.4
30-<35	53	(12.2)	72	12.5	35	(16.9)	46	17.1
35-<40	67	(16.5)	85	16.2	28	(13.5)	37	14.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	60 (15.7)	79	15.9	33 (16.2)	45	17.6
Back pain						
<30	4 (4.9)	4	3.7	2 (5.6)	2	4.2
30-<35	37 (8.5)	40	6.9	17 (8.2)	19	7.0
35-<40	34 (8.4)	41	7.8	15 (7.2)	15	5.8
>=40	32 (8.4)	36	7.2	20 (9.8)	20	7.8
Pain in extremity						
<30	1 (1.2)	1	0.9	0		
30-<35	7 (1.6)	9	1.6	6 (2.9)	8	3.0
35-<40	17 (4.2)	17	3.2	8 (3.8)	9	3.5
>=40	19 (5.0)	21	4.2	10 (4.9)	11	4.3
Musculoskeletal pain						
<30	1 (1.2)	1	0.9	0		
30-<35	8 (1.8)	8	1.4	5 (2.4)	5	1.9
35-<40	13 (3.2)	13	2.5	5 (2.4)	6	2.3
>=40	9 (2.3)	9	1.8	6 (2.9)	7	2.7
Neck pain						
<30	1 (1.2)	1	0.9	0		
30-<35	6 (1.4)	7	1.2	3 (1.4)	3	1.1
35-<40	5 (1.2)	5	1.0	3 (1.4)	3	1.2
>=40	7 (1.8)	8	1.6	3 (1.5)	3	1.2
Musculoskeletal stiffness						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Musculoskeletal chest pain						
<30	0			0		
30-<35	3 (0.7)	3	0.5	3 (1.4)	3	1.1
35-<40	3 (0.7)	3	0.6	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Plantar fasciitis						
<30	0			1 (2.8)	2	4.2
30-<35	1 (0.2)	1	0.2	2 (1.0)	2	0.7
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	3 (1.5)	3	1.2
Flank pain						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Axillary mass						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Musculoskeletal discomfort						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	2	0.4	0		
>=40	0			0		
Dupuytren's contracture						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Groin pain						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Limb mass						
<30	0			0		
30-<35	0			1 (0.5)	2	0.7
35-<40	0			0		
>=40	0			0		
Muscle contracture						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			2 (1.0)	2	0.8
>=40	0			0		
Neck mass						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Joint disorders						
<30	0			1 (2.8)	1	2.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	46 (10.6)	55	9.5	22 (10.6)	30	11.1
35-<40	45 (11.1)	65	12.4	27 (13.0)	36	14.0
>=40	42 (11.0)	49	9.9	25 (12.3)	27	10.6
Arthralgia						
<30	0			1 (2.8)	1	2.1
30-<35	25 (5.7)	26	4.5	11 (5.3)	12	4.4
35-<40	27 (6.7)	34	6.5	19 (9.1)	22	8.6
>=40	29 (7.6)	32	6.4	12 (5.9)	12	4.7
Osteoarthritis						
<30	0			0		
30-<35	9 (2.1)	11	1.9	6 (2.9)	7	2.6
35-<40	7 (1.7)	8	1.5	6 (2.9)	7	2.7
>=40	7 (1.8)	9	1.8	6 (2.9)	6	2.4
Spinal osteoarthritis						
<30	0			0		
30-<35	4 (0.9)	4	0.7	0		
35-<40	6 (1.5)	7	1.3	0		
>=40	2 (0.5)	2	0.4	0		
Arthritis						
<30	0			0		
30-<35	5 (1.1)	5	0.9	3 (1.4)	3	1.1
35-<40	1 (0.2)	1	0.2	3 (1.4)	3	1.2
>=40	2 (0.5)	2	0.4	0		
Joint swelling						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	2 (1.0)	2	0.8
Rotator cuff syndrome						
<30	0			0		
30-<35	3 (0.7)	3	0.5	1 (0.5)	1	0.4
35-<40	3 (0.7)	3	0.6	1 (0.5)	1	0.4
>=40	0			3 (1.5)	3	1.2
Joint stiffness						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		
>=40	1 (0.3)	1	0.2	0		
Vertebral foraminal stenosis						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	1 (0.2)	2	0.4	0		
>=40	0			0		
Facet joint syndrome						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	2	0.4	0		
>=40	0			0		
Arthropathy						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	2	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=40	0				1	(0.5)	1	0.4
Periarthritis								
<30	0				0			
30-<35	0				1	(0.5)	2	0.7
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Vertebral osteophyte								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Spondylitis								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Chondromalacia								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	0				1	(0.5)	1	0.4
Haemarthrosis								
<30	0				0			
30-<35	0				0			
35-<40	0				1	(0.5)	1	0.4
>=40	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Joint noise						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Joint range of motion decreased						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
Joint space narrowing						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Polyarthritis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Rheumatoid arthritis						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Spondyloarthropathy						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Muscle disorders								
<30	2	(2.5)	3	2.8	0			
30-<35	14	(3.2)	14	2.4	7	(3.4)	8	3.0
35-<40	26	(6.4)	28	5.3	8	(3.8)	9	3.5
>=40	16	(4.2)	19	3.8	8	(3.9)	12	4.7
Myalgia								
<30	1	(1.2)	2	1.9	0			
30-<35	5	(1.1)	5	0.9	4	(1.9)	5	1.9
35-<40	11	(2.7)	12	2.3	1	(0.5)	1	0.4
>=40	6	(1.6)	7	1.4	3	(1.5)	7	2.7
Muscle spasms								
<30	1	(1.2)	1	0.9	0			
30-<35	4	(0.9)	4	0.7	3	(1.4)	3	1.1
35-<40	7	(1.7)	7	1.3	5	(2.4)	6	2.3
>=40	7	(1.8)	7	1.4	2	(1.0)	2	0.8
Muscular weakness								
<30	0				0			
30-<35	0				0			
35-<40	2	(0.5)	3	0.6	0			
>=40	3	(0.8)	3	0.6	1	(0.5)	1	0.4
Fibromyalgia								
<30	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	3 (0.7)	3	0.6	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Myofascial pain syndrome						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	0			0		
Muscle twitching						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Myalgia intercostal						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Myosclerosis						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Torticollis						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Muscle disorder						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Muscle fatigue						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Muscle tightness						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Tendon, ligament and cartilage disorders						
<30	1 (1.2)	1	0.9	0		
30-<35	8 (1.8)	8	1.4	3 (1.4)	3	1.1
35-<40	7 (1.7)	9	1.7	6 (2.9)	8	3.1
>=40	9 (2.3)	9	1.8	4 (2.0)	4	1.6
Tendonitis						
<30	0			0		
30-<35	5 (1.1)	5	0.9	2 (1.0)	2	0.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	6 (1.5)	7	1.3	3 (1.4)	5	1.9
>=40	2 (0.5)	2	0.4	4 (2.0)	4	1.6
Tenosynovitis						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Costochondritis						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	2 (0.5)	2	0.4	0		
Tendon disorder						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Osteochondrosis						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Posterior tibial tendon dysfunction						
<30	0			0		
30-<35	0			0		
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	1 (0.3)	1	0.2	0		
Tendon discomfort						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Tendon pain						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Trigger finger						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Synovial and bursal disorders						
<30	1 (1.2)	1	0.9	0		
30-<35	6 (1.4)	6	1.0	2 (1.0)	2	0.7
35-<40	5 (1.2)	5	1.0	3 (1.4)	3	1.2
>=40	4 (1.0)	4	0.8	0		
Bursitis						
<30	0			0		
30-<35	4 (0.9)	4	0.7	2 (1.0)	2	0.7
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Synovial cyst						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	0		
Synovitis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Bursal fluid accumulation						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)						
<30	0			0		
30-<35	4 (0.9)	8	1.4	3 (1.4)	3	1.1
35-<40	8 (2.0)	9	1.7	1 (0.5)	1	0.4
>=40	7 (1.8)	7	1.4	7 (3.4)	9	3.5
Intervertebral disc protrusion						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	4 (1.0)	4	0.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	4 (1.0)	4	0.8	3 (1.5)	4	1.6
Intervertebral disc degeneration						
<30	0			0		
30-<35	1 (0.2)	3	0.5	0		
35-<40	3 (0.7)	3	0.6	0		
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Scoliosis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			0		
Cervical spinal stenosis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Spondylolisthesis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Finger deformity						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Intervertebral disc displacement						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Kyphoscoliosis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Spinal stenosis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Foot deformity						
<30	0			0		
30-<35	0			2 (1.0)	2	0.7
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Intervertebral disc annular tear						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Kyphosis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Bone disorders (excl congenital and fractures)						
<30	1 (1.2)	1	0.9	2 (5.6)	2	4.2
30-<35	3 (0.7)	3	0.5	5 (2.4)	5	1.9
35-<40	3 (0.7)	3	0.6	6 (2.9)	6	2.3
>=40	4 (1.0)	5	1.0	1 (0.5)	1	0.4
Osteopenia						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Pain in jaw						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	0		
Bone cyst						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	2	0.4	0		
Osteonecrosis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Exostosis						
<30	0			1 (2.8)	1	2.1
30-<35	0			2 (1.0)	2	0.7
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Metatarsalgia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	2 (1.0)	2	0.8
>=40	0			0		
Coccydynia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Osteoporosis						
<30	0			1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
Pubic pain						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Connective tissue disorders (excl congenital)						
<30	0			1 (2.8)	1	2.1
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Myofascitis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Sjogren's syndrome						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Systemic lupus erythematosus						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Systemic scleroderma						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
General disorders and administration site conditions						
<30	13 (16.0)	19	17.8	2 (5.6)	3	6.3
30-<35	101 (23.2)	158	27.4	40 (19.3)	76	28.2
35-<40	90 (22.2)	149	28.4	40 (19.2)	64	24.9
>=40	87 (22.7)	139	28.0	49 (24.0)	79	31.0
General system disorders NEC						
<30	12 (14.8)	17	15.9	1 (2.8)	1	2.1
30-<35	77 (17.7)	108	18.7	24 (11.6)	33	12.2
35-<40	67 (16.5)	101	19.2	27 (13.0)	31	12.1
>=40	69 (18.0)	98	19.7	34 (16.7)	48	18.8
Fatigue						
<30	6 (7.4)	6	5.6	0		
30-<35	38 (8.7)	43	7.5	12 (5.8)	13	4.8
35-<40	32 (7.9)	39	7.4	6 (2.9)	6	2.3
>=40	28 (7.3)	32	6.4	10 (4.9)	10	3.9
Asthenia						
<30	2 (2.5)	2	1.9	0		
30-<35	11 (2.5)	14	2.4	4 (1.9)	5	1.9
35-<40	12 (3.0)	16	3.0	4 (1.9)	4	1.6
>=40	10 (2.6)	21	4.2	3 (1.5)	3	1.2
Pain						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	2 (2.5)	2	1.9	0		
30-<35	5 (1.1)	6	1.0	1 (0.5)	1	0.4
35-<40	7 (1.7)	7	1.3	2 (1.0)	2	0.8
>=40	7 (1.8)	8	1.6	4 (2.0)	4	1.6
Early satiety						
<30	0			0		
30-<35	12 (2.8)	12	2.1	1 (0.5)	1	0.4
35-<40	8 (2.0)	8	1.5	1 (0.5)	1	0.4
>=40	6 (1.6)	6	1.2	0		
Malaise						
<30	2 (2.5)	4	3.7	0		
30-<35	7 (1.6)	7	1.2	0		
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	5 (1.3)	6	1.2	3 (1.5)	4	1.6
Influenza like illness						
<30	0			0		
30-<35	5 (1.1)	6	1.0	4 (1.9)	4	1.5
35-<40	7 (1.7)	7	1.3	1 (0.5)	1	0.4
>=40	5 (1.3)	5	1.0	8 (3.9)	8	3.1
Chest discomfort						
<30	1 (1.2)	1	0.9	0		
30-<35	3 (0.7)	3	0.5	0		
35-<40	3 (0.7)	3	0.6	2 (1.0)	3	1.2
>=40	2 (0.5)	2	0.4	0		
Chills						
<30	1 (1.2)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	0		
Non-cardiac chest pain						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	0		
>=40	3 (0.8)	3	0.6	3 (1.5)	3	1.2
Hunger						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	3 (0.7)	3	0.6	3 (1.4)	3	1.2
>=40	2 (0.5)	2	0.4	0		
Peripheral swelling						
<30	1 (1.2)	1	0.9	0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	2 (1.0)	2	0.8
>=40	0			2 (1.0)	2	0.8
Oedema peripheral						
<30	0			1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	2 (1.0)	2	0.7
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	1 (0.3)	1	0.2	3 (1.5)	3	1.2
Chest pain						
<30	0			0		
30-<35	2 (0.5)	2	0.3	2 (1.0)	2	0.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			2 (1.0)	2	0.8
>=40	1 (0.3)	1	0.2	3 (1.5)	3	1.2
Thirst						
<30	0			0		
30-<35	3 (0.7)	3	0.5	0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Hernia						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Swelling						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Swelling face						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Feeling cold						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	0			0		
Feeling hot						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Ill-defined disorder						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Sensation of foreign body						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Crying						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Hangover						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Fat tissue increased						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Inflammation						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	2	0.4	1 (0.5)	1	0.4
>=40	0			0		
Pseudocyst						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Sluggishness						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Axillary pain						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Sense of oppression						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	1	(0.2)	2	0.3	0			
35-<40	0				0			
>=40	0				0			
Discomfort								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	0				1	(0.5)	1	0.4
Facial pain								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Granuloma								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Gravitational oedema								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	0				1	(0.5)	1	0.4
Temperature intolerance								
<30	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Administration site reactions						
<30	0			1 (2.8)	2	4.2
30-<35	24 (5.5)	36	6.2	15 (7.2)	36	13.3
35-<40	17 (4.2)	29	5.5	13 (6.3)	22	8.6
>=40	24 (6.3)	34	6.8	15 (7.4)	22	8.6
Injection site bruising						
<30	0			0		
30-<35	13 (3.0)	14	2.4	7 (3.4)	10	3.7
35-<40	4 (1.0)	5	1.0	9 (4.3)	13	5.1
>=40	11 (2.9)	12	2.4	10 (4.9)	11	4.3
Injection site pain						
<30	0			1 (2.8)	1	2.1
30-<35	4 (0.9)	6	1.0	5 (2.4)	9	3.3
35-<40	6 (1.5)	6	1.1	5 (2.4)	6	2.3
>=40	9 (2.3)	12	2.4	5 (2.5)	5	2.0
Injection site pruritus						
<30	0			1 (2.8)	1	2.1
30-<35	5 (1.1)	5	0.9	0		
35-<40	3 (0.7)	3	0.6	0		
>=40	1 (0.3)	1	0.2	0		
Injection site mass						
<30	0			0		
30-<35	1 (0.2)	1	0.2	3 (1.4)	3	1.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	3 (0.7)	3	0.6	0		
>=40	0			0		
Injection site haematoma						
<30	0			0		
30-<35	0			1 (0.5)	9	3.3
35-<40	2 (0.5)	7	1.3	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Injection site erythema						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Injection site reaction						
<30	0			0		
30-<35	3 (0.7)	3	0.5	1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Injection site haemorrhage						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Injection site paraesthesia						
<30	0			0		
30-<35	0			2 (1.0)	2	0.7
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	2 (0.5)	2	0.4	0		
Application site haematoma						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Injection site inflammation						
<30	0			0		
30-<35	1 (0.2)	3	0.5	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Injection site induration						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Injection site swelling						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	2	0.8
>=40	1 (0.3)	1	0.2	0		
Vessel puncture site rash						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Injection site urticaria						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	2	0.4	0		
>=40	0			0		
Infusion site extravasation						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Vessel puncture site bruise						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Application site bruise						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Puncture site pain						
<30	0			0		
30-<35	0			1 (0.5)	2	0.7
35-<40	0			0		
>=40	0			0		
Body temperature conditions						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	2 (2.5)	2	1.9	0		
30-<35	9 (2.1)	11	1.9	4 (1.9)	5	1.9
35-<40	12 (3.0)	16	3.0	8 (3.8)	9	3.5
>=40	4 (1.0)	4	0.8	5 (2.5)	7	2.7
Pyrexia						
<30	2 (2.5)	2	1.9	0		
30-<35	9 (2.1)	11	1.9	4 (1.9)	5	1.9
35-<40	12 (3.0)	16	3.0	8 (3.8)	9	3.5
>=40	4 (1.0)	4	0.8	5 (2.5)	7	2.7
Tissue disorders NEC						
<30	0			0		
30-<35	2 (0.5)	2	0.3	2 (1.0)	2	0.7
35-<40	3 (0.7)	3	0.6	1 (0.5)	1	0.4
>=40	0			2 (1.0)	2	0.8
Cyst						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			1 (0.5)	1	0.4
Nodule						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Dysplasia						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Fat necrosis						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Hyperplasia						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Therapeutic and nontherapeutic effects (excl toxicity)						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Withdrawal syndrome						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Complications associated with device						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Injury associated with device						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Vascular stent occlusion						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Metabolism and nutrition disorders						
<30	13 (16.0)	17	15.9	4 (11.1)	5	10.5
30-<35	75 (17.2)	97	16.8	27 (13.0)	34	12.6
35-<40	61 (15.0)	88	16.7	31 (14.9)	42	16.3
>=40	50 (13.1)	65	13.1	21 (10.3)	27	10.6
Appetite and general nutritional disorders						
<30	11 (13.6)	12	11.2	1 (2.8)	2	4.2
30-<35	57 (13.1)	67	11.6	14 (6.8)	16	5.9
35-<40	40 (9.9)	53	10.1	8 (3.8)	10	3.9
>=40	33 (8.6)	40	8.1	5 (2.5)	8	3.1
Decreased appetite						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	10 (12.3)	10	9.4	1 (2.8)	2	4.2
30-<35	52 (11.9)	58	10.1	11 (5.3)	12	4.4
35-<40	32 (7.9)	37	7.0	7 (3.4)	8	3.1
>=40	30 (7.8)	34	6.8	3 (1.5)	4	1.6
Increased appetite						
<30	1 (1.2)	1	0.9	0		
30-<35	0			1 (0.5)	1	0.4
35-<40	4 (1.0)	4	0.8	0		
>=40	1 (0.3)	2	0.4	1 (0.5)	1	0.4
Food craving						
<30	0			0		
30-<35	4 (0.9)	4	0.7	1 (0.5)	1	0.4
35-<40	3 (0.7)	3	0.6	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Hyperphagia						
<30	0			0		
30-<35	3 (0.7)	3	0.5	1 (0.5)	1	0.4
35-<40	3 (0.7)	4	0.8	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	3	1.2
Malnutrition						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Food aversion						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	3	0.6	0		
>=40	2 (0.5)	2	0.4	0		
Lack of satiety						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	0			0		
Lipid metabolism disorders						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	5 (1.1)	6	1.0	6 (2.9)	6	2.2
35-<40	9 (2.2)	9	1.7	7 (3.4)	8	3.1
>=40	5 (1.3)	5	1.0	6 (2.9)	6	2.4
Dyslipidaemia						
<30	0			0		
30-<35	2 (0.5)	2	0.3	3 (1.4)	3	1.1
35-<40	5 (1.2)	5	1.0	4 (1.9)	5	1.9
>=40	3 (0.8)	3	0.6	2 (1.0)	2	0.8
Hypertriglyceridaemia						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Hypercholesterolaemia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	3 (1.4)	3	1.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Hyperlipidaemia						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			2 (1.0)	2	0.8
Cholesterosis						
<30	0			0		
30-<35	1 (0.2)	2	0.3	0		
35-<40	0			0		
>=40	0			0		
Vitamin related disorders						
<30	0			0		
30-<35	2 (0.5)	2	0.3	4 (1.9)	5	1.9
35-<40	11 (2.7)	16	3.0	3 (1.4)	3	1.2
>=40	9 (2.3)	10	2.0	3 (1.5)	4	1.6
Vitamin D deficiency						
<30	0			0		
30-<35	1 (0.2)	1	0.2	4 (1.9)	4	1.5
35-<40	8 (2.0)	8	1.5	2 (1.0)	2	0.8
>=40	8 (2.1)	8	1.6	2 (1.0)	2	0.8
Vitamin B12 deficiency						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	5 (1.2)	5	1.0	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=40	0				0			
Folate deficiency								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	1	(0.5)	1	0.4
>=40	1	(0.3)	1	0.2	1	(0.5)	1	0.4
Vitamin B complex deficiency								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	1	(0.3)	1	0.2	1	(0.5)	1	0.4
Vitamin A deficiency								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Vitamin B2 deficiency								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Glucose metabolism disorders (incl diabetes mellitus)								
<30	1	(1.2)	1	0.9	1	(2.8)	1	2.1
30-<35	5	(1.1)	10	1.7	4	(1.9)	4	1.5
35-<40	3	(0.7)	5	1.0	12	(5.8)	16	6.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	1 (0.3)	1	0.2	4 (2.0)	4	1.6
Hypoglycaemia						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	3 (0.7)	8	1.4	0		
35-<40	2 (0.5)	3	0.6	3 (1.4)	5	1.9
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Postprandial hypoglycaemia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	2	0.4	0		
>=40	0			0		
Glucose tolerance impaired						
<30	0			0		
30-<35	1 (0.2)	1	0.2	2 (1.0)	2	0.7
35-<40	0			2 (1.0)	2	0.8
>=40	0			0		
Type 2 diabetes mellitus						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			5 (2.4)	6	2.3
>=40	0			1 (0.5)	1	0.4
Diabetes mellitus						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hyperglycaemia						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Impaired fasting glucose						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			2 (1.0)	2	0.8
Insulin resistance						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Electrolyte and fluid balance conditions						
<30	1 (1.2)	2	1.9	1 (2.8)	1	2.1
30-<35	5 (1.1)	5	0.9	0		
35-<40	1 (0.2)	1	0.2	3 (1.4)	3	1.2
>=40	2 (0.5)	4	0.8	2 (1.0)	2	0.8
Hyponatraemia						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Dehydration						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Hypokalaemia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			2 (1.0)	2	0.8
>=40	2 (0.5)	4	0.8	0		
Hyperkalaemia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Electrolyte imbalance						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Polydipsia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Fluid retention						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Iron and trace metal metabolism disorders						
<30	0			0		
30-<35	1 (0.2)	1	0.2	3 (1.4)	3	1.1
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	0		
Iron deficiency						
<30	0			0		
30-<35	1 (0.2)	1	0.2	3 (1.4)	3	1.1
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	0		
Protein and amino acid metabolism disorders NEC						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Hypoalbuminaemia						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Purine and pyrimidine metabolism disorders						
<30	0			0		
30-<35	2 (0.5)	3	0.5	0		
35-<40	0			1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	3 (1.5)	3	1.2
Gout						
<30	0			0		
30-<35	2 (0.5)	3	0.5	0		
35-<40	0			1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
Hyperuricaemia						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Food intolerance syndromes						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Dairy intolerance						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Food intolerance								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Lactose intolerance								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Metabolism disorders NEC								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Hyperlipasaemia								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Bone, calcium, magnesium and phosphorus metabolism disorders								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hypomagnesaemia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Skin and subcutaneous tissue disorders						
<30	12 (14.8)	15	14.0	5 (13.9)	5	10.5
30-<35	62 (14.2)	81	14.0	21 (10.1)	28	10.4
35-<40	57 (14.0)	85	16.2	23 (11.1)	27	10.5
>=40	57 (14.9)	68	13.7	26 (12.7)	36	14.1
Epidermal and dermal conditions						
<30	7 (8.6)	7	6.6	3 (8.3)	3	6.3
30-<35	33 (7.6)	40	6.9	13 (6.3)	17	6.3
35-<40	34 (8.4)	46	8.8	18 (8.7)	21	8.2
>=40	31 (8.1)	36	7.2	18 (8.8)	24	9.4
Rash						
<30	1 (1.2)	1	0.9	0		
30-<35	11 (2.5)	14	2.4	3 (1.4)	5	1.9
35-<40	9 (2.2)	9	1.7	7 (3.4)	7	2.7
>=40	5 (1.3)	6	1.2	7 (3.4)	11	4.3
Pruritus						
<30	1 (1.2)	1	0.9	0		
30-<35	6 (1.4)	7	1.2	4 (1.9)	4	1.5
35-<40	4 (1.0)	4	0.8	0		
>=40	6 (1.6)	6	1.2	2 (1.0)	2	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Eczema						
<30	2 (2.5)	2	1.9	0		
30-<35	5 (1.1)	5	0.9	1 (0.5)	1	0.4
35-<40	3 (0.7)	3	0.6	2 (1.0)	2	0.8
>=40	3 (0.8)	3	0.6	1 (0.5)	1	0.4
Dry skin						
<30	0			1 (2.8)	1	2.1
30-<35	2 (0.5)	2	0.3	0		
35-<40	2 (0.5)	2	0.4	0		
>=40	4 (1.0)	4	0.8	2 (1.0)	2	0.8
Dermatitis						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Rash pruritic						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Pain of skin						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			1 (0.5)	1	0.4
Skin burning sensation						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	3 (0.7)	9	1.7	0		
>=40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
Dermatitis contact						
<30	0			0		
30-<35	2 (0.5)	3	0.5	0		
35-<40	2 (0.5)	3	0.6	4 (1.9)	4	1.6
>=40	1 (0.3)	1	0.2	0		
Skin lesion						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Erythema						
<30	0			0		
30-<35	0			3 (1.4)	3	1.1
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	0		
Skin irritation						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Psoriasis						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	2 (0.5)	2	0.3	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Blister						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	2 (1.0)	2	0.8
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Dermatitis allergic						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Skin disorder						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	2 (0.5)	3	0.6	0		
>=40	0			0		
Decubitus ulcer						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	0			0		
Dermatitis atopic						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Macule						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Prurigo						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Xanthelasma						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Papule						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Pityriasis rosea						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=40	0				0			
Rash maculo-papular								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Skin odour abnormal								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Perioral dermatitis								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Skin discolouration								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				2	(1.0)	2	0.8
>=40	0				0			
Drug eruption								
<30	0				0			
30-<35	0				0			
35-<40	0				1	(0.5)	1	0.4
>=40	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Photosensitivity reaction						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Rash erythematous						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Rash macular						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Skin reaction						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Skin appendage conditions						
<30	5 (6.2)	6	5.6	1 (2.8)	1	2.1
30-<35	30 (6.9)	33	5.7	5 (2.4)	7	2.6
35-<40	26 (6.4)	30	5.7	4 (1.9)	4	1.6
>=40	21 (5.5)	23	4.6	9 (4.4)	9	3.5
Alopecia						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	3 (3.7)	4	3.7	0		
30-<35	23 (5.3)	23	4.0	2 (1.0)	2	0.7
35-<40	17 (4.2)	17	3.2	3 (1.4)	3	1.2
>=40	10 (2.6)	11	2.2	0		
Hyperhidrosis						
<30	0			0		
30-<35	0			0		
35-<40	3 (0.7)	3	0.6	1 (0.5)	1	0.4
>=40	5 (1.3)	5	1.0	7 (3.4)	7	2.7
Cold sweat						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Miliaria						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Acne						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	3 (0.7)	3	0.6	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Hirsutism						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	2	0.4	0		
>=40	1 (0.3)	1	0.2	0		
Ingrowing nail						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	2	0.7
35-<40	2 (0.5)	2	0.4	0		
>=40	0			0		
Hidradenitis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Rosacea						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	2	0.4	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Hair growth abnormal						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	0			0		
Onychoclasis						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Nail bed inflammation								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Diffuse alopecia								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Hypertrichosis								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Nail discolouration								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Night sweats								
<30	0				0			
30-<35	1	(0.2)	1	0.2	1	(0.5)	1	0.4
35-<40	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	0			0		
Angioedema and urticaria						
<30	1 (1.2)	1	0.9	0		
30-<35	4 (0.9)	4	0.7	3 (1.4)	3	1.1
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	4 (1.0)	4	0.8	2 (1.0)	2	0.8
Urticaria						
<30	1 (1.2)	1	0.9	0		
30-<35	3 (0.7)	3	0.5	2 (1.0)	2	0.7
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	4 (1.0)	4	0.8	2 (1.0)	2	0.8
Cold urticaria						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Angioedema						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Cornification and dystrophic skin disorders						
<30	1 (1.2)	1	0.9	0		
30-<35	2 (0.5)	3	0.5	0		
35-<40	2 (0.5)	2	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	2 (0.5)	3	0.6	0		
Actinic keratosis						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	2	0.3	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Hyperkeratosis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Lichenoid keratosis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	2	0.4	0		
Skin striae						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Pigmentation disorders						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Ephelides						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Skin hyperpigmentation						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Cutaneous neoplasms benign						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Dermal cyst						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Skin vascular abnormalities						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Ecchymosis						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	1	(0.2)	1	0.2	1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Skin and subcutaneous tissue disorders NEC								
<30	0				0			
30-<35	0				0			
35-<40	0				1	(0.5)	1	0.4
>=40	0				1	(0.5)	1	0.4
Erythema nodosum								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	0				1	(0.5)	1	0.4
Skin ulcer								
<30	0				0			
30-<35	0				0			
35-<40	0				1	(0.5)	1	0.4
>=40	0				0			
Respiratory, thoracic and mediastinal disorders								
<30	15	(18.5)	17	15.9	3	(8.3)	3	6.3
30-<35	47	(10.8)	58	10.1	29	(14.0)	37	13.7
35-<40	59	(14.5)	75	14.3	32	(15.4)	39	15.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	52 (13.6)	75	15.1	40 (19.6)	55	21.6
Respiratory tract signs and symptoms						
<30	6 (7.4)	6	5.6	1 (2.8)	1	2.1
30-<35	19 (4.4)	22	3.8	8 (3.9)	9	3.3
35-<40	26 (6.4)	28	5.3	14 (6.7)	16	6.2
>=40	24 (6.3)	25	5.0	10 (4.9)	11	4.3
Oropharyngeal pain						
<30	1 (1.2)	1	0.9	0		
30-<35	13 (3.0)	16	2.8	4 (1.9)	5	1.9
35-<40	16 (3.9)	17	3.2	13 (6.3)	14	5.4
>=40	18 (4.7)	19	3.8	6 (2.9)	7	2.7
Upper respiratory tract inflammation						
<30	3 (3.7)	3	2.8	1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	2	0.4	1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
Upper-airway cough syndrome						
<30	1 (1.2)	1	0.9	0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	0			0		
Rhinorrhoea						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	3 (0.7)	3	0.6	0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Oropharyngeal discomfort						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Hiccups						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Dysphonia						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Catarrh						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			1 (0.5)	1	0.4
Paranasal sinus discomfort						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Sinus pain						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Diaphragmalgia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Pleuritic pain						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Yawning						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Upper respiratory tract congestion						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Upper respiratory tract disorders (excl infections)						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	8 (9.9)	8	7.5	1 (2.8)	1	2.1
30-<35	17 (3.9)	17	2.9	7 (3.4)	8	3.0
35-<40	10 (2.5)	11	2.1	2 (1.0)	4	1.6
>=40	16 (4.2)	17	3.4	8 (3.9)	8	3.1
Rhinitis allergic						
<30	3 (3.7)	3	2.8	0		
30-<35	2 (0.5)	2	0.3	2 (1.0)	3	1.1
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	3 (1.5)	3	1.2
Sinus congestion						
<30	0			1 (2.8)	1	2.1
30-<35	6 (1.4)	6	1.0	2 (1.0)	2	0.7
35-<40	2 (0.5)	2	0.4	1 (0.5)	3	1.2
>=40	5 (1.3)	5	1.0	1 (0.5)	1	0.4
Epistaxis						
<30	1 (1.2)	1	0.9	0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	4 (1.0)	4	0.8	0		
Nasal congestion						
<30	0			0		
30-<35	4 (0.9)	4	0.7	2 (1.0)	2	0.7
35-<40	3 (0.7)	3	0.6	0		
>=40	4 (1.0)	4	0.8	4 (2.0)	4	1.6
Tonsillar hypertrophy						
<30	1 (1.2)	1	0.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Nasal polyps								
<30	1	(1.2)	1	0.9	0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Nasal dryness								
<30	1	(1.2)	1	0.9	0			
30-<35	0				0			
35-<40	0				0			
>=40	0				0			
Paranasal cyst								
<30	1	(1.2)	1	0.9	0			
30-<35	0				0			
35-<40	0				0			
>=40	0				0			
Nasal septum deviation								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	1	(0.3)	1	0.2	0			
Paranasal sinus hypersecretion								
<30	0				0			
30-<35	2	(0.5)	2	0.3	0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			0		
>=40	0			0		
Vocal cord polyp						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Nasal adhesions						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Respiratory disorders NEC						
<30	2 (2.5)	2	1.9	1 (2.8)	1	2.1
30-<35	16 (3.7)	17	2.9	13 (6.3)	14	5.2
35-<40	23 (5.7)	26	4.9	16 (7.7)	17	6.6
>=40	20 (5.2)	25	5.0	21 (10.3)	24	9.4
Cough						
<30	1 (1.2)	1	0.9	0		
30-<35	14 (3.2)	14	2.4	8 (3.9)	9	3.3
35-<40	14 (3.4)	16	3.0	13 (6.3)	13	5.1
>=40	11 (2.9)	14	2.8	12 (5.9)	13	5.1
Sleep apnoea syndrome						
<30	1 (1.2)	1	0.9	0		
30-<35	0			2 (1.0)	2	0.7
35-<40	3 (0.7)	3	0.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
Dyspnoea						
<30	0			0		
30-<35	2 (0.5)	2	0.3	2 (1.0)	2	0.7
35-<40	3 (0.7)	3	0.6	2 (1.0)	2	0.8
>=40	3 (0.8)	3	0.6	4 (2.0)	4	1.6
Productive cough						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
Dyspnoea exertional						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Haemoptysis						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Respiratory disorder						
<30	0			1 (2.8)	1	2.1
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Respiratory tract congestion						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Hyperventilation						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Acute respiratory failure						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Pulmonary mass						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Bronchial disorders (excl neoplasms)						
<30	0			0		
30-<35	1 (0.2)	1	0.2	3 (1.4)	3	1.1
35-<40	9 (2.2)	9	1.7	2 (1.0)	2	0.8
>=40	4 (1.0)	4	0.8	8 (3.9)	11	4.3
Asthma						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	3 (1.4)	3	1.1
35-<40	7 (1.7)	7	1.3	2 (1.0)	2	0.8
>=40	3 (0.8)	3	0.6	4 (2.0)	6	2.4
Chronic obstructive pulmonary disease						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Wheezing						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Allergic bronchitis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	2	0.8
Lower respiratory tract disorders (excl obstruction and infection)						
<30	1 (1.2)	1	0.9	0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Atelectasis						
<30	1 (1.2)	1	0.9	0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Pulmonary fibrosis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Pleural disorders						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Pleural effusion						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Pleurisy						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Pulmonary vascular disorders						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Pulmonary embolism						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Injury, poisoning and procedural complications						
<30	6 (7.4)	6	5.6	8 (22.2)	11	23.0
30-<35	62 (14.2)	86	14.9	41 (19.8)	62	23.0
35-<40	60 (14.8)	84	16.0	27 (13.0)	46	17.9
>=40	60 (15.7)	88	17.7	45 (22.1)	57	22.4
Injuries NEC						
<30	1 (1.2)	1	0.9	6 (16.7)	8	16.7
30-<35	40 (9.2)	53	9.2	31 (15.0)	39	14.5
35-<40	46 (11.3)	58	11.0	22 (10.6)	36	14.0
>=40	39 (10.2)	56	11.3	37 (18.1)	47	18.4
Ligament sprain						
<30	0			1 (2.8)	1	2.1
30-<35	6 (1.4)	7	1.2	8 (3.9)	9	3.3
35-<40	7 (1.7)	9	1.7	2 (1.0)	2	0.8
>=40	8 (2.1)	8	1.6	8 (3.9)	8	3.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Fall						
<30	0			2 (5.6)	2	4.2
30-<35	4 (0.9)	4	0.7	1 (0.5)	1	0.4
35-<40	7 (1.7)	7	1.3	5 (2.4)	11	4.3
>=40	8 (2.1)	8	1.6	4 (2.0)	5	2.0
Muscle strain						
<30	0			2 (5.6)	2	4.2
30-<35	8 (1.8)	8	1.4	6 (2.9)	6	2.2
35-<40	1 (0.2)	1	0.2	4 (1.9)	4	1.6
>=40	8 (2.1)	9	1.8	3 (1.5)	3	1.2
Contusion						
<30	0			1 (2.8)	1	2.1
30-<35	4 (0.9)	4	0.7	5 (2.4)	5	1.9
35-<40	7 (1.7)	8	1.5	3 (1.4)	4	1.6
>=40	4 (1.0)	7	1.4	6 (2.9)	9	3.5
Arthropod sting						
<30	1 (1.2)	1	0.9	0		
30-<35	3 (0.7)	3	0.5	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Skin laceration						
<30	0			0		
30-<35	2 (0.5)	2	0.3	3 (1.4)	4	1.5
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	4 (2.0)	4	1.6
Arthropod bite						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	4 (0.9)	4	0.7	0		
35-<40	3 (0.7)	3	0.6	4 (1.9)	4	1.6
>=40	2 (0.5)	2	0.4	3 (1.5)	3	1.2
Limb injury						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	4 (1.0)	4	0.8	2 (1.0)	2	0.8
Skin abrasion						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	3 (0.7)	6	1.1	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Tooth fracture						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	3 (0.7)	3	0.6	0		
>=40	1 (0.3)	1	0.2	3 (1.5)	3	1.2
Ligament rupture						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Concussion						
<30	0			0		

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Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	0		
>=40	0			1 (0.5)	1	0.4
Epicondylitis						
<30	0			0		
30-<35	3 (0.7)	3	0.5	4 (1.9)	4	1.5
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Back injury						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Road traffic accident						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Muscle rupture						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Animal bite						
<30	0			0		
30-<35	3 (0.7)	3	0.5	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			0		
>=40	0			0		
Injury						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Wound						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Eyelid contusion						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Musculoskeletal injury						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Post-traumatic neck syndrome						
<30	0			0		
30-<35	0			0		
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Soft tissue foreign body						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Subdural haematoma						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Bone contusion						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Eye burns						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Foreign body in eye						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Head injury						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Ligament injury						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Muscle injury						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Nerve injury						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Post-traumatic pain						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Eyelid injury						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Face injury								
<30	0				1	(2.8)	1	2.1
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Skeletal injury								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Tendon injury								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Chest injury								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	0				1	(0.5)	1	0.4
Corneal abrasion								
<30	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
30-<35	0			1	(0.5)	1 0.4
35-<40	0			0		
>=40	0			1	(0.5)	1 0.4
Eye injury						
<30	0			0		
30-<35	0			0		
35-<40	0			1	(0.5)	1 0.4
>=40	0			0		
Gun shot wound						
<30	0			0		
30-<35	0			1	(0.5)	1 0.4
35-<40	0			0		
>=40	0			0		
Post concussion syndrome						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1	(0.5)	1 0.4
Scar						
<30	0			0		
30-<35	0			1	(0.5)	1 0.4
35-<40	0			0		
>=40	0			0		
Tendon rupture						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			2 (1.0)	3	1.2
>=40	0			0		
Bone and joint injuries						
<30	1 (1.2)	1	0.9	2 (5.6)	2	4.2
30-<35	9 (2.1)	11	1.9	6 (2.9)	6	2.2
35-<40	9 (2.2)	10	1.9	7 (3.4)	8	3.1
>=40	16 (4.2)	17	3.4	7 (3.4)	7	2.7
Foot fracture						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	2 (0.5)	3	0.5	2 (1.0)	2	0.7
35-<40	1 (0.2)	2	0.4	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Joint injury						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	0			0		
>=40	4 (1.0)	4	0.8	0		
Meniscus injury						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	2 (1.0)	3	1.2
>=40	3 (0.8)	3	0.6	2 (1.0)	2	0.8
Rib fracture						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Radius fracture						
<30	0			0		
30-<35	0			0		
35-<40	3 (0.7)	3	0.6	0		
>=40	0			1 (0.5)	1	0.4
Joint dislocation						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Hand fracture						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Fractured coccyx						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Stress fracture						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Thoracic vertebral fracture						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Upper limb fracture						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Wrist fracture						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Facial bones fracture						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Spinal compression fracture						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Ankle fracture						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			2 (1.0)	2	0.8
>=40	0			0		
Femur fracture						
<30	0			0		
30-<35	1 (0.2)	2	0.3	0		
35-<40	0			0		
>=40	0			0		
Tibia fracture						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Fibula fracture						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Torus fracture						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Procedural related injuries and complications NEC						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	11 (2.5)	15	2.6	7 (3.4)	9	3.3
35-<40	6 (1.5)	10	1.9	1 (0.5)	1	0.4
>=40	9 (2.3)	9	1.8	2 (1.0)	2	0.8
Procedural pain						
<30	0			1 (2.8)	1	2.1
30-<35	5 (1.1)	6	1.0	5 (2.4)	7	2.6
35-<40	2 (0.5)	2	0.4	0		
>=40	5 (1.3)	5	1.0	1 (0.5)	1	0.4
Injection related reaction						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Post procedural complication						
<30	0			0		
30-<35	3 (0.7)	4	0.7	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Administration related reaction						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Procedural nausea						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Anaphylactic transfusion reaction						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Suture related complication						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Anaemia postoperative						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Post procedural constipation						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Procedural haemorrhage						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Urinary retention postoperative						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Vaccination complication						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Post procedural haemorrhage						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Procedural vomiting						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Seroma						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	0			0		
Injuries by physical agents						
<30	2 (2.5)	2	1.9	0		
30-<35	2 (0.5)	2	0.3	3 (1.4)	3	1.1
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Heat exhaustion						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Heat illness						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Sunburn						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Thermal burn						
<30	0			0		
30-<35	0			2 (1.0)	2	0.7
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Hypobarism						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Burns second degree						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
Medication errors and other product use errors and issues						
<30	1 (1.2)	1	0.9	0		
30-<35	3 (0.7)	3	0.5	2 (1.0)	3	1.1
35-<40	4 (1.0)	4	0.8	0		
>=40	2 (0.5)	2	0.4	0		
Accidental overdose						
<30	0			0		
30-<35	2 (0.5)	2	0.3	2 (1.0)	3	1.1
35-<40	4 (1.0)	4	0.8	0		
>=40	1 (0.3)	1	0.2	0		
Medication error						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Incorrect dose administered						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Overdoses and underdoses NEC						
<30	0			0		
30-<35	0			2 (1.0)	2	0.7
35-<40	1 (0.2)	1	0.2	0		
>=40	3 (0.8)	3	0.6	0		
Overdose						
<30	0			0		
30-<35	0			2 (1.0)	2	0.7
35-<40	1 (0.2)	1	0.2	0		
>=40	3 (0.8)	3	0.6	0		
Exposures, chemical injuries and poisoning						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	0			0		
Exposure to toxic agent						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Reactive gastropathy						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Psychiatric disorders						
<30	4 (4.9)	6	5.6	4 (11.1)	4	8.4
30-<35	38 (8.7)	42	7.3	22 (10.6)	28	10.4
35-<40	39 (9.6)	50	9.5	26 (12.5)	40	15.6
>=40	43 (11.2)	62	12.5	31 (15.2)	41	16.1
Anxiety disorders and symptoms						
<30	1 (1.2)	1	0.9	2 (5.6)	2	4.2
30-<35	15 (3.4)	16	2.8	8 (3.9)	8	3.0
35-<40	16 (3.9)	16	3.0	10 (4.8)	10	3.9
>=40	14 (3.7)	15	3.0	11 (5.4)	12	4.7
Anxiety						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	10 (2.3)	10	1.7	8 (3.9)	8	3.0
35-<40	10 (2.5)	10	1.9	4 (1.9)	4	1.6
>=40	11 (2.9)	12	2.4	7 (3.4)	7	2.7
Stress						
<30	0			1 (2.8)	1	2.1
30-<35	4 (0.9)	4	0.7	0		
35-<40	2 (0.5)	2	0.4	3 (1.4)	3	1.2
>=40	2 (0.5)	2	0.4	2 (1.0)	2	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Panic attack						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Burnout syndrome						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Nervousness						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Post-traumatic stress disorder						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Acute stress disorder						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Agitation						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
Generalised anxiety disorder						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Depressed mood disorders and disturbances						
<30	3 (3.7)	3	2.8	1 (2.8)	1	2.1
30-<35	9 (2.1)	9	1.6	5 (2.4)	5	1.9
35-<40	6 (1.5)	8	1.5	8 (3.8)	10	3.9
>=40	15 (3.9)	19	3.8	13 (6.4)	13	5.1
Depressed mood						
<30	2 (2.5)	2	1.9	0		
30-<35	3 (0.7)	3	0.5	1 (0.5)	1	0.4
35-<40	3 (0.7)	4	0.8	2 (1.0)	2	0.8
>=40	6 (1.6)	6	1.2	6 (2.9)	6	2.4
Depression						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	4 (0.9)	4	0.7	2 (1.0)	2	0.7
35-<40	1 (0.2)	1	0.2	5 (2.4)	6	2.3
>=40	9 (2.3)	11	2.2	6 (2.9)	6	2.4
Major depression						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
<30	0			0		
30-<35	0			0		
35-<40	2	(0.5)	2 0.4	0		
>=40	1	(0.3)	1 0.2	0		
Anhedonia						
<30	0			0		
30-<35	1	(0.2)	1 0.2	0		
35-<40	1	(0.2)	1 0.2	0		
>=40	0			0		
Tearfulness						
<30	0			0		
30-<35	0			0		
35-<40	0			1	(0.5)	1 0.4
>=40	1	(0.3)	1 0.2	0		
Negative thoughts						
<30	0			0		
30-<35	1	(0.2)	1 0.2	0		
35-<40	0			0		
>=40	0			0		
Depressive symptom						
<30	0			0		
30-<35	0			1	(0.5)	1 0.4
35-<40	0			0		
>=40	0			0		
Persistent depressive disorder						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			1 (0.5)	1	0.4
35-<40	0			1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
Sleep disorders and disturbances						
<30	0			0		
30-<35	11 (2.5)	11	1.9	7 (3.4)	9	3.3
35-<40	14 (3.4)	15	2.9	11 (5.3)	13	5.1
>=40	15 (3.9)	16	3.2	11 (5.4)	11	4.3
Insomnia						
<30	0			0		
30-<35	8 (1.8)	8	1.4	5 (2.4)	5	1.9
35-<40	9 (2.2)	9	1.7	8 (3.8)	9	3.5
>=40	11 (2.9)	12	2.4	5 (2.5)	5	2.0
Sleep disorder						
<30	0			0		
30-<35	2 (0.5)	2	0.3	2 (1.0)	3	1.1
35-<40	3 (0.7)	3	0.6	2 (1.0)	2	0.8
>=40	1 (0.3)	1	0.2	3 (1.5)	3	1.2
Initial insomnia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	2	0.4	0		
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Middle insomnia						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Abnormal dreams						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Nightmare						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	2	0.8
>=40	0			1 (0.5)	1	0.4
Sleep terror						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Changes in physical activity						
<30	2 (2.5)	2	1.9	0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			0		
Restlessness						
<30	2 (2.5)	2	1.9	0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	0			0		
Tic						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Mood disorders and disturbances NEC						
<30	0			0		
30-<35	4 (0.9)	4	0.7	1 (0.5)	1	0.4
35-<40	3 (0.7)	3	0.6	2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	0		
Irritability						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	0			0		
Apathy						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Affective disorder						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Mood swings						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Sexual dysfunctions, disturbances and gender identity disorders						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Libido decreased						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Libido increased						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Suicidal and self-injurious behaviours NEC						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	2	0.7
35-<40	1 (0.2)	1	0.2	1 (0.5)	2	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Suicidal ideation						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	2	0.7
35-<40	1 (0.2)	1	0.2	1 (0.5)	2	0.8
>=40	2 (0.5)	2	0.4	0		
Suicide attempt						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Adjustment disorders (incl subtypes)						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
Adjustment disorder						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Grief reaction						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Adjustment disorder with depressed mood								
<30	0				1	(2.8)	1	2.1
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				2	(1.0)	2	0.8
Cognitive and attention disorders and disturbances								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	2	(0.5)	3	0.6	1	(0.5)	1	0.4
Attention deficit/hyperactivity disorder								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	1	(0.5)	1	0.4
Mental fatigue								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	2	0.4	0			
Manic and bipolar mood disorders and disturbances								
<30	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Bipolar disorder								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Deliria (incl confusion)								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	2	0.4	1	(0.5)	1	0.4
>=40	0				0			
Disorientation								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	2	0.4	1	(0.5)	1	0.4
>=40	0				0			
Psychiatric and behavioural symptoms NEC								
<30	0				0			
30-<35	1	(0.2)	1	0.2	1	(0.5)	1	0.4
35-<40	0				1	(0.5)	1	0.4
>=40	0				0			
Abulia								
<30	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Psychiatric symptom						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Psychiatric disorders NEC						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Alcoholic hangover						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Somatic symptom and related disorders						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Conversion disorder						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			0		
>=40	0			0		
Investigations						
<30	8 (9.9)	8	7.5	2 (5.6)	2	4.2
30-<35	28 (6.4)	32	5.5	9 (4.3)	16	5.9
35-<40	30 (7.4)	43	8.2	17 (8.2)	22	8.6
>=40	27 (7.0)	35	7.0	21 (10.3)	27	10.6
Protein and chemistry analyses NEC						
<30	2 (2.5)	2	1.9	0		
30-<35	0			0		
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	7 (1.8)	7	1.4	4 (2.0)	4	1.6
C-reactive protein increased						
<30	2 (2.5)	2	1.9	0		
30-<35	0			0		
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	7 (1.8)	7	1.4	4 (2.0)	4	1.6
Physical examination and organ system status topics						
<30	3 (3.7)	3	2.8	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	2 (0.5)	2	0.4	2 (1.0)	3	1.2
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Weight decreased						
<30	2 (2.5)	2	1.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Weight increased						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Body mass index decreased						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Respiratory rate increased						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Body temperature increased						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	2	0.8
>=40	0			0		
Cardiac and vascular investigations (excl enzyme tests)						
<30	2 (2.5)	2	1.9	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	3 (0.7)	4	0.7	0		
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	3 (0.8)	4	0.8	5 (2.5)	5	2.0
QRS axis abnormal						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Electrocardiogram ST segment depression						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Heart rate increased						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Blood pressure decreased						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Blood pressure increased						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	0			2 (1.0)	2	0.8
>=40	1 (0.3)	1	0.2	4 (2.0)	4	1.6
Cardiac murmur						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Pulse abnormal						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Blood pressure abnormal						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Electrocardiogram T wave amplitude decreased						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Electrocardiogram T wave inversion						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Electrocardiogram T wave abnormal						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Hepatobiliary investigations						
<30	0			0		
30-<35	6 (1.4)	7	1.2	4 (1.9)	6	2.2
35-<40	3 (0.7)	3	0.6	4 (1.9)	5	1.9
>=40	7 (1.8)	7	1.4	3 (1.5)	4	1.6
Gamma-glutamyltransferase increased						
<30	0			0		
30-<35	3 (0.7)	3	0.5	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	0		
Hepatic enzyme increased						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
Blood bilirubin increased						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			2 (1.0)	2	0.8
>=40	1 (0.3)	1	0.2	0		
Alanine aminotransferase increased						
<30	0			0		
30-<35	1 (0.2)	1	0.2	2 (1.0)	2	0.7
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Aspartate aminotransferase increased						
<30	0			0		
30-<35	1 (0.2)	1	0.2	2 (1.0)	2	0.7
35-<40	0			1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
Transaminases increased						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Gastrointestinal investigations						
<30	0			1 (2.8)	1	2.1
30-<35	2 (0.5)	2	0.3	0		
35-<40	7 (1.7)	8	1.5	1 (0.5)	1	0.4
>=40	4 (1.0)	5	1.0	0		
Lipase increased						
<30	0			1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	0		
35-<40	6 (1.5)	6	1.1	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	4 (1.0)	4	0.8	0		
Amylase increased						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Gastric pH						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Pancreatic enzymes increased						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Lipid analyses						
<30	0			0		
30-<35	3 (0.7)	5	0.9	2 (1.0)	3	1.1
35-<40	5 (1.2)	9	1.7	1 (0.5)	1	0.4
>=40	1 (0.3)	2	0.4	1 (0.5)	1	0.4
High density lipoprotein decreased						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	3 (0.7)	3	0.6	0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Blood cholesterol increased						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Low density lipoprotein increased						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Lipids increased						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	0			0		
Blood triglycerides increased						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Very low density lipoprotein increased						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Renal and urinary tract investigations and urinalyses						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	0			1 (0.5)	1	0.4
Blood creatinine increased						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Glomerular filtration rate decreased						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
White blood cells urine						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Blood urine present						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Endocrine investigations (incl sex hormones)						
<30	0			0		
30-<35	3 (0.7)	3	0.5	1 (0.5)	1	0.4
35-<40	3 (0.7)	5	1.0	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Blood calcitonin increased						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Blood thyroid stimulating hormone decreased						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	0		
>=40	1 (0.3)	1	0.2	0		
Thyroxine free increased						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Thyroxine increased						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
>=40	0			0		
Blood thyroid stimulating hormone abnormal						
<30	0			0		
30-<35	1	(0.2)	1 0.2	0		
35-<40	0			0		
>=40	0			0		
Blood thyroid stimulating hormone increased						
<30	0			0		
30-<35	0			0		
35-<40	0			1	(0.5)	1 0.4
>=40	0			0		
Enzyme investigations NEC						
<30	0			1	(2.8)	1 2.1
30-<35	2	(0.5)	2 0.3	2	(1.0)	2 0.7
35-<40	3	(0.7)	3 0.6	4	(1.9)	4 1.6
>=40	1	(0.3)	1 0.2	1	(0.5)	1 0.4
Blood creatine phosphokinase increased						
<30	0			1	(2.8)	1 2.1
30-<35	2	(0.5)	2 0.3	2	(1.0)	2 0.7
35-<40	2	(0.5)	2 0.4	3	(1.4)	3 1.2
>=40	1	(0.3)	1 0.2	1	(0.5)	1 0.4
Enzyme level increased						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Blood alkaline phosphatase increased						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Microbiology and serology investigations						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	2 (0.5)	2	0.4	0		
HIV test positive						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Human papilloma virus test positive						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Helicobacter test positive						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Haematology investigations (incl blood groups)						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			2 (1.0)	5	2.0
Haemoglobin decreased						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			1 (0.5)	1	0.4
Haematology test abnormal						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Haematocrit increased						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Haemoglobin increased						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Red blood cell count increased						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Red cell distribution width increased						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Investigations, imaging and histopathology procedures NEC						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Precancerous cells present						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Smear test						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1	(0.3)	1 0.2	0		
Endoscopy						
<30	0			0		
30-<35	0			1	(0.5)	1 0.4
35-<40	0			0		
>=40	0			0		
Water, electrolyte and mineral investigations						
<30	0			0		
30-<35	0			1	(0.5)	1 0.4
35-<40	2	(0.5)	2 0.4	1	(0.5)	1 0.4
>=40	0			1	(0.5)	1 0.4
Blood calcium decreased						
<30	0			0		
30-<35	0			0		
35-<40	1	(0.2)	1 0.2	0		
>=40	0			0		
Blood potassium increased						
<30	0			0		
30-<35	0			0		
35-<40	1	(0.2)	1 0.2	0		
>=40	0			0		
Blood iron decreased						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Blood sodium increased						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Serum ferritin decreased						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Metabolic, nutritional and blood gas investigations						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Blood glucose increased						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Blood uric acid increased						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Glycosylated haemoglobin increased								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	0				1	(0.5)	1	0.4
Vitamin D decreased								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	0				1	(0.5)	1	0.4
Cytogenetic investigations								
<30	0				0			
30-<35	2	(0.5)	2	0.3	1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Prostatic specific antigen increased								
<30	0				0			
30-<35	2	(0.5)	2	0.3	1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Reproductive organ and breast investigations (excl hormone analyses)								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	2	(0.5)	2	0.3	0			
35-<40	0				0			
>=40	0				0			
Biopsy breast								
<30	0				0			
30-<35	2	(0.5)	2	0.3	0			
35-<40	0				0			
>=40	0				0			
Musculoskeletal and soft tissue investigations (excl enzyme tests)								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Arthroscopy								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Immunology and allergy investigations								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	0				1	(0.5)	1	0.4
Antinuclear antibody positive								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Vascular disorders						
<30	5 (6.2)	6	5.6	2 (5.6)	2	4.2
30-<35	28 (6.4)	31	5.4	13 (6.3)	14	5.2
35-<40	31 (7.6)	32	6.1	18 (8.7)	19	7.4
>=40	26 (6.8)	28	5.6	12 (5.9)	15	5.9
Vascular hypertensive disorders						
<30	2 (2.5)	2	1.9	1 (2.8)	1	2.1
30-<35	11 (2.5)	11	1.9	8 (3.9)	9	3.3
35-<40	13 (3.2)	13	2.5	10 (4.8)	11	4.3
>=40	16 (4.2)	16	3.2	9 (4.4)	11	4.3
Hypertension						
<30	2 (2.5)	2	1.9	1 (2.8)	1	2.1
30-<35	11 (2.5)	11	1.9	8 (3.9)	9	3.3
35-<40	13 (3.2)	13	2.5	9 (4.3)	10	3.9
>=40	14 (3.7)	14	2.8	9 (4.4)	11	4.3
Essential hypertension						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Hypertensive emergency						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Hypertensive crisis						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Decreased and nonspecific blood pressure disorders and shock						
<30	1 (1.2)	1	0.9	0		
30-<35	8 (1.8)	9	1.6	1 (0.5)	1	0.4
35-<40	6 (1.5)	6	1.1	0		
>=40	4 (1.0)	5	1.0	1 (0.5)	1	0.4
Hypotension						
<30	1 (1.2)	1	0.9	0		
30-<35	4 (0.9)	4	0.7	1 (0.5)	1	0.4
35-<40	3 (0.7)	3	0.6	0		
>=40	2 (0.5)	3	0.6	1 (0.5)	1	0.4
Orthostatic hypotension						
<30	0			0		
30-<35	3 (0.7)	4	0.7	0		
35-<40	3 (0.7)	3	0.6	0		
>=40	2 (0.5)	2	0.4	0		
Circulatory collapse						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Vascular disorders NEC						
<30	2 (2.5)	3	2.8	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	4 (1.0)	4	0.8	4 (1.9)	4	1.6
>=40	2 (0.5)	2	0.4	0		
Hot flush						
<30	2 (2.5)	2	1.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	3 (0.7)	3	0.6	3 (1.4)	3	1.2
>=40	2 (0.5)	2	0.4	0		
Flushing						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Arteriosclerosis, stenosis, vascular insufficiency and necrosis						
<30	0			0		
30-<35	5 (1.1)	5	0.9	2 (1.0)	2	0.7
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
Peripheral venous disease						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	3 (0.7)	3	0.5	0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Peripheral coldness						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Aortic arteriosclerosis						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Arteriosclerosis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Raynaud's phenomenon						
<30	0			0		
30-<35	0			2 (1.0)	2	0.7
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Venous varices						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	3 (0.7)	3	0.6	0		
>=40	2 (0.5)	2	0.4	0		
Varicose vein						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	3 (0.7)	3	0.6	0		
>=40	2 (0.5)	2	0.4	0		
Vascular haemorrhagic disorders						
<30	0			1 (2.8)	1	2.1
30-<35	2 (0.5)	2	0.3	0		
35-<40	3 (0.7)	3	0.6	3 (1.4)	3	1.2
>=40	1 (0.3)	1	0.2	0		
Haematoma						
<30	0			1 (2.8)	1	2.1
30-<35	2 (0.5)	2	0.3	0		
35-<40	3 (0.7)	3	0.6	3 (1.4)	3	1.2
>=40	1 (0.3)	1	0.2	0		
Embolism and thrombosis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Thrombosis						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Thrombophlebitis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Deep vein thrombosis						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Thrombophlebitis superficial						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Vascular infections and inflammations						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Phlebitis						
<30	0			0		
30-<35	0			0		
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	1 (0.3)	1	0.2	0		
Arteritis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Lymphatic vessel disorders						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Lymphoedema						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Reproductive system and breast disorders						
<30	3 (3.7)	3	2.8	0		
30-<35	23 (5.3)	29	5.0	10 (4.8)	14	5.2
35-<40	38 (9.4)	49	9.3	8 (3.8)	10	3.9
>=40	32 (8.4)	41	8.3	14 (6.9)	15	5.9
Menstrual cycle and uterine bleeding disorders						
<30	2 (2.5)	2	1.9	0		
30-<35	9 (2.1)	9	1.6	1 (0.5)	4	1.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	17 (4.2)	22	4.2	0		
>=40	17 (4.4)	20	4.0	6 (2.9)	6	2.4
Menstruation irregular						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	9 (2.2)	9	1.7	0		
>=40	3 (0.8)	3	0.6	0		
Dysmenorrhoea						
<30	1 (1.2)	1	0.9	0		
30-<35	0			1 (0.5)	3	1.1
35-<40	3 (0.7)	4	0.8	0		
>=40	3 (0.8)	3	0.6	0		
Menorrhagia						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	3 (0.7)	4	0.8	0		
>=40	5 (1.3)	6	1.2	3 (1.5)	3	1.2
Metrorrhagia						
<30	0			0		
30-<35	3 (0.7)	3	0.5	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	3 (0.8)	3	0.6	1 (0.5)	1	0.4
Menstrual disorder						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	3 (0.8)	3	0.6	0		
Menstruation delayed						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Dysfunctional uterine bleeding						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	2 (0.5)	2	0.4	0		
Oligomenorrhoea						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Premenstrual syndrome						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Amenorrhoea						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Premenstrual pain						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Breast disorders						
<30	0			0		
30-<35	5 (1.1)	6	1.0	2 (1.0)	2	0.7
35-<40	8 (2.0)	9	1.7	3 (1.4)	4	1.6
>=40	4 (1.0)	5	1.0	2 (1.0)	2	0.8
Breast mass						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	3 (0.7)	3	0.6	1 (0.5)	2	0.8
>=40	3 (0.8)	3	0.6	0		
Breast cyst						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Fibrocystic breast disease						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Breast pain						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
<30	0			0		
30-<35	0			0		
35-<40	2	(0.5)	2 0.4	0		
>=40	0			1	(0.5)	1 0.4
Breast disorder						
<30	0			0		
30-<35	1	(0.2)	1 0.2	0		
35-<40	1	(0.2)	1 0.2	0		
>=40	0			0		
Nipple pain						
<30	0			0		
30-<35	0			0		
35-<40	1	(0.2)	1 0.2	0		
>=40	0			0		
Breast inflammation						
<30	0			0		
30-<35	1	(0.2)	1 0.2	0		
35-<40	0			0		
>=40	0			0		
Breast fibrosis						
<30	0			0		
30-<35	0			0		
35-<40	0			1	(0.5)	1 0.4
>=40	0			0		
Breast haematoma						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Menopause related conditions						
<30	1 (1.2)	1	0.9	0		
30-<35	3 (0.7)	3	0.5	2 (1.0)	3	1.1
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Menopausal symptoms						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	0			0		
Atrophic vulvovaginitis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Postmenopausal haemorrhage						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	2	0.7
35-<40	0			0		
>=40	0			0		
Uterine, pelvic and broad ligament disorders						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	4 (0.9)	4	0.7	0		
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	1 (0.5)	1	0.4
Uterine haemorrhage						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Endometriosis						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Uterine polyp						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Adenomyosis						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	0			0		
Vaginal prolapse						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Uterine enlargement						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Vulvovaginal disorders (excl infections and inflammations)						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	3 (0.7)	3	0.6	1 (0.5)	1	0.4
>=40	4 (1.0)	4	0.8	3 (1.5)	3	1.2
Vaginal haemorrhage						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	0		
>=40	3 (0.8)	3	0.6	1 (0.5)	1	0.4
Vulvovaginal pain						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Vulvovaginal dryness						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Vulvovaginal discomfort						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Vaginal polyp						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Vulvovaginal pruritus						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Ovarian and fallopian tube disorders						
<30	0			0		
30-<35	4 (0.9)	4	0.7	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	4 (1.0)	4	0.8	2 (1.0)	2	0.8
Ovarian cyst						
<30	0			0		
30-<35	3 (0.7)	3	0.5	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	3 (0.8)	3	0.6	1 (0.5)	1	0.4
Hydrosalpinx						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Polycystic ovaries						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Reproductive tract disorders NEC						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Pelvic pain						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Genital rash						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Genital pain						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Sexual function and fertility disorders						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Dyspareunia						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Erectile dysfunction						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Testicular and epididymal disorders						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Testicular mass						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Testicular pain						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Testicular disorder						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Cervix disorders (excl infections and inflammations)						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	0			0		
Cervical dysplasia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Cervical leukoplakia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Uterine cervical erosion						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Female reproductive tract infections and inflammations						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Uterine inflammation						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Prostatic disorders (excl infections and inflammations)						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	0			0		
Benign prostatic hyperplasia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Penile and scrotal disorders (excl infections and inflammations)						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Scrotal pain						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Cardiac disorders						
<30	3 (3.7)	3	2.8	1 (2.8)	3	6.3
30-<35	16 (3.7)	18	3.1	16 (7.7)	22	8.2
35-<40	22 (5.4)	23	4.4	12 (5.8)	15	5.8
>=40	13 (3.4)	18	3.6	4 (2.0)	4	1.6
Cardiac arrhythmias						
<30	2 (2.5)	2	1.9	1 (2.8)	1	2.1
30-<35	9 (2.1)	10	1.7	9 (4.3)	12	4.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	12 (3.0)	13	2.5	6 (2.9)	7	2.7
>=40	9 (2.3)	13	2.6	1 (0.5)	1	0.4
Atrial fibrillation						
<30	1 (1.2)	1	0.9	0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	2	0.7
35-<40	1 (0.2)	1	0.2	2 (1.0)	2	0.8
>=40	2 (0.5)	5	1.0	0		
Tachycardia						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	3 (1.4)	3	1.1
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	1 (0.3)	1	0.2	0		
Atrioventricular block first degree						
<30	0			0		
30-<35	1 (0.2)	1	0.2	3 (1.4)	3	1.1
35-<40	1 (0.2)	1	0.2	0		
>=40	3 (0.8)	3	0.6	1 (0.5)	1	0.4
Arrhythmia						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	0			0		
Ventricular extrasystoles						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
>=40	0			0		
Bundle branch block left						
<30	0			0		
30-<35	1	(0.2)	1 0.2	0		
35-<40	0			0		
>=40	1	(0.3)	1 0.2	0		
Sinus tachycardia						
<30	0			0		
30-<35	1	(0.2)	1 0.2	0		
35-<40	1	(0.2)	1 0.2	0		
>=40	0			0		
Cardiac flutter						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1	(0.3)	1 0.2	0		
Sinus bradycardia						
<30	0			1	(2.8)	1 2.1
30-<35	0			0		
35-<40	0			0		
>=40	1	(0.3)	1 0.2	0		
Supraventricular extrasystoles						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1	(0.3)	1 0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Atrial tachycardia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Atrioventricular block second degree						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Bradycardia						
<30	0			0		
30-<35	0			2 (1.0)	2	0.7
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Nodal rhythm						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Atrial flutter						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Atrioventricular block						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Bundle branch block right						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Defect conduction intraventricular						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Cardiac disorders, signs and symptoms NEC						
<30	1 (1.2)	1	0.9	0		
30-<35	5 (1.1)	5	0.9	5 (2.4)	7	2.6
35-<40	4 (1.0)	4	0.8	3 (1.4)	3	1.2
>=40	2 (0.5)	2	0.4	0		
Palpitations						
<30	1 (1.2)	1	0.9	0		
30-<35	4 (0.9)	4	0.7	4 (1.9)	6	2.2
35-<40	3 (0.7)	3	0.6	2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	0		
Cardiovascular disorder						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Hypertensive heart disease						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Coronary artery disorders						
<30	0			1 (2.8)	2	4.2
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	3 (0.7)	3	0.6	3 (1.4)	3	1.2
>=40	3 (0.8)	3	0.6	2 (1.0)	2	0.8
Angina pectoris						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	2 (1.0)	2	0.8
Acute myocardial infarction						
<30	0			1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Angina unstable						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
30-<35	0			0		
35-<40	0			0		
>=40	1	(0.3)	1 0.2	0		
Arteriosclerosis coronary artery						
<30	0			0		
30-<35	0			0		
35-<40	1	(0.2)	1 0.2	0		
>=40	0			0		
Coronary artery stenosis						
<30	0			0		
30-<35	0			0		
35-<40	1	(0.2)	1 0.2	0		
>=40	0			0		
Coronary artery disease						
<30	0			1	(2.8)	1 2.1
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Myocardial infarction						
<30	0			0		
30-<35	0			0		
35-<40	0			2	(1.0)	2 0.8
>=40	0			0		
Cardiac valve disorders						
<30	0			0		
30-<35	2	(0.5)	2 0.3	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			1 (0.5)	2	0.8
>=40	0			0		
Aortic valve incompetence						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Aortic valve sclerosis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Mitral valve incompetence						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Tricuspid valve incompetence						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Cardiac neoplasms						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=40	0				0			
Pericardial cyst								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Myocardial disorders								
<30	0				0			
30-<35	0				2	(1.0)	2	0.7
35-<40	1	(0.2)	1	0.2	0			
>=40	0				1	(0.5)	1	0.4
Left ventricular hypertrophy								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Cardiomegaly								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	0				1	(0.5)	1	0.4
Cardiomyopathy								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Myocarditis						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Pericardial disorders						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Pericardial disease						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Renal and urinary disorders						
<30	4 (4.9)	5	4.7	3 (8.3)	3	6.3
30-<35	13 (3.0)	16	2.8	4 (1.9)	4	1.5
35-<40	13 (3.2)	16	3.0	7 (3.4)	8	3.1
>=40	11 (2.9)	14	2.8	8 (3.9)	9	3.5
Urinary tract signs and symptoms						
<30	2 (2.5)	2	1.9	1 (2.8)	1	2.1
30-<35	8 (1.8)	9	1.6	1 (0.5)	1	0.4
35-<40	9 (2.2)	10	1.9	1 (0.5)	1	0.4
>=40	7 (1.8)	8	1.6	5 (2.5)	6	2.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Dysuria						
<30	1 (1.2)	1	0.9	0		
30-<35	3 (0.7)	4	0.7	0		
35-<40	4 (1.0)	5	1.0	0		
>=40	1 (0.3)	1	0.2	0		
Haematuria						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Pollakiuria						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Renal pain						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Chromaturia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Stress urinary incontinence						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	0			0		
Micturition urgency						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Renal colic						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	2	0.4	0		
Urine odour abnormal						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Nocturia						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Urine flow decreased						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Bladder pain						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Polyuria						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Urinary incontinence						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Urinary retention						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Urolithiases						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	3 (0.7)	3	0.5	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	2 (0.5)	3	0.6	3 (1.4)	3	1.2
>=40	5 (1.3)	5	1.0	2 (1.0)	2	0.8
Nephrolithiasis						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	2 (0.5)	2	0.3	0		
35-<40	2 (0.5)	2	0.4	3 (1.4)	3	1.2
>=40	3 (0.8)	3	0.6	2 (1.0)	2	0.8
Calculus urinary						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Ureterolithiasis						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Renal disorders (excl nephropathies)						
<30	1 (1.2)	2	1.9	1 (2.8)	1	2.1
30-<35	2 (0.5)	3	0.5	2 (1.0)	2	0.7
35-<40	3 (0.7)	3	0.6	3 (1.4)	4	1.6
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Acute kidney injury						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	1 (0.3)	1	0.2	0		
Renal impairment						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Renal cyst						
<30	0			0		
30-<35	1 (0.2)	1	0.2	2 (1.0)	2	0.7
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
Hydronephrosis						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Nephrectasia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Chronic kidney disease						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Hypertensive nephropathy								
<30	0				0			
30-<35	0				0			
35-<40	0				1	(0.5)	1	0.4
>=40	0				0			
Bladder and bladder neck disorders (excl calculi)								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Cystitis noninfective								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Urethral disorders (excl calculi)								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Urethritis noninfective								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
<30	2 (2.5)	2	1.9	3 (8.3)	3	6.3
30-<35	17 (3.9)	18	3.1	10 (4.8)	12	4.4
35-<40	16 (3.9)	18	3.4	6 (2.9)	6	2.3
>=40	11 (2.9)	14	2.8	6 (2.9)	6	2.4
Cutaneous neoplasms benign						
<30	0			1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	2 (1.0)	2	0.7
35-<40	6 (1.5)	8	1.5	1 (0.5)	1	0.4
>=40	3 (0.8)	5	1.0	2 (1.0)	2	0.8
Melanocytic naevus						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	4 (1.0)	5	1.0	0		
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Acrochordon						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Seborrhoeic keratosis						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Dysplastic naevus						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Skin papilloma						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			1 (0.5)	1	0.4
Pyogenic granuloma						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Soft tissue neoplasms benign						
<30	1 (1.2)	1	0.9	1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	0		
Leiomyoma						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Lipoma						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			1 (2.8)	1	2.1
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	0		
Reproductive neoplasms female benign						
<30	0			0		
30-<35	3 (0.7)	3	0.5	2 (1.0)	2	0.7
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Uterine leiomyoma						
<30	0			0		
30-<35	2 (0.5)	2	0.3	2 (1.0)	2	0.7
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Ovarian adenoma						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Gastrointestinal neoplasms malignant and unspecified						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Gastrointestinal stromal tumour						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Skin neoplasms malignant and unspecified						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	3 (0.8)	3	0.6	2 (1.0)	2	0.8
Basal cell carcinoma						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Malignant melanoma						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Malignant melanoma in situ						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Neoplasm skin						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Breast neoplasms malignant and unspecified (incl nipple)								
<30	0				1	(2.8)	1	2.1
30-<35	2	(0.5)	2	0.3	1	(0.5)	1	0.4
35-<40	2	(0.5)	2	0.4	0			
>=40	0				1	(0.5)	1	0.4
Intraductal proliferative breast lesion								
<30	0				0			
30-<35	1	(0.2)	1	0.2	1	(0.5)	1	0.4
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Invasive ductal breast carcinoma								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Breast cancer								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Lobular breast carcinoma in situ						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Phyllodes tumour						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Gastrointestinal neoplasms benign						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			0		
Colon adenoma						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			0		
Breast neoplasms benign (incl nipple)						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Benign breast neoplasm						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Miscellaneous and site unspecified neoplasms malignant and unspecified						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Neoplasm						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Squamous cell carcinoma						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Endocrine neoplasms benign						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	0			0		
Benign neoplasm of thyroid gland						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Parathyroid tumour benign								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Hepatic and biliary neoplasms benign								
<30	0				0			
30-<35	2	(0.5)	2	0.3	0			
35-<40	0				0			
>=40	0				0			
Haemangioma of liver								
<30	0				0			
30-<35	2	(0.5)	2	0.3	0			
35-<40	0				0			
>=40	0				0			
Miscellaneous and site unspecified neoplasms benign								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Fibroma								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Adenoma benign						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Skeletal neoplasms benign						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Haemangioma of bone						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Endocrine neoplasms malignant and unspecified						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Papillary thyroid cancer						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Hepatobiliary neoplasms malignant and unspecified								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Hepatic neoplasm								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Reproductive neoplasms female malignant and unspecified								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Cervix carcinoma stage 0								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
Reproductive neoplasms male malignant and unspecified								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Prostate cancer								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Soft tissue neoplasms malignant and unspecified								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Dermatofibrosarcoma protuberans								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Leukaemias								
<30	0				0			
30-<35	0				0			
35-<40	0				1	(0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	0			0		
Hairy cell leukaemia						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Nervous system neoplasms malignant and unspecified NEC						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Glioblastoma						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Ocular neoplasms						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Eyelid haemangioma						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=40	0				0			
Plasma cell neoplasms								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Paraproteinaemia								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Renal and urinary tract neoplasms benign								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Kidney angiomyolipoma								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Renal and urinary tract neoplasms malignant and unspecified								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			0		
>=40	0			0		
Urinary tract neoplasm						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Ear and labyrinth disorders						
<30	2 (2.5)	2	1.9	1 (2.8)	1	2.1
30-<35	17 (3.9)	21	3.6	7 (3.4)	8	3.0
35-<40	14 (3.4)	18	3.4	7 (3.4)	10	3.9
>=40	12 (3.1)	15	3.0	9 (4.4)	10	3.9
Inner ear and VIIIth cranial nerve disorders						
<30	0			1 (2.8)	1	2.1
30-<35	7 (1.6)	9	1.6	6 (2.9)	7	2.6
35-<40	8 (2.0)	10	1.9	4 (1.9)	6	2.3
>=40	7 (1.8)	7	1.4	7 (3.4)	8	3.1
Vertigo						
<30	0			1 (2.8)	1	2.1
30-<35	6 (1.4)	6	1.0	4 (1.9)	4	1.5
35-<40	7 (1.7)	7	1.3	2 (1.0)	3	1.2
>=40	4 (1.0)	4	0.8	5 (2.5)	5	2.0
Tinnitus						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
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Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	2	0.3	1 (0.5)	1	0.4
35-<40	0			1 (0.5)	2	0.8
>=40	2 (0.5)	2	0.4	0		
Vertigo positional						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	2 (0.5)	3	0.6	1 (0.5)	1	0.4
>=40	0			2 (1.0)	3	1.2
Meniere's disease						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Motion sickness						
<30	0			0		
30-<35	0			1 (0.5)	2	0.7
35-<40	0			0		
>=40	0			0		
Aural disorders NEC						
<30	1 (1.2)	1	0.9	0		
30-<35	4 (0.9)	4	0.7	1 (0.5)	1	0.4
35-<40	6 (1.5)	7	1.3	1 (0.5)	1	0.4
>=40	4 (1.0)	4	0.8	0		
Ear pain						
<30	1 (1.2)	1	0.9	0		
30-<35	4 (0.9)	4	0.7	1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	3 (0.7)	4	0.8	1 (0.5)	1	0.4
>=40	4 (1.0)	4	0.8	0		
Ear discomfort						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			0		
Ear congestion						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Hearing disorders						
<30	1 (1.2)	1	0.9	0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Sudden hearing loss						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Deafness neurosensory						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	1 (0.3)	1	0.2	0		
Hypoacusis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Deafness						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Hyperacusis						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Middle ear disorders (excl congenital)						
<30	0			0		
30-<35	3 (0.7)	4	0.7	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Eustachian tube dysfunction						
<30	0			0		
30-<35	2 (0.5)	3	0.5	0		
35-<40	0			1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Eustachian tube disorder						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Tympanic membrane disorder						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
External ear disorders (excl congenital)						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Cerumen impaction						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Excessive cerumen production						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Eye disorders						
<30	2 (2.5)	4	3.7	1 (2.8)	1	2.1
30-<35	21 (4.8)	31	5.4	3 (1.4)	3	1.1
35-<40	11 (2.7)	11	2.1	11 (5.3)	16	6.2
>=40	10 (2.6)	12	2.4	9 (4.4)	11	4.3
Vision disorders						
<30	1 (1.2)	2	1.9	1 (2.8)	1	2.1
30-<35	4 (0.9)	6	1.0	0		
35-<40	3 (0.7)	3	0.6	3 (1.4)	3	1.2
>=40	6 (1.6)	6	1.2	0		
Diplopia						
<30	1 (1.2)	2	1.9	0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Vision blurred						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	0		
Myopia						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Visual impairment						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Photopsia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Anisometropia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Astigmatism						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Scintillating scotoma						
<30	0			1 (2.8)	1	2.1
30-<35	0			0		
35-<40	0			0		
>=40	0			0		
Ocular infections, irritations and inflammations						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	1 (1.2)	2	1.9	0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	4 (1.0)	4	0.8	3 (1.4)	5	1.9
>=40	1 (0.3)	2	0.4	3 (1.5)	4	1.6
Eye pruritus						
<30	1 (1.2)	1	0.9	0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			0		
Conjunctivitis allergic						
<30	1 (1.2)	1	0.9	0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Meibomian gland dysfunction						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Swelling of eyelid						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Conjunctival irritation						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Eczema eyelids								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Eye allergy								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Eye discharge								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Ocular hyperaemia								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	0				0			
Blepharitis								
<30	0				0			
30-<35	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
35-<40	0			0		
>=40	0			1	(0.5)	1 0.4
Conjunctival hyperaemia						
<30	0			0		
30-<35	0			0		
35-<40	0			1	(0.5)	1 0.4
>=40	0			0		
Erythema of eyelid						
<30	0			0		
30-<35	0			0		
35-<40	0			1	(0.5)	1 0.4
>=40	0			0		
Eye inflammation						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1	(0.5)	2 0.8
Eye irritation						
<30	0			0		
30-<35	0			0		
35-<40	0			1	(0.5)	1 0.4
>=40	0			0		
Keratitis						
<30	0			0		
30-<35	0			0		
35-<40	0			1	(0.5)	1 0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
>=40	0				0			
Ulcerative keratitis								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	0				1	(0.5)	1	0.4
Eye disorders NEC								
<30	0				0			
30-<35	5	(1.1)	5	0.9	2	(1.0)	2	0.7
35-<40	2	(0.5)	2	0.4	2	(1.0)	2	0.8
>=40	1	(0.3)	1	0.2	2	(1.0)	2	0.8
Dry eye								
<30	0				0			
30-<35	2	(0.5)	2	0.3	2	(1.0)	2	0.7
35-<40	2	(0.5)	2	0.4	1	(0.5)	1	0.4
>=40	0				1	(0.5)	1	0.4
Eyelid disorder								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Eye pain								
<30	0				0			
30-<35	1	(0.2)	1	0.2	0			
35-<40	0				1	(0.5)	1	0.4
>=40	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Lacrimation increased						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Ocular discomfort						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Anterior eye structural change, deposit and degeneration						
<30	0			0		
30-<35	7 (1.6)	8	1.4	0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			2 (1.0)	3	1.2
Cataract						
<30	0			0		
30-<35	6 (1.4)	7	1.2	0		
35-<40	0			0		
>=40	0			1 (0.5)	2	0.8
Xerophthalmia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Ectropion						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Pterygium						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Glaucoma and ocular hypertension						
<30	0			0		
30-<35	4 (0.9)	4	0.7	0		
35-<40	0			1 (0.5)	2	0.8
>=40	0			0		
Glaucoma						
<30	0			0		
30-<35	4 (0.9)	4	0.7	0		
35-<40	0			1 (0.5)	2	0.8
>=40	0			0		
Ocular structural change, deposit and degeneration NEC						
<30	0			0		
30-<35	2 (0.5)	3	0.5	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Macular degeneration						
<30	0			0		
30-<35	2 (0.5)	3	0.5	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Vitreous detachment						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
Ocular haemorrhages and vascular disorders NEC						
<30	0			0		
30-<35	3 (0.7)	3	0.5	0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Optic ischaemic neuropathy						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	0			0		
Eyelid haematoma						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Conjunctival haemorrhage						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Retina, choroid and vitreous haemorrhages and vascular disorders						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	2 (0.5)	2	0.4	0		
Retinopathy						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Retinal aneurysm						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Ocular neuromuscular disorders						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Blepharospasm						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Ocular sensory symptoms NEC						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Asthenopia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Hepatobiliary disorders						
<30	1 (1.2)	2	1.9	0		
30-<35	15 (3.4)	20	3.5	6 (2.9)	6	2.2
35-<40	14 (3.4)	17	3.2	1 (0.5)	1	0.4
>=40	14 (3.7)	17	3.4	6 (2.9)	7	2.7
Gallbladder disorders						
<30	1 (1.2)	2	1.9	0		
30-<35	10 (2.3)	11	1.9	1 (0.5)	1	0.4
35-<40	9 (2.2)	11	2.1	0		
>=40	11 (2.9)	14	2.8	4 (2.0)	4	1.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Cholelithiasis						
<30	1 (1.2)	2	1.9	0		
30-<35	6 (1.4)	6	1.0	1 (0.5)	1	0.4
35-<40	8 (2.0)	8	1.5	0		
>=40	8 (2.1)	8	1.6	3 (1.5)	3	1.2
Cholecystitis						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	3 (0.8)	3	0.6	1 (0.5)	1	0.4
Cholecystitis acute						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Gallbladder disorder						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Cholecystitis chronic						
<30	0			0		
30-<35	0			0		
35-<40	2 (0.5)	2	0.4	0		
>=40	0			0		
Biliary dyskinesia						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Hepatic and hepatobiliary disorders						
<30	0			0		
30-<35	6 (1.4)	9	1.6	5 (2.4)	5	1.9
35-<40	4 (1.0)	4	0.8	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	3 (1.5)	3	1.2
Hepatic steatosis						
<30	0			0		
30-<35	3 (0.7)	3	0.5	3 (1.4)	3	1.1
35-<40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	3 (1.5)	3	1.2
Hepatic function abnormal						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Hepatic cyst						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Granulomatous liver disease						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Hepatic pain						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Hypertransaminasaemia						
<30	0			0		
30-<35	1 (0.2)	3	0.5	0		
35-<40	0			0		
>=40	0			0		
Nonalcoholic fatty liver disease						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Portal vein thrombosis						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Bile duct disorders						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	2 (0.5)	2	0.4	0		
>=40	0			0		
Bile duct stone						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Biliary colic						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Blood and lymphatic system disorders						
<30	2 (2.5)	3	2.8	1 (2.8)	1	2.1
30-<35	10 (2.3)	10	1.7	4 (1.9)	5	1.9
35-<40	15 (3.7)	16	3.0	6 (2.9)	10	3.9
>=40	8 (2.1)	8	1.6	5 (2.5)	5	2.0
Anaemias nonhaemolytic and marrow depression						
<30	2 (2.5)	3	2.8	0		
30-<35	10 (2.3)	10	1.7	2 (1.0)	2	0.7
35-<40	8 (2.0)	8	1.5	4 (1.9)	5	1.9
>=40	4 (1.0)	4	0.8	4 (2.0)	4	1.6
Anaemia						
<30	2 (2.5)	3	2.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	6 (1.4)	6	1.0	2 (1.0)	2	0.7
35-<40	8 (2.0)	8	1.5	3 (1.4)	4	1.6
>=40	3 (0.8)	3	0.6	4 (2.0)	4	1.6
Iron deficiency anaemia						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	0			0		
Pernicious anaemia						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Blood loss anaemia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Hypochromic anaemia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Pancytopenia						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Spleen, lymphatic and reticuloendothelial system disorders						
<30	0			0		
30-<35	0			0		
35-<40	5 (1.2)	5	1.0	2 (1.0)	3	1.2
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Lymphadenopathy						
<30	0			0		
30-<35	0			0		
35-<40	3 (0.7)	3	0.6	1 (0.5)	2	0.8
>=40	1 (0.3)	1	0.2	0		
Splenic haemorrhage						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Hypersplenism						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Splenomegaly						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
White blood cell disorders						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	0		
>=40	1 (0.3)	1	0.2	0		
Leukocytosis						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Eosinophilia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Platelet disorders						
<30	0			1 (2.8)	1	2.1
30-<35	0			1 (0.5)	1	0.4
35-<40	0			2 (1.0)	2	0.8
>=40	1 (0.3)	1	0.2	0		
Thrombocytopenia						
<30	0			1 (2.8)	1	2.1
30-<35	0			1 (0.5)	1	0.4
35-<40	0			2 (1.0)	2	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	1 (0.3)	1	0.2	0		
Red blood cell disorders						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Polycythaemia						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Microcytosis						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Immune system disorders						
<30	0			1 (2.8)	1	2.1
30-<35	8 (1.8)	8	1.4	5 (2.4)	5	1.9
35-<40	13 (3.2)	13	2.5	8 (3.8)	9	3.5
>=40	7 (1.8)	7	1.4	7 (3.4)	8	3.1
Allergic conditions						
<30	0			1 (2.8)	1	2.1
30-<35	8 (1.8)	8	1.4	5 (2.4)	5	1.9
35-<40	13 (3.2)	13	2.5	8 (3.8)	9	3.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
>=40	6 (1.6)	6	1.2	7 (3.4)	8	3.1
Seasonal allergy						
<30	0			1 (2.8)	1	2.1
30-<35	4 (0.9)	4	0.7	4 (1.9)	4	1.5
35-<40	9 (2.2)	9	1.7	6 (2.9)	6	2.3
>=40	2 (0.5)	2	0.4	3 (1.5)	3	1.2
Hypersensitivity						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	2 (1.0)	2	0.8
>=40	1 (0.3)	1	0.2	3 (1.5)	3	1.2
Allergy to arthropod bite						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Drug hypersensitivity						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Food allergy						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Allergy to arthropod sting						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Rubber sensitivity						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Mite allergy						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Multiple allergies						
<30	0			0		
30-<35	0			0		
35-<40	0			1 (0.5)	1	0.4
>=40	0			0		
Immune disorders NEC						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Immunisation reaction						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Endocrine disorders						
<30	2 (2.5)	2	1.9	0		
30-<35	5 (1.1)	5	0.9	2 (1.0)	2	0.7
35-<40	3 (0.7)	5	1.0	2 (1.0)	2	0.8
>=40	4 (1.0)	4	0.8	2 (1.0)	3	1.2
Thyroid gland disorders						
<30	2 (2.5)	2	1.9	0		
30-<35	5 (1.1)	5	0.9	2 (1.0)	2	0.7
35-<40	2 (0.5)	4	0.8	2 (1.0)	2	0.8
>=40	4 (1.0)	4	0.8	2 (1.0)	2	0.8
Hypothyroidism						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	0			2 (1.0)	2	0.8
>=40	2 (0.5)	2	0.4	1 (0.5)	1	0.4
Thyroid mass						
<30	1 (1.2)	1	0.9	0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Goitre						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Hyperthyroidism						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	1 (0.2)	2	0.4	0		
>=40	0			0		
Thyroid cyst						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Primary hyperthyroidism						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Adrenal gland disorders						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Hyperadrenocorticism						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Endocrine disorders of gonadal function						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Hypogonadism						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	0			1 (0.5)	1	0.4
Surgical and medical procedures						
<30	0			0		
30-<35	8 (1.8)	8	1.4	4 (1.9)	4	1.5
35-<40	6 (1.5)	7	1.3	1 (0.5)	1	0.4
>=40	4 (1.0)	4	0.8	3 (1.5)	3	1.2
Head and neck therapeutic procedures						
<30	0			0		
30-<35	3 (0.7)	3	0.5	1 (0.5)	1	0.4
35-<40	2 (0.5)	2	0.4	0		
>=40	1 (0.3)	1	0.2	0		
Tooth extraction						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Dental operation						
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Dental implantation						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Sinus operation						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Therapeutic procedures and supportive care NEC						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	1 (0.3)	1	0.2	0		
Polypectomy						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	1 (0.5)	1	0.4
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Spinal anaesthesia						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Cyst removal						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Skin and subcutaneous tissue therapeutic procedures						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Acrochordon excision						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Skin neoplasm excision						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Gastrointestinal therapeutic procedures						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Gastric bypass						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	1 (0.5)	1	0.4
Abdominoplasty						
<30	0			0		
30-<35	0			1 (0.5)	1	0.4
35-<40	0			0		
>=40	0			0		
Bone and joint therapeutic procedures						
<30	0			0		
30-<35	0			0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	0			1 (0.5)	1	0.4
Synovial cyst removal						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Bone prosthesis insertion								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	0				1	(0.5)	1	0.4
Hip surgery								
<30	0				0			
30-<35	0				0			
35-<40	0				1	(0.5)	1	0.4
>=40	0				0			
Hepatobiliary therapeutic procedures								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				1	(0.5)	1	0.4
Cholecystectomy								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				1	(0.5)	1	0.4
Obstetric and gynaecological therapeutic procedures								

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Abortion induced								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Ovarian operation								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Soft tissue therapeutic procedures								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Lipoma excision								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Eye therapeutic procedures								
<30	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Glaucoma surgery						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Nervous system, skull and spine therapeutic procedures						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Intervertebral disc operation						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Social circumstances						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	1 (0.2)	1	0.2	1 (0.5)	1	0.4
>=40	3 (0.8)	3	0.6	0		
Economic and housing issues						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Stress at work						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			1 (0.5)	1	0.4
>=40	1 (0.3)	1	0.2	0		
Age related factors						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Menopause						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	1 (0.2)	1	0.2	0		
>=40	0			0		
Family issues						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Family stress						
<30	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
30-<35	0			0		
35-<40	0			0		
>=40	1	(0.3)	1 0.2	0		
Lifestyle issues						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1	(0.3)	1 0.2	0		
Bedridden						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1	(0.3)	1 0.2	0		
Pregnancy, puerperium and perinatal conditions						
<30	0			0		
30-<35	0			0		
35-<40	2	(0.5)	2 0.4	0		
>=40	3	(0.8)	3 0.6	0		
Abortions and stillbirth						
<30	0			0		
30-<35	0			0		
35-<40	2	(0.5)	2 0.4	0		
>=40	1	(0.3)	1 0.2	0		
Abortion spontaneous						

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R
<30	0			0		
30-<35	0			0		
35-<40	1	(0.2)	1 0.2	0		
>=40	1	(0.3)	1 0.2	0		
Abortion						
<30	0			0		
30-<35	0			0		
35-<40	1	(0.2)	1 0.2	0		
>=40	0			0		
Maternal complications of pregnancy						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	2	(0.5)	2 0.4	0		
Ectopic pregnancy						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1	(0.3)	1 0.2	0		
Morning sickness						
<30	0			0		
30-<35	0			0		
35-<40	0			0		
>=40	1	(0.3)	1 0.2	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R
Congenital, familial and genetic disorders						
<30	0			0		
30-<35	2 (0.5)	2	0.3	1 (0.5)	1	0.4
35-<40	0			0		
>=40	2 (0.5)	2	0.4	0		
Metabolic and nutritional disorders congenital						
<30	0			0		
30-<35	2 (0.5)	2	0.3	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Type V hyperlipidaemia						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	1 (0.3)	1	0.2	0		
Gilbert's syndrome						
<30	0			0		
30-<35	1 (0.2)	1	0.2	0		
35-<40	0			0		
>=40	0			0		
Musculoskeletal and connective tissue disorders congenital						
<30	0			0		
30-<35	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Carpus curvus								
<30	0				0			
30-<35	0				0			
35-<40	0				0			
>=40	1	(0.3)	1	0.2	0			
Skin and subcutaneous tissue disorders congenital								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Dermoid cyst								
<30	0				0			
30-<35	0				1	(0.5)	1	0.4
35-<40	0				0			
>=40	0				0			
Product issues								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Device issues								
<30	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 1

	Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			
Device expulsion								
<30	0				0			
30-<35	0				0			
35-<40	1	(0.2)	1	0.2	0			
>=40	0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

21 Adverse events by BMI at baseline - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N	PYE			N	PYE			N	PYE		
<30	66	82.8			68	91.0			77	97.8		
30-<35	163	214.0			139	177.2			135	179.2		
35-<40	99	131.0			103	140.6			97	129.1		
>=40	74	102.0			93	124.2			93	122.3		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Events												
<30	58	(87.9)	255	307.9	62	(91.2)	397	436.0	55	(71.4)	208	212.7
30-<35	132	(81.0)	720	336.5	118	(84.9)	761	429.6	107	(79.3)	462	257.9
35-<40	77	(77.8)	495	378.0	89	(86.4)	521	370.4	76	(78.4)	348	269.6
>=40	62	(83.8)	389	381.2	84	(90.3)	518	417.1	71	(76.3)	370	302.6
Serious												
Yes												
<30	5	(7.6)	5	6.0	6	(8.8)	6	6.6	7	(9.1)	8	8.2
30-<35	11	(6.7)	26	12.2	16	(11.5)	25	14.1	13	(9.6)	22	12.3
35-<40	10	(10.1)	16	12.2	6	(5.8)	12	8.5	11	(11.3)	17	13.2
>=40	5	(6.8)	6	5.9	12	(12.9)	28	22.5	6	(6.5)	6	4.9
No												
<30	58	(87.9)	250	301.9	62	(91.2)	391	429.4	54	(70.1)	200	204.5
30-<35	130	(79.8)	694	324.4	118	(84.9)	736	415.5	106	(78.5)	440	245.6
35-<40	76	(76.8)	479	365.8	89	(86.4)	509	361.9	76	(78.4)	331	256.4
>=40	62	(83.8)	383	375.4	83	(89.2)	490	394.5	71	(76.3)	364	297.7

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by BMI at baseline - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Severity									
Severe									
<30	1 (1.5)	1	1.2	5 (7.4)	7	7.7	4 (5.2)	4	4.1
30-<35	13 (8.0)	23	10.7	8 (5.8)	14	7.9	11 (8.1)	16	8.9
35-<40	5 (5.1)	16	12.2	3 (2.9)	4	2.8	9 (9.3)	14	10.8
>=40	3 (4.1)	3	2.9	11 (11.8)	26	20.9	4 (4.3)	5	4.1
Moderate									
<30	23 (34.8)	63	76.1	25 (36.8)	73	80.2	20 (26.0)	32	32.7
30-<35	47 (28.8)	97	45.3	62 (44.6)	184	103.9	41 (30.4)	91	50.8
35-<40	35 (35.4)	104	79.4	43 (41.7)	124	88.2	30 (30.9)	66	51.1
>=40	30 (40.5)	51	50.0	43 (46.2)	127	102.3	27 (29.0)	75	61.3
Mild									
<30	52 (78.8)	191	230.6	60 (88.2)	317	348.2	49 (63.6)	172	175.9
30-<35	123 (75.5)	600	280.4	105 (75.5)	563	317.8	91 (67.4)	355	198.1
35-<40	72 (72.7)	375	286.3	87 (84.5)	393	279.4	72 (74.2)	268	207.6
>=40	59 (79.7)	335	328.3	76 (81.7)	365	293.9	67 (72.0)	290	237.2
Relationship to trial product									
Missing									
<30	0			1 (1.5)	1	1.1	0		
30-<35	4 (2.5)	4	1.9	3 (2.2)	3	1.7	3 (2.2)	3	1.7
35-<40	3 (3.0)	3	2.3	3 (2.9)	3	2.1	3 (3.1)	4	3.1
>=40	3 (4.1)	4	3.9	3 (3.2)	3	2.4	0		
Probable									
<30	28 (42.4)	63	76.1	29 (42.6)	75	82.4	7 (9.1)	10	10.2
30-<35	54 (33.1)	133	62.2	62 (44.6)	216	121.9	27 (20.0)	47	26.2
35-<40	23 (23.2)	84	64.1	36 (35.0)	64	45.5	18 (18.6)	31	24.0
>=40	28 (37.8)	64	62.7	42 (45.2)	101	81.3	10 (10.8)	12	9.8

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by BMI at baseline - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Relationship to trial product									
Possible									
<30	26 (39.4)	47	56.7	28 (41.2)	92	101.0	14 (18.2)	17	17.4
30-<35	62 (38.0)	168	78.5	61 (43.9)	183	103.3	28 (20.7)	51	28.5
35-<40	36 (36.4)	97	74.1	48 (46.6)	141	100.2	26 (26.8)	57	44.2
>=40	29 (39.2)	95	93.1	45 (48.4)	118	95.0	25 (26.9)	45	36.8
Unlikely									
<30	47 (71.2)	145	175.1	56 (82.4)	229	251.5	51 (66.2)	181	185.1
30-<35	122 (74.8)	415	194.0	100 (71.9)	359	202.7	99 (73.3)	361	201.5
35-<40	69 (69.7)	311	237.5	73 (70.9)	313	222.5	70 (72.2)	256	198.3
>=40	58 (78.4)	226	221.5	72 (77.4)	296	238.3	69 (74.2)	313	256.0
Outcome									
Fatal									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Recovered									
<30	55 (83.3)	215	259.6	59 (86.8)	328	360.3	51 (66.2)	150	153.4
30-<35	128 (78.5)	568	265.5	113 (81.3)	657	370.9	98 (72.6)	361	201.5
35-<40	73 (73.7)	403	307.7	83 (80.6)	410	291.5	71 (73.2)	265	205.3
>=40	59 (79.7)	317	310.7	78 (83.9)	417	335.8	65 (69.9)	278	227.4
Recovering									
<30	3 (4.5)	3	3.6	0			3 (3.9)	3	3.1
30-<35	9 (5.5)	10	4.7	4 (2.9)	5	2.8	5 (3.7)	7	3.9
35-<40	2 (2.0)	5	3.8	7 (6.8)	9	6.4	3 (3.1)	3	2.3
>=40	5 (6.8)	14	13.7	6 (6.5)	12	9.7	6 (6.5)	6	4.9

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by BMI at baseline - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Outcome									
Recovered With Sequelae									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	3 (3.0)	3	2.3	2 (1.9)	2	1.4	0		
>=40	1 (1.4)	1	1.0	3 (3.2)	3	2.4	0		
Not Recovered									
<30	18 (27.3)	37	44.7	29 (42.6)	69	75.8	29 (37.7)	53	54.2
30-<35	65 (39.9)	141	65.9	50 (36.0)	95	53.6	48 (35.6)	92	51.3
35-<40	35 (35.4)	84	64.1	47 (45.6)	98	69.7	41 (42.3)	79	61.2
>=40	29 (39.2)	57	55.9	37 (39.8)	83	66.8	38 (40.9)	86	70.3
Unknown									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			1 (0.7)	4	2.3	1 (0.7)	1	0.6
35-<40	0			2 (1.9)	2	1.4	1 (1.0)	1	0.8
>=40	0			1 (1.1)	2	1.6	0		
Leading to									
Permanent treatment discontinuation									
<30	8 (12.1)	9	10.9	4 (5.9)	5	5.5	5 (6.5)	5	5.1
30-<35	9 (5.5)	10	4.7	10 (7.2)	10	5.6	4 (3.0)	6	3.3
35-<40	2 (2.0)	3	2.3	4 (3.9)	4	2.8	4 (4.1)	6	4.6
>=40	1 (1.4)	1	1.0	7 (7.5)	15	12.1	1 (1.1)	1	0.8
Temporary interruption of trial product									
<30	4 (6.1)	6	7.2	4 (5.9)	6	6.6	2 (2.6)	2	2.0
30-<35	8 (4.9)	15	7.0	15 (10.8)	35	19.8	5 (3.7)	5	2.8
35-<40	9 (9.1)	19	14.5	3 (2.9)	7	5.0	5 (5.2)	10	7.7
>=40	5 (6.8)	7	6.9	15 (16.1)	42	33.8	3 (3.2)	3	2.5

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

Adverse events by BMI at baseline - overview - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Leading to												
Dose reduction of trial product												
<30	2	(3.0)	2	2.4	6	(8.8)	9	9.9	0			
30-<35	5	(3.1)	7	3.3	11	(7.9)	29	16.4	1	(0.7)	1	0.6
35-<40	8	(8.1)	13	9.9	11	(10.7)	18	12.8	1	(1.0)	1	0.8
>=40	3	(4.1)	6	5.9	7	(7.5)	10	8.1	1	(1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.

22 Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects and exposure	N		PYE		N		PYE		N		PYE	
<30	66		82.8		68		91.0		77		97.8	
30-<35	163		214.0		139		177.2		135		179.2	
35-<40	99		131.0		103		140.6		97		129.1	
>=40	74		102.0		93		124.2		93		122.3	
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Adverse events												
<30	58	(87.9)	255	307.9	62	(91.2)	397	436.0	55	(71.4)	208	212.7
30-<35	132	(81.0)	720	336.5	118	(84.9)	761	429.6	107	(79.3)	462	257.9
35-<40	77	(77.8)	495	378.0	89	(86.4)	521	370.4	76	(78.4)	348	269.6
>=40	62	(83.8)	389	381.2	84	(90.3)	518	417.1	71	(76.3)	370	302.6
Gastrointestinal disorders												
<30	42	(63.6)	105	126.8	41	(60.3)	145	159.3	24	(31.2)	37	37.8
30-<35	100	(61.3)	294	137.4	89	(64.0)	362	204.3	46	(34.1)	91	50.8
35-<40	46	(46.5)	184	140.5	68	(66.0)	207	147.2	30	(30.9)	66	51.1
>=40	43	(58.1)	141	138.2	58	(62.4)	210	169.1	38	(40.9)	68	55.6
Gastrointestinal signs and symptoms												
<30	37	(56.1)	65	78.5	30	(44.1)	97	106.5	9	(11.7)	12	12.3
30-<35	78	(47.9)	156	72.9	68	(48.9)	257	145.1	25	(18.5)	42	23.4
35-<40	38	(38.4)	131	100.0	50	(48.5)	111	78.9	20	(20.6)	30	23.2
>=40	34	(45.9)	80	78.4	52	(55.9)	136	109.5	22	(23.7)	31	25.4
Nausea												
<30	28	(42.4)	40	48.3	20	(29.4)	41	45.0	6	(7.8)	6	6.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	53 (32.5)	70	32.7	45 (32.4)	94	53.1	12 (8.9)	18	10.0
35-<40	27 (27.3)	56	42.8	34 (33.0)	51	36.3	7 (7.2)	7	5.4
>=40	21 (28.4)	32	31.4	37 (39.8)	63	50.7	12 (12.9)	14	11.5
Vomiting									
<30	7 (10.6)	10	12.1	15 (22.1)	25	27.5	0		
30-<35	16 (9.8)	26	12.2	35 (25.2)	108	61.0	5 (3.7)	5	2.8
35-<40	21 (21.2)	40	30.5	17 (16.5)	28	19.9	2 (2.1)	2	1.5
>=40	10 (13.5)	17	16.7	21 (22.6)	27	21.7	4 (4.3)	5	4.1
Dyspepsia									
<30	4 (6.1)	4	4.8	5 (7.4)	5	5.5	1 (1.3)	1	1.0
30-<35	12 (7.4)	12	5.6	8 (5.8)	9	5.1	2 (1.5)	2	1.1
35-<40	7 (7.1)	7	5.3	5 (4.9)	6	4.3	1 (1.0)	1	0.8
>=40	4 (5.4)	4	3.9	7 (7.5)	10	8.1	1 (1.1)	1	0.8
Abdominal distension									
<30	1 (1.5)	1	1.2	4 (5.9)	6	6.6	0		
30-<35	2 (1.2)	3	1.4	10 (7.2)	11	6.2	8 (5.9)	8	4.5
35-<40	2 (2.0)	2	1.5	3 (2.9)	3	2.1	1 (1.0)	3	2.3
>=40	4 (5.4)	6	5.9	7 (7.5)	10	8.1	2 (2.2)	2	1.6
Eructation									
<30	0			4 (5.9)	5	5.5	1 (1.3)	1	1.0
30-<35	6 (3.7)	8	3.7	5 (3.6)	8	4.5	0		
35-<40	3 (3.0)	6	4.6	3 (2.9)	3	2.1	0		
>=40	2 (2.7)	2	2.0	4 (4.3)	5	4.0	0		
Flatulence									
<30	2 (3.0)	2	2.4	2 (2.9)	2	2.2	1 (1.3)	1	1.0
30-<35	6 (3.7)	8	3.7	3 (2.2)	5	2.8	2 (1.5)	3	1.7

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	6 (6.1)	8	6.1	6 (5.8)	6	4.3	2 (2.1)	3	2.3
>=40	7 (9.5)	7	6.9	5 (5.4)	8	6.4	2 (2.2)	2	1.6
Abdominal pain upper									
<30	2 (3.0)	2	2.4	2 (2.9)	3	3.3	1 (1.3)	1	1.0
30-<35	0			5 (3.6)	6	3.4	1 (0.7)	2	1.1
35-<40	3 (3.0)	3	2.3	4 (3.9)	6	4.3	5 (5.2)	6	4.6
>=40	6 (8.1)	6	5.9	5 (5.4)	6	4.8	4 (4.3)	4	3.3
Abdominal pain									
<30	3 (4.5)	4	4.8	4 (5.9)	4	4.4	0		
30-<35	9 (5.5)	9	4.2	2 (1.4)	4	2.3	1 (0.7)	1	0.6
35-<40	4 (4.0)	5	3.8	4 (3.9)	4	2.8	3 (3.1)	3	2.3
>=40	1 (1.4)	2	2.0	3 (3.2)	3	2.4	1 (1.1)	1	0.8
Abdominal discomfort									
<30	1 (1.5)	1	1.2	3 (4.4)	5	5.5	1 (1.3)	1	1.0
30-<35	12 (7.4)	14	6.5	5 (3.6)	5	2.8	2 (1.5)	2	1.1
35-<40	2 (2.0)	2	1.5	3 (2.9)	3	2.1	3 (3.1)	3	2.3
>=40	0			2 (2.2)	2	1.6	1 (1.1)	1	0.8
Regurgitation									
<30	0			0			0		
30-<35	0			2 (1.4)	2	1.1	0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			1 (1.1)	1	0.8	0		
Abdominal pain lower									
<30	0			0			1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	3 (2.2)	3	1.7	0		
35-<40	0			0			1 (1.0)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	2 (2.7)	2	2.0	0			1 (1.1)	1	0.8
Gastrointestinal sounds abnormal									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Abnormal faeces									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	0		
Aerophagia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Epigastric discomfort									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Gastrointestinal pain									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Abdominal rigidity									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Anal incontinence									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Breath odour									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Dysphagia									
<30	1	(1.5)	1 1.2	0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Faeces discoloured									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Faeces soft									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Retching									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Gastrointestinal motility and defaecation conditions									
<30	17 (25.8)	25	30.2	22 (32.4)	34	37.3	10 (13.0)	11	11.2
30-<35	51 (31.3)	113	52.8	46 (33.1)	77	43.5	24 (17.8)	35	19.5
35-<40	27 (27.3)	48	36.7	40 (38.8)	67	47.6	15 (15.5)	27	20.9
>=40	30 (40.5)	57	55.9	35 (37.6)	61	49.1	21 (22.6)	28	22.9
Diarrhoea									
<30	13 (19.7)	17	20.5	9 (13.2)	16	17.6	5 (6.5)	5	5.1
30-<35	32 (19.6)	70	32.7	28 (20.1)	51	28.8	22 (16.3)	31	17.3
35-<40	22 (22.2)	34	26.0	22 (21.4)	37	26.3	8 (8.2)	13	10.1
>=40	22 (29.7)	37	36.3	27 (29.0)	37	29.8	13 (14.0)	17	13.9
Constipation									
<30	3 (4.5)	6	7.2	15 (22.1)	15	16.5	4 (5.2)	4	4.1
30-<35	27 (16.6)	36	16.8	19 (13.7)	21	11.9	3 (2.2)	3	1.7
35-<40	9 (9.1)	13	9.9	19 (18.4)	24	17.1	7 (7.2)	11	8.5
>=40	12 (16.2)	15	14.7	17 (18.3)	22	17.7	8 (8.6)	8	6.5
Gastrooesophageal reflux disease									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	2 (3.0)	2	2.4	2 (2.9)	2	2.2	1 (1.3)	1	1.0
30-<35	5 (3.1)	6	2.8	4 (2.9)	4	2.3	1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	5 (4.9)	5	3.6	3 (3.1)	3	2.3
>=40	5 (6.8)	5	4.9	1 (1.1)	2	1.6	2 (2.2)	2	1.6
Change of bowel habit									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Irritable bowel syndrome									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Gastrointestinal motility disorder									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Gastrointestinal hypermotility									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Gastrooesophageal sphincter insufficiency									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Gastrointestinal conditions NEC									
<30	2 (3.0)	3	3.6	1 (1.5)	3	3.3	2 (2.6)	2	2.0
30-<35	3 (1.8)	3	1.4	8 (5.8)	9	5.1	1 (0.7)	1	0.6
35-<40	2 (2.0)	2	1.5	5 (4.9)	5	3.6	2 (2.1)	2	1.5
>=40	0			4 (4.3)	4	3.2	1 (1.1)	1	0.8
Hyperchlorhydria									
<30	1 (1.5)	2	2.4	1 (1.5)	3	3.3	0		
30-<35	2 (1.2)	2	0.9	6 (4.3)	7	4.0	1 (0.7)	1	0.6
35-<40	2 (2.0)	2	1.5	3 (2.9)	3	2.1	1 (1.0)	1	0.8
>=40	0			1 (1.1)	1	0.8	0		
Food poisoning									
<30	1 (1.5)	1	1.2	0			0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			2 (2.2)	2	1.6	0		
Gastrointestinal disorder									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			1 (1.1)	1	0.8	0		
Barrett's oesophagus									
<30	0			0			1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Gastric disorder									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Gastrointestinal melanosis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Gastrointestinal inflammatory conditions									
<30	3 (4.5)	3	3.6	0			0		
30-<35	4 (2.5)	4	1.9	8 (5.8)	8	4.5	4 (3.0)	5	2.8
35-<40	1 (1.0)	1	0.8	9 (8.7)	12	8.5	0		
>=40	1 (1.4)	1	1.0	0			2 (2.2)	3	2.5
Gastritis									
<30	3 (4.5)	3	3.6	0			0		
30-<35	1 (0.6)	1	0.5	6 (4.3)	6	3.4	2 (1.5)	3	1.7
35-<40	1 (1.0)	1	0.8	5 (4.9)	7	5.0	0		
>=40	1 (1.4)	1	1.0	0			2 (2.2)	3	2.5
Enteritis									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	0			2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Enterocolitis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			2 (1.9)	2	1.4	0		
>=40	0			0			0		
Chronic gastritis									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Duodenitis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Colitis									
<30	0			0			0		
30-<35	2 (1.2)	2	0.9	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Dental and gingival conditions									
<30	1 (1.5)	1	1.2	4 (5.9)	5	5.5	1 (1.3)	1	1.0
30-<35	5 (3.1)	6	2.8	4 (2.9)	4	2.3	4 (3.0)	4	2.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	2 (2.0)	2	1.5	2 (1.9)	2	1.4	0		
>=40	0			0			2 (2.2)	2	1.6
Toothache									
<30	0			3 (4.4)	3	3.3	1 (1.3)	1	1.0
30-<35	3 (1.8)	4	1.9	0			0		
35-<40	1 (1.0)	1	0.8	2 (1.9)	2	1.4	0		
>=40	0			0			1 (1.1)	1	0.8
Dental caries									
<30	0			2 (2.9)	2	2.2	0		
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	4 (3.0)	4	2.2
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			1 (1.1)	1	0.8
Gingival swelling									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Tooth deposit									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Periodontal disease									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			0			0		
Gastrointestinal vascular conditions									
<30	2 (3.0)	4	4.8	1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	0		
35-<40	0			3 (2.9)	3	2.1	1 (1.0)	1	0.8
>=40	0			3 (3.2)	3	2.4	0		
Haemorrhoids									
<30	1 (1.5)	2	2.4	1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	0		
35-<40	0			3 (2.9)	3	2.1	1 (1.0)	1	0.8
>=40	0			3 (3.2)	3	2.4	0		
Haemorrhoids thrombosed									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Varices oesophageal									
<30	1 (1.5)	1	1.2	0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Abdominal hernias and other abdominal wall conditions									
<30	1 (1.5)	1	1.2	2 (2.9)	2	2.2	4 (5.2)	4	4.1
30-<35	0			0			0		
35-<40	0			2 (1.9)	2	1.4	1 (1.0)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			0			0		
Hiatus hernia									
<30	0			1 (1.5)	1	1.1	2 (2.6)	2	2.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Umbilical hernia									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Abdominal hernia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Abdominal wall haematoma									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			0			0		
Inguinal hernia									
<30	1 (1.5)	1	1.2	0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gastrointestinal haemorrhages NEC									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	2 (2.7)	2	2.0	2 (2.2)	2	1.6	2 (2.2)	2	1.6
Intra-abdominal haemorrhage									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Haematochezia									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	2 (2.7)	2	2.0	1 (1.1)	1	0.8	0		
Mallory-Weiss syndrome									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Upper gastrointestinal haemorrhage									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Intra-abdominal haematoma									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Rectal haemorrhage									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Salivary gland conditions									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	2 (2.2)	3	2.4	0		
Dry mouth									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	0			0		
Parotid gland enlargement									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Salivary hypersecretion									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	2	1.6	0		
Noninfective sialoadenitis									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Benign neoplasms gastrointestinal									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	2 (2.6)	2	2.0
30-<35	4 (2.5)	5	2.3	0			1 (0.7)	1	0.6
35-<40	0			2 (1.9)	2	1.4	1 (1.0)	1	0.8
>=40	0			0			0		
Gastric polyps									
<30	0			0			1 (1.3)	1	1.0
30-<35	2 (1.2)	2	0.9	0			1 (0.7)	1	0.6
35-<40	0			2 (1.9)	2	1.4	0		
>=40	0			0			0		
Large intestine polyp									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	3 (1.8)	3	1.4	0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Oral soft tissue conditions									
<30	0			1 (1.5)	1	1.1	3 (3.9)	3	3.1
30-<35	0			1 (0.7)	1	0.6	1 (0.7)	1	0.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
35-<40	0			0			0		
>=40	0			0			0		
Stomatitis									
<30	0			1	(1.5)	1 1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Mouth ulceration									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Aphthous ulcer									
<30	0			0			2	(2.6)	2 2.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Lip swelling									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Odynophagia									
<30	0			0			1	(1.3)	1 1.0
30-<35	0			0			0		
35-<40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			0			0		
Diverticular disorders									
<30	1 (1.5)	1	1.2	0			0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
Diverticulum intestinal									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Diverticulum									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			1 (1.1)	1	0.8
Exocrine pancreas conditions									
<30	0			0			1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Pancreatitis acute									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Obstructive pancreatitis									
<30	0			0			1	(1.3)	1 1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Pancreatic cyst									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Anal and rectal conditions NEC									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Anal fissure									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Gastrointestinal stenosis and obstruction									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Small intestinal obstruction									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Gastrointestinal ulceration and perforation									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	1	(0.7)	1 0.6	0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Gastritis erosive									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Diverticular perforation									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Gastric ulcer									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Malabsorption conditions									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Malabsorption									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Peritoneal and retroperitoneal conditions									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Retroperitoneal mass									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Tongue conditions									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Glossodynia									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Infections and infestations									
<30	26 (39.4)	54	65.2	31 (45.6)	73	80.2	29 (37.7)	57	58.3
30-<35	64 (39.3)	122	57.0	64 (46.0)	117	66.0	59 (43.7)	112	62.5
35-<40	37 (37.4)	76	58.0	45 (43.7)	82	58.3	42 (43.3)	75	58.1
>=40	39 (52.7)	66	64.7	39 (41.9)	73	58.8	45 (48.4)	115	94.1
Infections - pathogen unspecified									
<30	22 (33.3)	39	47.1	29 (42.6)	63	69.2	26 (33.8)	49	50.1
30-<35	58 (35.6)	99	46.3	58 (41.7)	97	54.8	46 (34.1)	86	48.0
35-<40	33 (33.3)	61	46.6	40 (38.8)	68	48.3	36 (37.1)	59	45.7
>=40	33 (44.6)	51	50.0	35 (37.6)	61	49.1	39 (41.9)	87	71.2
Nasopharyngitis									
<30	13 (19.7)	21	25.4	16 (23.5)	28	30.8	15 (19.5)	22	22.5
30-<35	14 (8.6)	20	9.3	24 (17.3)	44	24.8	23 (17.0)	39	21.8
35-<40	8 (8.1)	12	9.2	16 (15.5)	24	17.1	8 (8.2)	11	8.5
>=40	12 (16.2)	16	15.7	12 (12.9)	19	15.3	13 (14.0)	20	16.4
Upper respiratory tract infection									
<30	2 (3.0)	2	2.4	7 (10.3)	10	11.0	5 (6.5)	7	7.2
30-<35	13 (8.0)	24	11.2	14 (10.1)	15	8.5	13 (9.6)	16	8.9
35-<40	12 (12.1)	16	12.2	9 (8.7)	9	6.4	8 (8.2)	13	10.1
>=40	10 (13.5)	12	11.8	12 (12.9)	14	11.3	12 (12.9)	14	11.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gastroenteritis									
<30	8 (12.1)	11	13.3	4 (5.9)	4	4.4	3 (3.9)	3	3.1
30-<35	6 (3.7)	7	3.3	6 (4.3)	6	3.4	2 (1.5)	3	1.7
35-<40	7 (7.1)	7	5.3	2 (1.9)	2	1.4	3 (3.1)	3	2.3
>=40	3 (4.1)	3	2.9	2 (2.2)	3	2.4	5 (5.4)	6	4.9
Bronchitis									
<30	0			2 (2.9)	2	2.2	2 (2.6)	2	2.0
30-<35	6 (3.7)	6	2.8	3 (2.2)	4	2.3	4 (3.0)	5	2.8
35-<40	3 (3.0)	3	2.3	5 (4.9)	6	4.3	3 (3.1)	3	2.3
>=40	1 (1.4)	2	2.0	4 (4.3)	4	3.2	4 (4.3)	5	4.1
Urinary tract infection									
<30	2 (3.0)	2	2.4	3 (4.4)	3	3.3	3 (3.9)	5	5.1
30-<35	9 (5.5)	12	5.6	3 (2.2)	6	3.4	2 (1.5)	4	2.2
35-<40	3 (3.0)	4	3.1	3 (2.9)	3	2.1	2 (2.1)	2	1.5
>=40	3 (4.1)	3	2.9	4 (4.3)	4	3.2	5 (5.4)	5	4.1
Sinusitis									
<30	2 (3.0)	2	2.4	1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	3 (2.2)	3	1.7	2 (1.5)	3	1.7
35-<40	1 (1.0)	1	0.8	6 (5.8)	10	7.1	1 (1.0)	1	0.8
>=40	2 (2.7)	2	2.0	4 (4.3)	5	4.0	7 (7.5)	8	6.5
Conjunctivitis									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	1 (1.0)	3	2.3	0			1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	2 (2.2)	2	1.6	2 (2.2)	3	2.5
Cystitis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			1 (1.5)	1	1.1	0		
30-<35	2 (1.2)	2	0.9	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			2 (1.9)	2	1.4	1 (1.0)	2	1.5
>=40	1 (1.4)	1	1.0	0			1 (1.1)	2	1.6
Pneumonia									
<30	0			0			1 (1.3)	1	1.0
30-<35	2 (1.2)	2	0.9	0			1 (0.7)	1	0.6
35-<40	0			2 (1.9)	2	1.4	1 (1.0)	1	0.8
>=40	0			2 (2.2)	3	2.4	2 (2.2)	2	1.6
Paronychia									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	0		
>=40	1 (1.4)	1	1.0	0			0		
Tonsillitis									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			2 (1.4)	2	1.1	0		
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	3 (3.1)	3	2.3
>=40	0			0			1 (1.1)	1	0.8
Pharyngitis									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	0			3 (2.2)	3	1.7
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			1 (1.1)	1	0.8	2 (2.2)	2	1.6
Lower respiratory tract infection									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	3 (1.8)	3	1.4	1 (0.7)	1	0.6	0		
35-<40	0			0			3 (3.1)	3	2.3
>=40	0			1 (1.1)	1	0.8	2 (2.2)	2	1.6
Gastrointestinal infection									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	1 (0.7)	2	1.1	0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Localised infection									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Otitis externa									
<30	0			0			0		
30-<35	2 (1.2)	2	0.9	0			0		
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	0		
Tooth infection									
<30	0			0			0		
30-<35	2 (1.2)	3	1.4	0			0		
35-<40	0			2 (1.9)	2	1.4	0		
>=40	1 (1.4)	1	1.0	0			1 (1.1)	1	0.8
Acute sinusitis									
<30	0			0			0		
30-<35	2 (1.2)	2	0.9	1 (0.7)	1	0.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	1 (1.0)	1	0.8	0			2 (2.1)	4	3.1
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
Abscess									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Breast abscess									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Mastitis									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Otitis media acute									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Periodontitis									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
>=40	0				0				1	(1.1)	2	1.6
Tooth abscess												
<30	0				1	(1.5)	1	1.1	0			
30-<35	2	(1.2)	2	0.9	0				0			
35-<40	1	(1.0)	1	0.8	0				1	(1.0)	2	1.5
>=40	1	(1.4)	1	1.0	0				0			
Urosepsis												
<30	0				1	(1.5)	1	1.1	0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				0			
Kidney infection												
<30	0				0				0			
30-<35	0				0				1	(0.7)	1	0.6
35-<40	0				0				1	(1.0)	1	0.8
>=40	0				1	(1.1)	1	0.8	0			
Vulvovaginitis												
<30	0				0				0			
30-<35	0				0				0			
35-<40	1	(1.0)	1	0.8	0				0			
>=40	0				1	(1.1)	2	1.6	0			
Appendicitis												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				1	(1.0)	1	0.7	0			
>=40	0				0				1	(1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Chronic sinusitis												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				1	(1.0)	1	0.7	0			
>=40	0				0				0			
Post procedural infection												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				1	(1.0)	1	0.7	0			
>=40	0				0				0			
Diverticulitis												
<30	0				0				0			
30-<35	0				1	(0.7)	1	0.6	1	(0.7)	1	0.6
35-<40	0				0				1	(1.0)	1	0.8
>=40	1	(1.4)	1	1.0	0				1	(1.1)	1	0.8
Implant site infection												
<30	0				0				0			
30-<35	0				1	(0.7)	1	0.6	0			
35-<40	0				0				0			
>=40	0				0				0			
Infected dermal cyst												
<30	0				0				0			
30-<35	0				1	(0.7)	1	0.6	0			
35-<40	0				0				0			
>=40	0				0				0			
Respiratory tract infection												

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			3 (3.2)	3	2.5
Rhinitis									
<30	0			0			2 (2.6)	2	2.0
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			1 (1.1)	1	0.8
Skin infection									
<30	0			0			0		
30-<35	0			1 (0.7)	2	1.1	0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Colonic abscess									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Ear infection									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			1 (1.1)	1	0.8
Empyema									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Eye infection									
<30	1	(1.5)	1 1.2	0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Gingival abscess									
<30	0			0			1	(1.3)	1 1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Gingivitis									
<30	0			0			1	(1.3)	1 1.0
30-<35	0			0			0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			1	(1.1)	1 0.8
Hordeolum									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	1	(1.4)	1 1.0	0			0		
Joint abscess									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
35-<40	0			0			0		
>=40	0			0			0		
Labyrinthitis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1	(1.4)	1 1.0	0			0		
Laryngitis									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	1	(1.0)	1 0.8	0			0		
>=40	1	(1.4)	2 2.0	0			0		
Mastoiditis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1	(1.1)	1 0.8
Osteomyelitis									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Otitis media									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			0			1 (1.1)	1	0.8
Otitis media chronic									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Pericoronitis									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Postoperative wound infection									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Pulpitis dental									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Pyelonephritis acute									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Sepsis									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	2	(2.0)	2 1.5	0			0		
>=40	0			0			0		
Sialoadenitis									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Sinobronchitis									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Subcutaneous abscess									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Tracheitis									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Tracheobronchitis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Vaginal infection									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Wound infection									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Viral infectious disorders									
<30	6 (9.1)	8	9.7	4 (5.9)	5	5.5	5 (6.5)	5	5.1
30-<35	15 (9.2)	16	7.5	14 (10.1)	15	8.5	12 (8.9)	12	6.7
35-<40	8 (8.1)	10	7.6	9 (8.7)	12	8.5	8 (8.2)	11	8.5
>=40	6 (8.1)	7	6.9	9 (9.7)	9	7.2	11 (11.8)	14	11.5
Influenza									
<30	3 (4.5)	3	3.6	1 (1.5)	1	1.1	3 (3.9)	3	3.1
30-<35	6 (3.7)	7	3.3	3 (2.2)	3	1.7	8 (5.9)	8	4.5
35-<40	4 (4.0)	4	3.1	5 (4.9)	6	4.3	2 (2.1)	5	3.9
>=40	4 (5.4)	5	4.9	6 (6.5)	6	4.8	5 (5.4)	6	4.9
Gastroenteritis viral									
<30	1 (1.5)	1	1.2	1 (1.5)	2	2.2	1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	3 (1.8)	3	1.4	4 (2.9)	4	2.3	1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	0			1 (1.0)	1	0.8
>=40	0			1 (1.1)	1	0.8	4 (4.3)	4	3.3
Viral infection									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	1 (1.0)	1	0.8	2 (1.9)	3	2.1	2 (2.1)	2	1.5
>=40	0			1 (1.1)	1	0.8	1 (1.1)	2	1.6
Herpes zoster									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	0		
30-<35	2 (1.2)	2	0.9	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			1 (1.1)	1	0.8
Viral pharyngitis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Herpes virus infection									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Respiratory tract infection viral									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	0			0		
Gastroenteritis norovirus									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Herpes simplex									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Ophthalmic herpes zoster									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Oral herpes									
<30	1 (1.5)	2	2.4	0			1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Pneumonia influenzal									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=40	0			0			0		
Viral diarrhoea									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Chikungunya virus infection									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Ear infection viral									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Rhinovirus infection									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Viral upper respiratory tract infection									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	2	(2.0)	3 2.3	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			0			1 (1.1)	1	0.8
Bacterial infectious disorders									
<30	2 (3.0)	2	2.4	3 (4.4)	3	3.3	1 (1.3)	1	1.0
30-<35	4 (2.5)	4	1.9	2 (1.4)	2	1.1	7 (5.2)	9	5.0
35-<40	2 (2.0)	3	2.3	1 (1.0)	1	0.7	1 (1.0)	3	2.3
>=40	2 (2.7)	4	3.9	2 (2.2)	2	1.6	3 (3.2)	5	4.1
Cellulitis									
<30	1 (1.5)	1	1.2	2 (2.9)	2	2.2	0		
30-<35	2 (1.2)	2	0.9	0			2 (1.5)	2	1.1
35-<40	2 (2.0)	3	2.3	0			1 (1.0)	1	0.8
>=40	0			0			1 (1.1)	2	1.6
Staphylococcal infection									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			1 (0.7)	2	1.1
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Ear infection bacterial									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	3	2.9	1 (1.1)	1	0.8	0		
Pharyngitis streptococcal									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			2 (1.5)	2	1.1
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	1 (1.1)	2	1.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Bacterial vaginosis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Breast cellulitis									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Furuncle									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	1	(0.7)	1 0.6
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Clostridium difficile colitis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1	(1.4)	1 1.0	0			0		
Helicobacter gastritis									
<30	0			0			1	(1.3)	1 1.0
30-<35	0			0			0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Helicobacter infection									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	1 (1.5)	1	1.2	0			0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Wound infection staphylococcal									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Fungal infectious disorders									
<30	5 (7.6)	5	6.0	2 (2.9)	2	2.2	2 (2.6)	2	2.0
30-<35	3 (1.8)	3	1.4	3 (2.2)	3	1.7	5 (3.7)	5	2.8
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	2 (2.1)	2	1.5
>=40	4 (5.4)	4	3.9	1 (1.1)	1	0.8	6 (6.5)	8	6.5
Onychomycosis									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	1 (1.4)	1	1.0	0			1 (1.1)	1	0.8
Vulvovaginal candidiasis									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			3 (3.2)	4	3.3
Fungal infection									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	0		
Fungal skin infection									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Tinea pedis									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			2 (2.2)	2	1.6
Vulvovaginal mycotic infection									
<30	1 (1.5)	1	1.2	0			1 (1.3)	1	1.0
30-<35	0			1 (0.7)	1	0.6	2 (1.5)	2	1.1
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Balanitis candida									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Candida infection									
<30	0			0			0		
30-<35	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Dermatophytosis of nail									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Genital candidiasis									
<30	2 (3.0)	2	2.4	0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Genital infection fungal									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Skin candida									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Tinea infection									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			1 (1.0)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	1 (1.4)	1	1.0	0			0		
Tinea versicolour									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Ectoparasitic disorders									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Acarodermatitis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Musculoskeletal and connective tissue disorders									
<30	10 (15.2)	13	15.7	21 (30.9)	36	39.5	9 (11.7)	12	12.3
30-<35	44 (27.0)	62	29.0	32 (23.0)	47	26.5	32 (23.7)	50	27.9
35-<40	25 (25.3)	45	34.4	23 (22.3)	39	27.7	25 (25.8)	34	26.3
>=40	20 (27.0)	27	26.5	22 (23.7)	29	23.4	18 (19.4)	30	24.5
Musculoskeletal and connective tissue disorders NEC									
<30	5 (7.6)	5	6.0	16 (23.5)	16	17.6	4 (5.2)	5	5.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	28 (17.2)	34	15.9	18 (12.9)	20	11.3	14 (10.4)	14	7.8
35-<40	14 (14.1)	16	12.2	13 (12.6)	19	13.5	10 (10.3)	12	9.3
>=40	10 (13.5)	11	10.8	9 (9.7)	11	8.9	5 (5.4)	7	5.7
Back pain									
<30	1 (1.5)	1	1.2	5 (7.4)	5	5.5	2 (2.6)	3	3.1
30-<35	16 (9.8)	18	8.4	10 (7.2)	11	6.2	5 (3.7)	5	2.8
35-<40	7 (7.1)	7	5.3	8 (7.8)	10	7.1	4 (4.1)	4	3.1
>=40	4 (5.4)	4	3.9	4 (4.3)	4	3.2	3 (3.2)	3	2.5
Pain in extremity									
<30	2 (3.0)	2	2.4	6 (8.8)	6	6.6	1 (1.3)	1	1.0
30-<35	2 (1.2)	2	0.9	2 (1.4)	2	1.1	4 (3.0)	4	2.2
35-<40	4 (4.0)	4	3.1	4 (3.9)	4	2.8	3 (3.1)	3	2.3
>=40	4 (5.4)	4	3.9	4 (4.3)	4	3.2	2 (2.2)	2	1.6
Neck pain									
<30	1 (1.5)	1	1.2	3 (4.4)	3	3.3	0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			2 (1.9)	2	1.4	2 (2.1)	2	1.5
>=40	0			2 (2.2)	2	1.6	0		
Musculoskeletal pain									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	3 (1.8)	3	1.4	4 (2.9)	4	2.3	2 (1.5)	2	1.1
35-<40	3 (3.0)	3	2.3	2 (1.9)	2	1.4	2 (2.1)	2	1.5
>=40	2 (2.7)	2	2.0	0			1 (1.1)	1	0.8
Rheumatic disorder									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		

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BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			0			0		
>=40	0			0			0		
Flank pain									
<30	1 (1.5)	1	1.2	0			0		
30-<35	2 (1.2)	2	0.9	0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Musculoskeletal chest pain									
<30	0			0			0		
30-<35	2 (1.2)	3	1.4	0			1 (0.7)	1	0.6
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	0		
>=40	1 (1.4)	1	1.0	0			0		
Muscle contracture									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Neck mass									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Axillary mass									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			0			0		
Limb mass									
<30	0			0			0		
30-<35	1 (0.6)	2	0.9	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Musculoskeletal discomfort									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Musculoskeletal stiffness									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Plantar fasciitis									
<30	0			0			0		
30-<35	2 (1.2)	2	0.9	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Joint disorders									
<30	5 (7.6)	6	7.2	9 (13.2)	11	12.1	3 (3.9)	3	3.1
30-<35	12 (7.4)	14	6.5	12 (8.6)	16	9.0	14 (10.4)	20	11.2
35-<40	13 (13.1)	18	13.7	11 (10.7)	15	10.7	12 (12.4)	12	9.3
>=40	8 (10.8)	8	7.8	12 (12.9)	15	12.1	12 (12.9)	14	11.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Arthralgia									
<30	1 (1.5)	2	2.4	3 (4.4)	3	3.3	1 (1.3)	1	1.0
30-<35	8 (4.9)	8	3.7	7 (5.0)	8	4.5	9 (6.7)	9	5.0
35-<40	9 (9.1)	11	8.4	5 (4.9)	8	5.7	6 (6.2)	6	4.6
>=40	6 (8.1)	6	5.9	8 (8.6)	10	8.1	4 (4.3)	4	3.3
Osteoarthritis									
<30	1 (1.5)	1	1.2	3 (4.4)	4	4.4	0		
30-<35	0			2 (1.4)	3	1.7	2 (1.5)	2	1.1
35-<40	1 (1.0)	1	0.8	3 (2.9)	3	2.1	5 (5.2)	5	3.9
>=40	0			3 (3.2)	4	3.2	5 (5.4)	6	4.9
Periarthritis									
<30	0			2 (2.9)	3	3.3	0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	1 (1.0)	2	1.4	0		
>=40	1 (1.4)	1	1.0	0			0		
Rotator cuff syndrome									
<30	1 (1.5)	1	1.2	0			0		
30-<35	2 (1.2)	4	1.9	2 (1.4)	3	1.7	0		
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	0		
>=40	0			0			0		
Spinal osteoarthritis									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	0			1 (0.7)	1	0.6	3 (2.2)	3	1.7
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			2 (2.2)	2	1.6
Arthritis									

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BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			0			1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			1 (1.1)	1	0.8	0		
Joint swelling									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			0			0		
Arthritis climacteric									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Arthropathy									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Femoroacetabular impingement									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Gouty arthritis									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				1	(1.1)	1	0.8
Joint effusion												
<30	1	(1.5)	1	1.2	0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				0			
Neuropathic arthropathy												
<30	0				0				0			
30-<35	0				0				1	(0.7)	1	0.6
35-<40	0				0				0			
>=40	0				0				0			
Psoriatic arthropathy												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				1	(1.1)	1	0.8
Rheumatoid arthritis												
<30	0				0				0			
30-<35	0				0				1	(0.7)	2	1.1
35-<40	0				0				0			
>=40	0				0				0			
Sacroiliitis												
<30	0				0				0			
30-<35	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Muscle disorders									
<30	0			2 (2.9)	4	4.4	1 (1.3)	1	1.0
30-<35	6 (3.7)	7	3.3	5 (3.6)	5	2.8	5 (3.7)	6	3.3
35-<40	3 (3.0)	5	3.8	1 (1.0)	1	0.7	2 (2.1)	2	1.5
>=40	3 (4.1)	4	3.9	2 (2.2)	2	1.6	0		
Muscle spasms									
<30	0			1 (1.5)	1	1.1	0		
30-<35	3 (1.8)	4	1.9	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	2 (2.7)	2	2.0	1 (1.1)	1	0.8	0		
Myalgia									
<30	0			1 (1.5)	3	3.3	0		
30-<35	3 (1.8)	3	1.4	3 (2.2)	3	1.7	4 (3.0)	5	2.8
35-<40	2 (2.0)	3	2.3	0			0		
>=40	1 (1.4)	2	2.0	1 (1.1)	1	0.8	0		
Diastasis recti abdominis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Muscular weakness									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			0			0		
Tendon, ligament and cartilage disorders									
<30	1 (1.5)	1	1.2	2 (2.9)	2	2.2	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	3 (2.2)	3	1.7
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	3 (3.1)	4	3.1
>=40	3 (4.1)	3	2.9	0			2 (2.2)	2	1.6
Trigger finger									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			0			0		
Tendon disorder									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Osteochondrosis									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Tendonitis									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			1 (0.7)	1	0.6	2 (1.5)	2	1.1
35-<40	0			0			2 (2.1)	2	1.5

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	1 (1.4)	1	1.0	0			1 (1.1)	1	0.8
Costochondritis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	0			0		
Ligament calcification									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Meniscal degeneration									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Tendon pain									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Synovial and bursal disorders									
<30	0			1 (1.5)	1	1.1	0		
30-<35	2 (1.2)	2	0.9	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	3 (3.1)	4	3.1
>=40	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Bursitis									
<30	0			1 (1.5)	1	1.1	0		
30-<35	2 (1.2)	2	0.9	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	3 (3.1)	4	3.1
>=40	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
Bone disorders (excl congenital and fractures)									
<30	0			1 (1.5)	2	2.2	1 (1.3)	1	1.0
30-<35	4 (2.5)	4	1.9	1 (0.7)	1	0.6	2 (1.5)	2	1.1
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	0		
>=40	1 (1.4)	1	1.0	0			1 (1.1)	1	0.8
Bone lesion									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Osteopenia									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Exostosis									
<30	0			0			1 (1.3)	1	1.0
30-<35	2 (1.2)	2	0.9	0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	1 (1.4)	1	1.0	0			1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Osteoporosis									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Bone pain									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Metatarsalgia									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Osteitis									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)									
<30	1 (1.5)	1	1.2	0			1 (1.3)	1	1.0
30-<35	0			2 (1.4)	2	1.1	4 (3.0)	4	2.2
35-<40	4 (4.0)	4	3.1	1 (1.0)	1	0.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
>=40	0				0				3	(3.2)	4	3.3
Intervertebral disc protrusion												
<30	0				0				0			
30-<35	0				2	(1.4)	2	1.1	2	(1.5)	2	1.1
35-<40	1	(1.0)	1	0.8	1	(1.0)	1	0.7	0			
>=40	0				0				1	(1.1)	1	0.8
Foot deformity												
<30	1	(1.5)	1	1.2	0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				1	(1.1)	2	1.6
Intervertebral disc degeneration												
<30	0				0				0			
30-<35	0				0				0			
35-<40	1	(1.0)	1	0.8	0				0			
>=40	0				0				0			
Scoliosis												
<30	0				0				0			
30-<35	0				0				2	(1.5)	2	1.1
35-<40	1	(1.0)	1	0.8	0				0			
>=40	0				0				0			
Spinal flattening												
<30	0				0				1	(1.3)	1	1.0
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Spondylolisthesis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			1 (1.1)	1	0.8
Connective tissue disorders (excl congenital)									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Polymyalgia rheumatica									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Nervous system disorders									
<30	6 (9.1)	6	7.2	16 (23.5)	23	25.3	6 (7.8)	9	9.2
30-<35	25 (15.3)	34	15.9	28 (20.1)	39	22.0	26 (19.3)	33	18.4
35-<40	20 (20.2)	35	26.7	20 (19.4)	29	20.6	14 (14.4)	25	19.4
>=40	12 (16.2)	30	29.4	18 (19.4)	27	21.7	17 (18.3)	25	20.4
Headaches									
<30	4 (6.1)	4	4.8	9 (13.2)	10	11.0	3 (3.9)	4	4.1
30-<35	16 (9.8)	19	8.9	12 (8.6)	16	9.0	9 (6.7)	9	5.0
35-<40	8 (8.1)	14	10.7	9 (8.7)	11	7.8	5 (5.2)	8	6.2

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	8 (10.8)	19	18.6	7 (7.5)	9	7.2	7 (7.5)	11	9.0
Headache									
<30	4 (6.1)	4	4.8	7 (10.3)	8	8.8	3 (3.9)	4	4.1
30-<35	14 (8.6)	16	7.5	9 (6.5)	13	7.3	8 (5.9)	8	4.5
35-<40	8 (8.1)	11	8.4	9 (8.7)	11	7.8	4 (4.1)	7	5.4
>=40	7 (9.5)	17	16.7	6 (6.5)	8	6.4	5 (5.4)	8	6.5
Migraine									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	0		
Migraine with aura									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Tension headache									
<30	0			0			0		
30-<35	2 (1.2)	2	0.9	1 (0.7)	1	0.6	0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	1 (1.4)	1	1.0	0			2 (2.2)	2	1.6
Occipital neuralgia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Sinus headache												
<30	0				0				0			
30-<35	0				0				1	(0.7)	1	0.6
35-<40	1	(1.0)	2	1.5	0				0			
>=40	0				0				0			
Neurological disorders NEC												
<30	1	(1.5)	1	1.2	6	(8.8)	10	11.0	4	(5.2)	4	4.1
30-<35	7	(4.3)	9	4.2	14	(10.1)	15	8.5	14	(10.4)	18	10.0
35-<40	12	(12.1)	14	10.7	9	(8.7)	12	8.5	7	(7.2)	9	7.0
>=40	8	(10.8)	9	8.8	7	(7.5)	9	7.2	6	(6.5)	7	5.7
Dizziness												
<30	0				4	(5.9)	4	4.4	0			
30-<35	6	(3.7)	7	3.3	5	(3.6)	5	2.8	9	(6.7)	11	6.1
35-<40	7	(7.1)	8	6.1	5	(4.9)	5	3.6	3	(3.1)	3	2.3
>=40	5	(6.8)	6	5.9	5	(5.4)	6	4.8	1	(1.1)	1	0.8
Paraesthesia												
<30	1	(1.5)	1	1.2	1	(1.5)	1	1.1	2	(2.6)	2	2.0
30-<35	0				2	(1.4)	2	1.1	1	(0.7)	1	0.6
35-<40	1	(1.0)	1	0.8	2	(1.9)	4	2.8	1	(1.0)	1	0.8
>=40	0				0				2	(2.2)	3	2.5
Dysgeusia												
<30	0				1	(1.5)	5	5.5	0			
30-<35	0				3	(2.2)	3	1.7	0			
35-<40	0				0				1	(1.0)	1	0.8
>=40	0				0				0			
Hypoaesthesia												

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BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<30	0			0			0		
30-<35	0			3	(2.2)	3 1.7	0		
35-<40	0			0			2	(2.1)	2 1.5
>=40	0			0			0		
Somnolence									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			1	(1.1)	1 0.8	1	(1.1)	1 0.8
Hyperaesthesia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			2	(1.9)	2 1.4	0		
>=40	1	(1.4)	1 1.0	0			0		
Dizziness postural									
<30	0			0			0		
30-<35	1	(0.6)	2 0.9	1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Syncope									
<30	0			0			1	(1.3)	1 1.0
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	2	(2.0)	2 1.5	0			0		
>=40	0			1	(1.1)	1 0.8	0		
Ageusia									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
30-<35	0				0				1	(0.7)	1	0.6
35-<40	0				0				0			
>=40	0				0				0			
Aphasia												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	1	(1.4)	1	1.0	0				0			
Coordination abnormal												
<30	0				0				0			
30-<35	0				0				1	(0.7)	1	0.6
35-<40	0				0				0			
>=40	0				0				0			
Dysaesthesia												
<30	0				0				0			
30-<35	0				0				0			
35-<40	1	(1.0)	1	0.8	0				0			
>=40	0				0				0			
Head discomfort												
<30	0				0				0			
30-<35	0				0				0			
35-<40	1	(1.0)	1	0.8	0				0			
>=40	0				0				0			
Hypogeusia												
<30	0				0				0			
30-<35	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Lethargy									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Loss of consciousness									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Neuralgia									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Phantom limb syndrome									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Presyncope									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			0			1 (1.1)	1	0.8
Restless legs syndrome									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Central nervous system vascular disorders									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	3 (2.2)	4	2.3	1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	2	1.5
>=40	1 (1.4)	1	1.0	3 (3.2)	5	4.0	0		
Cerebrovascular accident									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Carotid arteriosclerosis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			2 (2.2)	2	1.6	0		
Carotid artery stenosis									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
>=40	0			1	(1.1)	1	0.8	0			
Spinal epidural haematoma											
<30	0			0				0			
30-<35	0			0				0			
35-<40	0			0				0			
>=40	0			1	(1.1)	1	0.8	0			
Subarachnoid haemorrhage											
<30	0			0				0			
30-<35	0			0				0			
35-<40	0			0				0			
>=40	0			1	(1.1)	1	0.8	0			
Cerebral artery stenosis											
<30	0			0				0			
30-<35	0			0				0			
35-<40	0			1	(1.0)	1	0.7	0			
>=40	0			0				0			
Cerebral artery thrombosis											
<30	0			0				0			
30-<35	0			1	(0.7)	1	0.6	0			
35-<40	0			0				0			
>=40	0			0				0			
Cerebral infarction											
<30	0			0				0			
30-<35	0			1	(0.7)	1	0.6	0			
35-<40	0			0				0			
>=40	0			0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Ischaemic stroke									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	2	1.5
>=40	1 (1.4)	1	1.0	0			0		
Peripheral neuropathies									
<30	1 (1.5)	1	1.2	0			0		
30-<35	3 (1.8)	3	1.4	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	2 (2.0)	3	2.3	1 (1.0)	1	0.7	3 (3.1)	3	2.3
>=40	0			1 (1.1)	1	0.8	3 (3.2)	4	3.3
Meralgia paraesthetica									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Neuropathy peripheral									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	0		
>=40	0			0			1 (1.1)	2	1.6
Carpal tunnel syndrome									
<30	0			0			0		
30-<35	2 (1.2)	2	0.9	1 (0.7)	1	0.6	0		
35-<40	1 (1.0)	2	1.5	0			2 (2.1)	2	1.5
>=40	0			0			0		
Diabetic neuropathy									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			1 (1.1)	1	0.8
Nerve compression									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Polyneuropathy									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Spinal cord and nerve root disorders									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	4 (4.0)	4	3.1	0			1 (1.0)	1	0.8
>=40	0			1 (1.1)	2	1.6	2 (2.2)	2	1.6
Sciatica									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	2 (2.0)	2	1.5	0			1 (1.0)	1	0.8
>=40	0			0			0		
Radiculopathy									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Sacral radiculopathy									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Cervical radiculopathy									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			0			0		
Cervicobrachial syndrome									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Lumbar radiculopathy									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			0			2	(2.2)	2 1.6
Cranial nerve disorders (excl neoplasms)									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			1	(1.1)	1 0.8	0		
Facial paralysis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Anosmia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Encephalopathies									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Hyponatraemic encephalopathy									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Hepatic encephalopathy									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
35-<40	0			0			0		
>=40	0			0			0		
Sleep disturbances (incl subtypes)									
<30	0			1	(1.5)	1 1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Hypersomnia									
<30	0			1	(1.5)	1 1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Mental impairment disorders									
<30	0			0			1	(1.3)	1 1.0
30-<35	0			0			2	(1.5)	2 1.1
35-<40	0			1	(1.0)	1 0.7	1	(1.0)	1 0.8
>=40	1	(1.4)	1 1.0	0			0		
Memory impairment									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Amnesia									
<30	0			0			0		
30-<35	0			0			2	(1.5)	2 1.1
35-<40	0			0			1	(1.0)	1 0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=40	0			0			0		
Dementia Alzheimer's type									
<30	0			0			1	(1.3)	1 1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Vascular dementia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1	(1.4)	1 1.0	0			0		
Structural brain disorders									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Cerebral ventricle dilatation									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Movement disorders (incl parkinsonism)									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Tremor									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Neurological disorders of the eye									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Visual field defect									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Seizures (incl subtypes)									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1	(1.1)	1 0.8
Partial seizures									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1	(1.1)	1 0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
General disorders and administration site conditions									
<30	10 (15.2)	13	15.7	16 (23.5)	20	22.0	6 (7.8)	10	10.2
30-<35	17 (10.4)	26	12.2	21 (15.1)	25	14.1	14 (10.4)	21	11.7
35-<40	12 (12.1)	15	11.5	16 (15.5)	21	14.9	13 (13.4)	14	10.8
>=40	12 (16.2)	15	14.7	16 (17.2)	27	21.7	13 (14.0)	16	13.1
General system disorders NEC									
<30	10 (15.2)	11	13.3	13 (19.1)	15	16.5	2 (2.6)	2	2.0
30-<35	12 (7.4)	20	9.3	18 (12.9)	22	12.4	10 (7.4)	10	5.6
35-<40	10 (10.1)	11	8.4	15 (14.6)	18	12.8	8 (8.2)	9	7.0
>=40	8 (10.8)	10	9.8	11 (11.8)	13	10.5	8 (8.6)	9	7.4
Fatigue									
<30	7 (10.6)	8	9.7	6 (8.8)	6	6.6	0		
30-<35	7 (4.3)	11	5.1	11 (7.9)	12	6.8	4 (3.0)	4	2.2
35-<40	2 (2.0)	2	1.5	5 (4.9)	5	3.6	0		
>=40	3 (4.1)	5	4.9	6 (6.5)	6	4.8	0		
Asthenia									
<30	2 (3.0)	2	2.4	1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	0			4 (2.9)	4	2.3	0		
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	0		
>=40	1 (1.4)	1	1.0	1 (1.1)	2	1.6	0		
Influenza like illness									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	3 (2.9)	4	2.8	2 (2.1)	2	1.5
>=40	0			1 (1.1)	1	0.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Malaise									
<30	0			2 (2.9)	2	2.2	0		
30-<35	1 (0.6)	2	0.9	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Early satiety									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	2 (2.1)	2	1.5
>=40	1 (1.4)	1	1.0	2 (2.2)	2	1.6	0		
Non-cardiac chest pain									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	2 (1.9)	2	1.4	0		
>=40	0			0			0		
Pain									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	3 (3.0)	3	2.3	1 (1.0)	1	0.7	2 (2.1)	2	1.5
>=40	0			0			0		
Peripheral swelling									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			2 (1.5)	2	1.1
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	2 (2.2)	2	1.6
Oedema peripheral									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			2	(1.9)	2 1.4	1	(1.0)	1 0.8
>=40	0			0			3	(3.2)	3 2.5
Chest discomfort									
<30	0			1	(1.5)	1 1.1	0		
30-<35	0			0			0		
35-<40	1	(1.0)	1 0.8	0			1	(1.0)	1 0.8
>=40	0			0			1	(1.1)	1 0.8
Hunger									
<30	0			1	(1.5)	1 1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Swelling									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Face oedema									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Thirst decreased									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Chest pain									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	0			2 (2.2)	3	2.5
Feeling cold									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Chills									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Discomfort									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Inflammation									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			0			0		
>=40	0			0			0		
Polyp									
<30	0			0			0		
30-<35	1 (0.6)	2	0.9	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Sensation of foreign body									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Thirst									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Administration site reactions									
<30	0			1 (1.5)	2	2.2	1 (1.3)	3	3.1
30-<35	4 (2.5)	4	1.9	3 (2.2)	3	1.7	4 (3.0)	10	5.6
35-<40	1 (1.0)	2	1.5	2 (1.9)	2	1.4	2 (2.1)	2	1.5
>=40	1 (1.4)	1	1.0	7 (7.5)	12	9.7	3 (3.2)	3	2.5
Injection site pain									
<30	0			1 (1.5)	2	2.2	1 (1.3)	1	1.0
30-<35	3 (1.8)	3	1.4	0			2 (1.5)	6	3.3
35-<40	1 (1.0)	1	0.8	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			6 (6.5)	7	5.6	0		
Injection site erythema									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			1 (1.1)	1	0.8	0		
Injection site bruising									
<30	0			0			1 (1.3)	2	2.0
30-<35	1 (0.6)	1	0.5	0			2 (1.5)	2	1.1
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
Injection site reaction									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Injection site mass									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	2	1.6	1 (1.1)	1	0.8
Implant site pain									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Injection site discomfort									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Injection site haemorrhage									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Injection site urticaria									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Body temperature conditions									
<30	2 (3.0)	2	2.4	3 (4.4)	3	3.3	3 (3.9)	5	5.1
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	2 (2.1)	2	1.5
>=40	4 (5.4)	4	3.9	0			3 (3.2)	4	3.3
Pyrexia									
<30	2 (3.0)	2	2.4	3 (4.4)	3	3.3	3 (3.9)	5	5.1
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	2 (2.1)	2	1.5
>=40	4 (5.4)	4	3.9	0			3 (3.2)	4	3.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Therapeutic and nontherapeutic effects (excl toxicity)												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				1	(1.1)	1	0.8	0			
Drug intolerance												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				1	(1.1)	1	0.8	0			
Tissue disorders NEC												
<30	0				0				0			
30-<35	1	(0.6)	1	0.5	0				0			
35-<40	0				0				0			
>=40	0				1	(1.1)	1	0.8	0			
Mass												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				1	(1.1)	1	0.8	0			
Nodule												
<30	0				0				0			
30-<35	1	(0.6)	1	0.5	0				0			
35-<40	0				0				0			
>=40	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Complications associated with device									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Complication associated with device									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Metabolism and nutrition disorders									
<30	9 (13.6)	10	12.1	15 (22.1)	17	18.7	10 (13.0)	11	11.2
30-<35	13 (8.0)	20	9.3	23 (16.5)	26	14.7	12 (8.9)	15	8.4
35-<40	17 (17.2)	25	19.1	12 (11.7)	16	11.4	18 (18.6)	19	14.7
>=40	9 (12.2)	13	12.7	6 (6.5)	7	5.6	13 (14.0)	16	13.1
Appetite and general nutritional disorders									
<30	8 (12.1)	8	9.7	12 (17.6)	13	14.3	3 (3.9)	3	3.1
30-<35	8 (4.9)	14	6.5	18 (12.9)	20	11.3	7 (5.2)	7	3.9
35-<40	12 (12.1)	14	10.7	7 (6.8)	9	6.4	4 (4.1)	4	3.1
>=40	4 (5.4)	4	3.9	4 (4.3)	4	3.2	2 (2.2)	4	3.3
Decreased appetite									
<30	7 (10.6)	7	8.5	12 (17.6)	13	14.3	3 (3.9)	3	3.1
30-<35	8 (4.9)	11	5.1	17 (12.2)	18	10.2	7 (5.2)	7	3.9
35-<40	12 (12.1)	14	10.7	7 (6.8)	8	5.7	3 (3.1)	3	2.3

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	2 (2.7)	2	2.0	2 (2.2)	2	1.6	2 (2.2)	4	3.3
Hyperphagia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			1 (1.1)	1	0.8	0		
Increased appetite									
<30	1 (1.5)	1	1.2	0			0		
30-<35	2 (1.2)	3	1.4	0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	0		
Overweight									
<30	0			0			0		
30-<35	0			1 (0.7)	2	1.1	0		
35-<40	0			0			0		
>=40	0			0			0		
Cachexia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Obesity									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Electrolyte and fluid balance conditions									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	3 (2.2)	3	1.7	0		
35-<40	4 (4.0)	4	3.1	2 (1.9)	2	1.4	2 (2.1)	2	1.5
>=40	1 (1.4)	2	2.0	1 (1.1)	1	0.8	0		
Dehydration									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	2 (2.1)	2	1.5
>=40	0			0			0		
Hypokalaemia									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	0		
>=40	1 (1.4)	2	2.0	1 (1.1)	1	0.8	0		
Hyponatraemia									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Hyperkalaemia									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Lipid metabolism disorders									
<30	1 (1.5)	1	1.2	2 (2.9)	2	2.2	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	0			2 (1.5)	2	1.1
35-<40	1 (1.0)	1	0.8	2 (1.9)	2	1.4	4 (4.1)	4	3.1
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	2 (2.2)	2	1.6
Dyslipidaemia									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	2 (1.9)	2	1.4	3 (3.1)	3	2.3
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
Hyperlipidaemia									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Hypertriglyceridaemia									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Hypercholesterolaemia									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Purine and pyrimidine metabolism disorders									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	2	1.1
35-<40	1 (1.0)	2	1.5	0			0		
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	2	1.6
Gout									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	2	1.1
35-<40	1 (1.0)	2	1.5	0			0		
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	2	1.6
Hyperuricaemia									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Vitamin related disorders									
<30	1 (1.5)	1	1.2	0			1 (1.3)	1	1.0
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Vitamin B complex deficiency									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Folate deficiency									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Vitamin D deficiency									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Bone, calcium, magnesium and phosphorus metabolism disorders									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	2 (2.1)	2	1.5
>=40	3 (4.1)	3	2.9	0			0		
Hypomagnesaemia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	0		
>=40	0			0			0		
Hypercalcaemia									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	2 (2.7)	2	2.0	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Hypercalcitoninaemia									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Hypocalcaemia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Glucose metabolism disorders (incl diabetes mellitus)									
<30	0			0			3 (3.9)	3	3.1
30-<35	1 (0.6)	1	0.5	0			3 (2.2)	3	1.7
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	6 (6.2)	6	4.6
>=40	1 (1.4)	2	2.0	0			8 (8.6)	8	6.5
Diabetes mellitus									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			2 (1.5)	2	1.1
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			3 (3.2)	3	2.5
Diabetes mellitus inadequate control									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			3 (3.1)	3	2.3
>=40	1 (1.4)	2	2.0	0			2 (2.2)	2	1.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Hyperglycaemia									
<30	0			0			1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			2 (2.1)	2	1.5
>=40	0			0			2 (2.2)	2	1.6
Hyperinsulinaemia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Hypoglycaemia									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Type 2 diabetes mellitus									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			1 (1.1)	1	0.8
Acid-base disorders									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Ketoacidosis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Lactic acidosis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			0			0		
Diabetic complications									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Diabetic ketoacidosis									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Diabetic metabolic decompensation									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Iron and trace metal metabolism disorders									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<30	0			0			0		
30-<35	0			0			0		
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			0			0		
Iron deficiency									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			0			0		
Metabolism disorders NEC									
<30	0			0			0		
30-<35	1	(0.6)	2 0.9	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Hyperamylasaemia									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Hyperlipasaemia									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Eye disorders									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	8 (12.1)	9	10.9	9 (13.2)	14	15.4	10 (13.0)	12	12.3
30-<35	23 (14.1)	35	16.4	14 (10.1)	17	9.6	17 (12.6)	25	14.0
35-<40	9 (9.1)	13	9.9	13 (12.6)	19	13.5	7 (7.2)	9	7.0
>=40	6 (8.1)	8	7.8	14 (15.1)	19	15.3	8 (8.6)	10	8.2
Retina, choroid and vitreous haemorrhages and vascular disorders									
<30	1 (1.5)	1	1.2	6 (8.8)	6	6.6	2 (2.6)	2	2.0
30-<35	6 (3.7)	6	2.8	2 (1.4)	2	1.1	6 (4.4)	7	3.9
35-<40	3 (3.0)	4	3.1	7 (6.8)	8	5.7	1 (1.0)	1	0.8
>=40	2 (2.7)	2	2.0	6 (6.5)	7	5.6	2 (2.2)	2	1.6
Diabetic retinopathy									
<30	1 (1.5)	1	1.2	5 (7.4)	5	5.5	2 (2.6)	2	2.0
30-<35	5 (3.1)	5	2.3	2 (1.4)	2	1.1	6 (4.4)	7	3.9
35-<40	3 (3.0)	4	3.1	4 (3.9)	4	2.8	1 (1.0)	1	0.8
>=40	2 (2.7)	2	2.0	4 (4.3)	5	4.0	2 (2.2)	2	1.6
Non-proliferative retinopathy									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			1 (1.1)	1	0.8	0		
Retinal haemorrhage									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			1 (1.1)	1	0.8	0		
Retinopathy hypertensive									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			2 (1.9)	2	1.4	0		
>=40	0			0			0		
Retinal artery occlusion									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Retinopathy									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Anterior eye structural change, deposit and degeneration									
<30	1 (1.5)	1	1.2	0			4 (5.2)	5	5.1
30-<35	6 (3.7)	6	2.8	3 (2.2)	4	2.3	4 (3.0)	5	2.8
35-<40	1 (1.0)	1	0.8	3 (2.9)	4	2.8	3 (3.1)	4	3.1
>=40	0			3 (3.2)	3	2.4	1 (1.1)	1	0.8
Cataract									
<30	1 (1.5)	1	1.2	0			3 (3.9)	4	4.1
30-<35	3 (1.8)	3	1.4	3 (2.2)	4	2.3	2 (1.5)	2	1.1
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	2 (2.1)	2	1.5
>=40	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
Cataract cortical									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Dermatochalasis									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			2	(1.5)	2 1.1
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Cataract subcapsular									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Narrow anterior chamber angle									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	2 1.4	0		
>=40	0			0			0		
Cataract nuclear									
<30	0			0			0		
30-<35	2	(1.2)	2 0.9	0			0		
35-<40	0			0			1	(1.0)	2 1.5
>=40	0			0			0		
Pinguecula									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Posterior capsule opacification									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Ocular infections, irritations and inflammations									
<30	4 (6.1)	4	4.8	2 (2.9)	2	2.2	1 (1.3)	1	1.0
30-<35	5 (3.1)	5	2.3	3 (2.2)	3	1.7	4 (3.0)	4	2.2
35-<40	3 (3.0)	3	2.3	1 (1.0)	2	1.4	0		
>=40	1 (1.4)	1	1.0	2 (2.2)	3	2.4	1 (1.1)	1	0.8
Blepharitis									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	0			2 (1.5)	2	1.1
35-<40	2 (2.0)	2	1.5	0			0		
>=40	0			1 (1.1)	2	1.6	0		
Macular oedema									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	2	1.4	0		
>=40	0			1 (1.1)	1	0.8	0		
Eyelid rash									
<30	0			1 (1.5)	1	1.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Keratitis									
<30	1	(1.5)	1 1.2	0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Meibomian gland dysfunction									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Ocular hyperaemia									
<30	0			0			1	(1.3)	1 1.0
30-<35	0			1	(0.7)	1 0.6	1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Conjunctivitis allergic									
<30	0			0			0		
30-<35	2	(1.2)	2 0.9	0			0		
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			0			0		
Episcleritis									
<30	0			0			0		
30-<35	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Eye pruritus									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Punctate keratitis									
<30	1 (1.5)	1	1.2	0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Swelling of eyelid									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Uveitis									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Eye disorders NEC									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	0		
30-<35	3 (1.8)	3	1.4	4 (2.9)	4	2.3	4 (3.0)	4	2.2
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	1 (1.0)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	2 (2.7)	2	2.0	2 (2.2)	2	1.6	2 (2.2)	2	1.6
Dry eye									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	3 (2.2)	3	1.7	3 (2.2)	3	1.7
35-<40	1 (1.0)	1	0.8	0			1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	2 (2.2)	2	1.6	1 (1.1)	1	0.8
Vitreous disorder									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	0		
>=40	0			0			0		
Lacrimation increased									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Eyelid disorder									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Retinal disorder									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Ocular structural change, deposit and degeneration NEC									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	7 (4.3)	9	4.2	2 (1.4)	2	1.1	1 (0.7)	2	1.1
35-<40	1 (1.0)	1	0.8	2 (1.9)	2	1.4	1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	0		
Optic disc disorder									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Retinal depigmentation									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Detachment of retinal pigment epithelium									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Vitreous detachment									
<30	0			0			0		
30-<35	1 (0.6)	2	0.9	0			1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=40	0			0			0		
Macular fibrosis									
<30	0			0			0		
30-<35	1	(0.6)	2 0.9	1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Retinal degeneration									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Age-related macular degeneration									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	1	(1.4)	1 1.0	0			0		
Choroidal dystrophy									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Macular degeneration									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Optic atrophy									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Retinal drusen									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Vitreous floaters									
<30	1 (1.5)	1	1.2	0			1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Vision disorders									
<30	1 (1.5)	1	1.2	0			1 (1.3)	1	1.0
30-<35	4 (2.5)	4	1.9	2 (1.4)	2	1.1	2 (1.5)	2	1.1
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	2 (2.1)	2	1.5
>=40	2 (2.7)	2	2.0	2 (2.2)	2	1.6	3 (3.2)	3	2.5
Vision blurred									
<30	0			0			0		
30-<35	2 (1.2)	2	0.9	1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	2 (2.7)	2	2.0	2 (2.2)	2	1.6	2 (2.2)	2	1.6
Visual impairment									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			0			1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			1 (1.1)	1	0.8
Myopia									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Astigmatism									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			2 (2.1)	2	1.5
>=40	0			0			0		
Hypermetropia									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Pathologic myopia									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Presbyopia									
<30	1 (1.5)	1	1.2	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Glaucoma and ocular hypertension									
<30	0			1 (1.5)	2	2.2	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
Glaucoma									
<30	0			1 (1.5)	2	2.2	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
Ocular haemorrhages and vascular disorders NEC									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Eye haemorrhage									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Conjunctival haemorrhage									
<30	0			0			1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Optic disc haemorrhage									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Ocular sensory symptoms NEC									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Asthenopia									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Ocular neuromuscular disorders									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Eyelid ptosis									
<30	0			0			0		
30-<35	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Respiratory, thoracic and mediastinal disorders									
<30	4 (6.1)	4	4.8	11 (16.2)	13	14.3	4 (5.2)	4	4.1
30-<35	11 (6.7)	14	6.5	8 (5.8)	9	5.1	8 (5.9)	9	5.0
35-<40	10 (10.1)	11	8.4	17 (16.5)	22	15.6	12 (12.4)	17	13.2
>=40	11 (14.9)	15	14.7	11 (11.8)	18	14.5	12 (12.9)	13	10.6
Respiratory disorders NEC									
<30	2 (3.0)	2	2.4	7 (10.3)	7	7.7	0		
30-<35	4 (2.5)	4	1.9	1 (0.7)	1	0.6	2 (1.5)	2	1.1
35-<40	3 (3.0)	3	2.3	4 (3.9)	4	2.8	6 (6.2)	8	6.2
>=40	7 (9.5)	8	7.8	6 (6.5)	7	5.6	7 (7.5)	8	6.5
Cough									
<30	1 (1.5)	1	1.2	2 (2.9)	2	2.2	0		
30-<35	3 (1.8)	3	1.4	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	3 (2.9)	3	2.1	4 (4.1)	4	3.1
>=40	5 (6.8)	6	5.9	3 (3.2)	3	2.4	2 (2.2)	3	2.5
Productive cough									
<30	1 (1.5)	1	1.2	3 (4.4)	3	3.3	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Pulmonary mass									
<30	0			1 (1.5)	1	1.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			2 (2.2)	2	1.6	0		
Respiratory disorder									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	2 (2.0)	2	1.5	0			2 (2.1)	2	1.5
>=40	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
Acute respiratory failure									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	0		
Sleep apnoea syndrome									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	0		
>=40	1 (1.4)	1	1.0	0			3 (3.2)	3	2.5
Dyspnoea									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			1 (1.1)	1	0.8
Hypoxia									
<30	0			0			0		
30-<35	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Respiratory tract signs and symptoms									
<30	1 (1.5)	1	1.2	2 (2.9)	2	2.2	3 (3.9)	3	3.1
30-<35	4 (2.5)	4	1.9	6 (4.3)	6	3.4	2 (1.5)	2	1.1
35-<40	4 (4.0)	4	3.1	11 (10.7)	11	7.8	1 (1.0)	1	0.8
>=40	4 (5.4)	4	3.9	0			3 (3.2)	3	2.5
Oropharyngeal pain									
<30	0			1 (1.5)	1	1.1	3 (3.9)	3	3.1
30-<35	3 (1.8)	3	1.4	2 (1.4)	2	1.1	2 (1.5)	2	1.1
35-<40	3 (3.0)	3	2.3	4 (3.9)	4	2.8	0		
>=40	2 (2.7)	2	2.0	0			1 (1.1)	1	0.8
Rhinorrhoea									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	0		
35-<40	1 (1.0)	1	0.8	2 (1.9)	2	1.4	0		
>=40	1 (1.4)	1	1.0	0			0		
Dysphonia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			2 (1.9)	2	1.4	0		
>=40	0			0			0		
Dry throat									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=40	0			0			0		
Oropharyngeal discomfort									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			1	(1.1)	1 0.8
Painful respiration									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Upper respiratory tract congestion									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Aphonia									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Hiccups									
<30	1	(1.5)	1 1.2	0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	1	(1.4)	1 1.0	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Nasal discomfort									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Upper-airway cough syndrome									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Upper respiratory tract disorders (excl infections)									
<30	0			1 (1.5)	1	1.1	0		
30-<35	3 (1.8)	4	1.9	1 (0.7)	1	0.6	4 (3.0)	4	2.2
35-<40	3 (3.0)	3	2.3	3 (2.9)	3	2.1	3 (3.1)	4	3.1
>=40	0			5 (5.4)	7	5.6	1 (1.1)	1	0.8
Epistaxis									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	0			3 (2.2)	3	1.7
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			2 (2.2)	3	2.4	1 (1.1)	1	0.8
Rhinitis allergic									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	0		
>=40	0			2 (2.2)	2	1.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Nasal congestion									
<30	0			0			0		
30-<35	1 (0.6)	2	0.9	0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	1 (1.0)	2	1.5
>=40	0			1 (1.1)	1	0.8	0		
Sinus congestion									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	1 (1.0)	1	0.8	0			1 (1.0)	1	0.8
>=40	0			1 (1.1)	1	0.8	0		
Bronchial disorders (excl neoplasms)									
<30	1 (1.5)	1	1.2	2 (2.9)	3	3.3	1 (1.3)	1	1.0
30-<35	0			0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	3 (2.9)	3	2.1	3 (3.1)	3	2.3
>=40	3 (4.1)	3	2.9	2 (2.2)	3	2.4	1 (1.1)	1	0.8
Asthma									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			2 (1.9)	2	1.4	2 (2.1)	2	1.5
>=40	2 (2.7)	2	2.0	2 (2.2)	3	2.4	0		
Bronchospasm									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Chronic obstructive pulmonary disease									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	1 (1.4)	1	1.0	0			0		
Childhood asthma									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Lower respiratory tract disorders (excl obstruction and infection)									
<30	0			0			0		
30-<35	1 (0.6)	2	0.9	1 (0.7)	1	0.6	0		
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			0			0		
Atelectasis									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			0			0		
Idiopathic interstitial pneumonia									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			0			0		
Emphysema									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Pleural disorders									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Pneumothorax									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Injury, poisoning and procedural complications									
<30	12 (18.2)	14	16.9	7 (10.3)	8	8.8	7 (9.1)	8	8.2
30-<35	11 (6.7)	14	6.5	18 (12.9)	29	16.4	20 (14.8)	28	15.6
35-<40	18 (18.2)	31	23.7	9 (8.7)	9	6.4	13 (13.4)	16	12.4
>=40	10 (13.5)	12	11.8	14 (15.1)	22	17.7	9 (9.7)	9	7.4
Injuries NEC									
<30	8 (12.1)	8	9.7	4 (5.9)	4	4.4	4 (5.2)	4	4.1
30-<35	7 (4.3)	7	3.3	12 (8.6)	17	9.6	16 (11.9)	18	10.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	16 (16.2)	27	20.6	8 (7.8)	8	5.7	8 (8.2)	10	7.7
>=40	6 (8.1)	7	6.9	8 (8.6)	10	8.1	8 (8.6)	8	6.5
Muscle strain									
<30	0			1 (1.5)	1	1.1	0		
30-<35	2 (1.2)	2	0.9	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	2 (2.0)	2	1.5	2 (1.9)	2	1.4	0		
>=40	1 (1.4)	1	1.0	3 (3.2)	3	2.4	0		
Fall									
<30	1 (1.5)	1	1.2	0			0		
30-<35	1 (0.6)	1	0.5	3 (2.2)	4	2.3	1 (0.7)	1	0.6
35-<40	3 (3.0)	3	2.3	0			1 (1.0)	2	1.5
>=40	3 (4.1)	3	2.9	2 (2.2)	2	1.6	0		
Ligament sprain									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	3 (2.2)	3	1.7
35-<40	4 (4.0)	6	4.6	0			0		
>=40	0			1 (1.1)	1	0.8	2 (2.2)	2	1.6
Limb injury									
<30	0			0			0		
30-<35	0			0			0		
35-<40	3 (3.0)	3	2.3	3 (2.9)	3	2.1	0		
>=40	0			0			0		
Skin laceration									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			1 (0.7)	1	0.6	2 (1.5)	2	1.1
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=40	0			1	(1.1)	1 0.8	0		
Bone contusion									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			1	(1.1)	1 0.8	0		
Arthropod sting									
<30	0			1	(1.5)	1 1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Face injury									
<30	0			1	(1.5)	1 1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Contusion									
<30	0			0			2	(2.6)	2 2.0
30-<35	0			2	(1.4)	3 1.7	2	(1.5)	2 1.1
35-<40	0			0			3	(3.1)	4 3.1
>=40	0			0			1	(1.1)	1 0.8
Road traffic accident									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			1	(1.1)	1 0.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Traumatic haemothorax									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Tooth fracture									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	3 (3.0)	3	2.3	1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			0			2 (2.2)	2	1.6
Animal bite									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Epicondylitis									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Head injury									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Muscle injury									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Post-traumatic pain									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Skin abrasion									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			0			0		
Abdominal injury									
<30	1	(1.5)	1 1.2	0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Arthropod bite									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Chest injury									
<30	0			0			0		

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BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
30-<35	0				0				1	(0.7)	1	0.6
35-<40	0				0				0			
>=40	0				0				0			
Craniocerebral injury												
<30	0				0				0			
30-<35	1	(0.6)	1	0.5	0				0			
35-<40	0				0				0			
>=40	0				0				0			
Foreign body in eye												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				1	(1.1)	1	0.8
Injury corneal												
<30	0				0				0			
30-<35	0				0				1	(0.7)	1	0.6
35-<40	0				0				0			
>=40	0				0				0			
Ligament rupture												
<30	2	(3.0)	2	2.4	0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				0			
Muscle rupture												
<30	0				0				0			
30-<35	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Post-traumatic neck syndrome									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			1 (1.0)	1	0.8
>=40	0			0			0		
Soft tissue injury									
<30	0			0			0		
30-<35	0			0			0		
35-<40	2 (2.0)	2	1.5	0			0		
>=40	3 (4.1)	3	2.9	0			0		
Spinal column injury									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Subdural haematoma									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Tendon injury									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			0			1 (1.1)	1	0.8
Tendon rupture									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			1 (1.0)	1	0.8
>=40	0			0			0		
Wound									
<30	0			0			0		
30-<35	0			0			2 (1.5)	2	1.1
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Bone and joint injuries									
<30	2 (3.0)	2	2.4	1 (1.5)	1	1.1	4 (5.2)	4	4.1
30-<35	4 (2.5)	5	2.3	6 (4.3)	6	3.4	6 (4.4)	6	3.3
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	3 (3.1)	3	2.3
>=40	0			6 (6.5)	11	8.9	0		
Rib fracture									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			2 (2.2)	2	1.6	0		
Foot fracture									
<30	0			0			2 (2.6)	2	2.0
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			2 (2.2)	2	1.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Humerus fracture									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	0		
35-<40	0			0			0		
>=40	0			0			0		
Cervical vertebral fracture									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Joint injury									
<30	0			0			1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	0			3 (2.2)	3	1.7
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			1 (1.1)	1	0.8	0		
Spinal compression fracture									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Stress fracture									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Thoracic vertebral fracture									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Upper limb fracture									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Wrist fracture									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Meniscus injury									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Radius fracture									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Ankle fracture									
<30	1	(1.5)	1 1.2	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Bone fissure									
<30	1	(1.5)	1 1.2	0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Cartilage injury									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Hand fracture									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Hip fracture									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			0			0		
Joint dislocation									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			1	(0.7)	1 0.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			0			0		
>=40	0			0			0		
Lisfranc fracture									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Spinal fracture									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Sternal fracture									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Procedural related injuries and complications NEC									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	3 (2.2)	3	1.7	2 (1.5)	2	1.1
35-<40	1 (1.0)	1	0.8	0			3 (3.1)	3	2.3
>=40	0			1 (1.1)	1	0.8	0		
Post procedural haemorrhage									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			1 (0.7)	1	0.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
35-<40	0				0				0			
>=40	0				0				0			
Anaemia postoperative												
<30	0				0				0			
30-<35	0				0				1	(0.7)	1	0.6
35-<40	0				0				0			
>=40	0				1	(1.1)	1	0.8	0			
Graft complication												
<30	0				0				0			
30-<35	0				1	(0.7)	1	0.6	0			
35-<40	0				0				0			
>=40	0				0				0			
Procedural pain												
<30	0				0				0			
30-<35	0				1	(0.7)	1	0.6	0			
35-<40	1	(1.0)	1	0.8	0				1	(1.0)	1	0.8
>=40	0				0				0			
Dental restoration failure												
<30	0				0				0			
30-<35	0				0				1	(0.7)	1	0.6
35-<40	0				0				0			
>=40	0				0				0			
Incision site pain												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				0				1	(1.0)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
>=40	0				0				0			
Post procedural complication												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				0				1	(1.0)	1	0.8
>=40	0				0				0			
Surgical skin tear												
<30	0				0				0			
30-<35	1	(0.6)	1	0.5	0				0			
35-<40	0				0				0			
>=40	0				0				0			
Injuries by physical agents												
<30	0				1	(1.5)	1	1.1	0			
30-<35	1	(0.6)	1	0.5	2	(1.4)	2	1.1	0			
35-<40	0				0				0			
>=40	1	(1.4)	1	1.0	0				0			
Sunburn												
<30	0				1	(1.5)	1	1.1	0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				0			
Hypobarism												
<30	0				0				0			
30-<35	0				1	(0.7)	1	0.6	0			
35-<40	0				0				0			
>=40	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Thermal burn									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Heat illness									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Medication errors and other product use errors and issues									
<30	2 (3.0)	4	4.8	1 (1.5)	1	1.1	0		
30-<35	0			1 (0.7)	1	0.6	1 (0.7)	2	1.1
35-<40	1 (1.0)	1	0.8	0			0		
>=40	2 (2.7)	3	2.9	0			1 (1.1)	1	0.8
Extra dose administered									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Accidental overdose									
<30	2 (3.0)	4	4.8	0			0		
30-<35	0			1 (0.7)	1	0.6	1 (0.7)	2	1.1
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Dose calculation error									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Incorrect dose administered									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	2	2.0	0			0		
Overdoses and underdoses NEC									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Intentional overdose									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Investigations									
<30	2 (3.0)	3	3.6	7 (10.3)	7	7.7	2 (2.6)	2	2.0
30-<35	7 (4.3)	11	5.1	11 (7.9)	15	8.5	12 (8.9)	15	8.4
35-<40	4 (4.0)	4	3.1	13 (12.6)	16	11.4	10 (10.3)	13	10.1
>=40	5 (6.8)	5	4.9	9 (9.7)	10	8.1	9 (9.7)	12	9.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Cardiac and vascular investigations (excl enzyme tests)									
<30	0			1 (1.5)	1	1.1	0		
30-<35	2 (1.2)	2	0.9	2 (1.4)	3	1.7	2 (1.5)	2	1.1
35-<40	0			3 (2.9)	3	2.1	0		
>=40	0			2 (2.2)	2	1.6	2 (2.2)	2	1.6
Heart rate increased									
<30	0			0			0		
30-<35	2 (1.2)	2	0.9	0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			1 (1.1)	1	0.8	0		
Electrocardiogram QT prolonged									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Blood pressure decreased									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Blood pressure increased									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Electrocardiogram Q waves												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				1	(1.0)	1	0.7	0			
>=40	0				0				0			
Cardiac murmur												
<30	0				0				0			
30-<35	0				1	(0.7)	1	0.6	0			
35-<40	0				0				0			
>=40	0				0				1	(1.1)	1	0.8
Cardiac stress test abnormal												
<30	0				0				0			
30-<35	0				1	(0.7)	1	0.6	0			
35-<40	0				0				0			
>=40	0				0				0			
Carotid pulse decreased												
<30	0				0				0			
30-<35	0				1	(0.7)	1	0.6	0			
35-<40	0				0				0			
>=40	0				0				0			
Electrocardiogram PR prolongation												
<30	0				0				0			
30-<35	0				0				1	(0.7)	1	0.6
35-<40	0				0				0			
>=40	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Electrocardiogram ST-T segment abnormal									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Gastrointestinal investigations									
<30	1 (1.5)	1	1.2	2 (2.9)	2	2.2	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	1 (0.7)	2	1.1
35-<40	1 (1.0)	1	0.8	2 (1.9)	2	1.4	0		
>=40	2 (2.7)	2	2.0	0			1 (1.1)	1	0.8
Lipase increased									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	0		
>=40	1 (1.4)	1	1.0	0			1 (1.1)	1	0.8
Occult blood positive									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Colonoscopy normal									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Occult blood									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Amylase increased									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Faecal volume increased									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1	(1.4)	1 1.0	0			0		
Pancreatic enzymes increased									
<30	0			0			1	(1.3)	1 1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Renal and urinary tract investigations and urinalyses									
<30	0			0			0		
30-<35	0			4	(2.9)	4 2.3	0		
35-<40	0			2	(1.9)	2 1.4	0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Glomerular filtration rate decreased									
<30	0			0			0		
30-<35	0			2	(1.4)	2 1.1	0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Urine albumin/creatinine ratio increased									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Urine albumin/creatinine ratio abnormal									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Endocrine investigations (incl sex hormones)									
<30	0			1	(1.5)	1 1.1	0		
30-<35	0			1	(0.7)	1 0.6	2	(1.5)	2 1.1
35-<40	0			2	(1.9)	2 1.4	0		
>=40	2	(2.7)	2 2.0	0			0		
Blood thyroid stimulating hormone increased									
<30	0			1	(1.5)	1 1.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
30-<35	0				1	(0.7)	1	0.6	2	(1.5)	2	1.1
35-<40	0				0				0			
>=40	1	(1.4)	1	1.0	0				0			
Blood thyroid stimulating hormone decreased												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				2	(1.9)	2	1.4	0			
>=40	0				0				0			
Blood parathyroid hormone increased												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	1	(1.4)	1	1.0	0				0			
Haematology investigations (incl blood groups)												
<30	0				0				1	(1.3)	1	1.0
30-<35	0				0				0			
35-<40	0				2	(1.9)	4	2.8	0			
>=40	0				2	(2.2)	2	1.6	0			
Haemoglobin decreased												
<30	0				0				1	(1.3)	1	1.0
30-<35	0				0				0			
35-<40	0				2	(1.9)	2	1.4	0			
>=40	0				1	(1.1)	1	0.8	0			
Haematocrit decreased												

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			2 (1.9)	2	1.4	0		
>=40	0			0			0		
Platelet count decreased									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Enzyme investigations NEC									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	0		
>=40	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
Blood creatine phosphokinase increased									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	0		
>=40	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
Hepatobiliary investigations									
<30	0			0			0		
30-<35	2 (1.2)	3	1.4	3 (2.2)	3	1.7	1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	0			3 (3.1)	5	3.9
>=40	0			0			3 (3.2)	4	3.3
Hepatic enzyme increased									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			0			1	(1.1)	1 0.8
Liver function test abnormal									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Liver function test increased									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Alanine aminotransferase increased									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			2	(2.1)	2 1.5
>=40	0			0			2	(2.2)	2 1.6
Aspartate aminotransferase increased									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			1	(1.1)	1 0.8
Blood bilirubin increased									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Transaminases increased									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	0			0			0		
Lipid analyses									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			1	(1.0)	1 0.7	1	(1.0)	1 0.8
>=40	0			0			1	(1.1)	1 0.8
Low density lipoprotein increased									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Lipids abnormal									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Blood cholesterol increased									
<30	0			0			0		
30-<35	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Blood triglycerides increased									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Microbiology and serology investigations									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Helicobacter test positive									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Physical examination and organ system status topics									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Weight decreased									
<30	0			1 (1.5)	1	1.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Weight increased									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Investigations, imaging and histopathology procedures NEC									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Endoscopy abnormal									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Neurological, special senses and psychiatric investigations									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	2	1.6	0		
Intraocular pressure increased									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	2	1.6	0		
Protein and chemistry analyses NEC									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	0			0			2 (2.1)	2	1.5
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
C-reactive protein increased									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	0			0			2 (2.1)	2	1.5
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
Reproductive organ and breast investigations (excl hormone analyses)									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Mammogram abnormal									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Metabolic, nutritional and blood gas investigations									
<30	1 (1.5)	1	1.2	0			0		
30-<35	2 (1.2)	2	0.9	0			3 (2.2)	4	2.2
35-<40	0			1 (1.0)	1	0.7	5 (5.2)	5	3.9
>=40	0			0			0		
Vitamin B12 decreased									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			0			0		
Blood glucose decreased									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Blood glucose increased									
<30	0			0			0		
30-<35	0			0			3 (2.2)	3	1.7
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Blood uric acid increased									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg				Sema 2.4 mg				Placebo			
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Brain natriuretic peptide increased												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				0				1	(1.0)	1	0.8
>=40	0				0				0			
Glycosylated haemoglobin increased												
<30	0				0				0			
30-<35	1	(0.6)	1	0.5	0				1	(0.7)	1	0.6
35-<40	0				0				2	(2.1)	2	1.5
>=40	0				0				0			
Water, electrolyte and mineral investigations												
<30	1	(1.5)	1	1.2	0				0			
30-<35	0				1	(0.7)	1	0.6	0			
35-<40	1	(1.0)	1	0.8	0				0			
>=40	0				0				1	(1.1)	1	0.8
Blood potassium increased												
<30	1	(1.5)	1	1.2	0				0			
30-<35	0				1	(0.7)	1	0.6	0			
35-<40	0				0				0			
>=40	0				0				0			
Blood potassium decreased												
<30	0				0				0			
30-<35	0				0				0			
35-<40	1	(1.0)	1	0.8	0				0			
>=40	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Blood sodium increased									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1	(1.1)	1 0.8
Cytogenetic investigations									
<30	0			0			0		
30-<35	0			0			2	(1.5)	2 1.1
35-<40	0			0			0		
>=40	0			0			0		
Prostatic specific antigen increased									
<30	0			0			0		
30-<35	0			0			2	(1.5)	2 1.1
35-<40	0			0			0		
>=40	0			0			0		
Immunology and allergy investigations									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1	(1.1)	1 0.8
Antinuclear antibody increased									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1	(1.1)	1 0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Skin and subcutaneous tissue disorders									
<30	5 (7.6)	5	6.0	7 (10.3)	10	11.0	7 (9.1)	8	8.2
30-<35	18 (11.0)	21	9.8	15 (10.8)	16	9.0	14 (10.4)	16	8.9
35-<40	6 (6.1)	6	4.6	7 (6.8)	12	8.5	10 (10.3)	10	7.7
>=40	9 (12.2)	11	10.8	11 (11.8)	16	12.9	6 (6.5)	8	6.5
Epidermal and dermal conditions									
<30	3 (4.5)	3	3.6	5 (7.4)	8	8.8	5 (6.5)	6	6.1
30-<35	10 (6.1)	11	5.1	12 (8.6)	13	7.3	6 (4.4)	6	3.3
35-<40	5 (5.1)	5	3.8	5 (4.9)	6	4.3	7 (7.2)	7	5.4
>=40	5 (6.8)	6	5.9	5 (5.4)	8	6.4	4 (4.3)	4	3.3
Rash									
<30	1 (1.5)	1	1.2	2 (2.9)	3	3.3	1 (1.3)	1	1.0
30-<35	2 (1.2)	2	0.9	1 (0.7)	1	0.6	3 (2.2)	3	1.7
35-<40	2 (2.0)	2	1.5	2 (1.9)	2	1.4	0		
>=40	0			2 (2.2)	4	3.2	0		
Eczema									
<30	0			0			1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	0		
35-<40	1 (1.0)	1	0.8	2 (1.9)	2	1.4	1 (1.0)	1	0.8
>=40	2 (2.7)	2	2.0	0			0		
Dry skin									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Blister									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<30	0			1	(1.5)	2 2.2	0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Intertrigo									
<30	0			1	(1.5)	1 1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Pain of skin									
<30	0			1	(1.5)	1 1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Rash pruritic									
<30	0			0			0		
30-<35	1	(0.6)	2 0.9	2	(1.4)	2 1.1	1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Dermatitis allergic									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Skin exfoliation									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Skin lesion									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			1 (1.0)	1	0.8
>=40	0			1 (1.1)	1	0.8	0		
Dermatitis contact									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			1 (1.1)	1	0.8
Pruritus									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	3 (3.1)	3	2.3
>=40	1 (1.4)	1	1.0	0			0		
Decubitus ulcer									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Drug eruption									
<30	0			0			2 (2.6)	3	3.1
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Perioral dermatitis									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Psoriasis									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Sensitive skin									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Skin burning sensation									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Dermatitis									
<30	0			0			0		
30-<35	2 (1.2)	2	0.9	0			0		
35-<40	0			0			1 (1.0)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
>=40	0			0			1	(1.1)	1 0.8
Erythema									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1	(1.4)	2 2.0	0			0		
Neurodermatitis									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Parapsoriasis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1	(1.1)	1 0.8
Rash erythematous									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			0			0		
Stasis dermatitis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1	(1.4)	1 1.0	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Xanthelasma									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Skin appendage conditions									
<30	2 (3.0)	2	2.4	1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	5 (3.1)	5	2.3	1 (0.7)	1	0.6	3 (2.2)	3	1.7
35-<40	0			1 (1.0)	2	1.4	2 (2.1)	2	1.5
>=40	4 (5.4)	4	3.9	6 (6.5)	8	6.4	2 (2.2)	2	1.6
Alopecia									
<30	2 (3.0)	2	2.4	0			1 (1.3)	1	1.0
30-<35	3 (1.8)	3	1.4	0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			4 (4.3)	5	4.0	0		
Alopecia areata									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Ingrowing nail									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
Onychomadesis									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1	(1.1)	2 1.6	0		
Hyperhidrosis									
<30	0			0			0		
30-<35	2	(1.2)	2 0.9	0			1	(0.7)	1 0.6
35-<40	0			1	(1.0)	2 1.4	1	(1.0)	1 0.8
>=40	0			0			1	(1.1)	1 0.8
Acne									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	1	(1.4)	1 1.0	0			0		
Miliaria									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1	(1.0)	1 0.8
>=40	1	(1.4)	1 1.0	0			0		
Nail dystrophy									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1	(1.4)	1 1.0	0			0		
Cornification and dystrophic skin disorders									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
<30	0				1	(1.5)	1	1.1	0			
30-<35	2	(1.2)	2	0.9	0				0			
35-<40	0				0				1	(1.0)	1	0.8
>=40	0				0				1	(1.1)	1	0.8
Actinic keratosis												
<30	0				1	(1.5)	1	1.1	0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				0			
Dermatitis papillaris capillitii												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				1	(1.1)	1	0.8
Hyperkeratosis												
<30	0				0				0			
30-<35	1	(0.6)	1	0.5	0				0			
35-<40	0				0				1	(1.0)	1	0.8
>=40	0				0				0			
Punctate keratosis												
<30	0				0				0			
30-<35	1	(0.6)	1	0.5	0				0			
35-<40	0				0				0			
>=40	0				0				0			
Skin and subcutaneous tissue disorders NEC												

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
<30	0			0			0		
30-<35	0			0			2	(1.5)	2 1.1
35-<40	0			1	(1.0)	4 2.8	0		
>=40	1	(1.4)	1 1.0	0			0		
Diabetic foot									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	3 2.1	0		
>=40	0			0			0		
Skin ulcer									
<30	0			0			0		
30-<35	0			0			2	(1.5)	2 1.1
35-<40	0			1	(1.0)	1 0.7	0		
>=40	1	(1.4)	1 1.0	0			0		
Angioedema and urticaria									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	1	(0.7)	1 0.6	2	(1.5)	2 1.1
35-<40	0			0			0		
>=40	0			0			0		
Urticaria									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	2	(1.5)	2 1.1
35-<40	0			0			0		
>=40	0			0			0		
Chronic spontaneous urticaria									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Cutaneous neoplasms benign									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			1 (0.7)	1	0.6	1 (0.7)	2	1.1
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			1 (1.1)	1	0.8
Dermal cyst									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			1 (0.7)	1	0.6	1 (0.7)	2	1.1
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			1 (1.1)	1	0.8
Skin vascular abnormalities									
<30	0			0			0		
30-<35	2 (1.2)	2	0.9	0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Ecchymosis									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Haemorrhage subcutaneous									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			0			0		
>=40	0			0			0		
Renal and urinary disorders									
<30	1 (1.5)	1	1.2	4 (5.9)	4	4.4	6 (7.8)	8	8.2
30-<35	7 (4.3)	7	3.3	9 (6.5)	11	6.2	8 (5.9)	10	5.6
35-<40	5 (5.1)	8	6.1	7 (6.8)	8	5.7	6 (6.2)	7	5.4
>=40	6 (8.1)	6	5.9	11 (11.8)	14	11.3	8 (8.6)	9	7.4
Urinary tract signs and symptoms									
<30	0			2 (2.9)	2	2.2	2 (2.6)	3	3.1
30-<35	2 (1.2)	2	0.9	6 (4.3)	6	3.4	5 (3.7)	7	3.9
35-<40	2 (2.0)	2	1.5	3 (2.9)	3	2.1	4 (4.1)	4	3.1
>=40	3 (4.1)	3	2.9	6 (6.5)	6	4.8	5 (5.4)	5	4.1
Microalbuminuria									
<30	0			0			0		
30-<35	2 (1.2)	2	0.9	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	2 (2.2)	2	1.6	0		
Nocturia									
<30	0			2 (2.9)	2	2.2	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Haematuria									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
Dysuria									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			0			1 (1.1)	1	0.8
Proteinuria									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			1 (1.1)	1	0.8	0		
Renal colic									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Pollakiuria									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	0			0		
>=40	2 (2.7)	2	2.0	1 (1.1)	1	0.8	2 (2.2)	2	1.6
Lower urinary tract symptoms									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			0			0		
Micturition disorder									
<30	0			0			0		
30-<35	0			0			1 (0.7)	2	1.1
35-<40	0			0			0		
>=40	0			0			0		
Polyuria									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Urethral pain									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Urinary incontinence									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Nephropathies									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	0			0		
>=40	1 (1.4)	1	1.0	3 (3.2)	3	2.4	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Diabetic nephropathy									
<30	0			1 (1.5)	1	1.1	0		
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			2 (2.2)	2	1.6	0		
Nephropathy									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	0		
Renal disorders (excl nephropathies)									
<30	0			0			4 (5.2)	4	4.1
30-<35	1 (0.6)	1	0.5	1 (0.7)	2	1.1	0		
35-<40	3 (3.0)	3	2.3	2 (1.9)	2	1.4	2 (2.1)	2	1.5
>=40	1 (1.4)	1	1.0	3 (3.2)	4	3.2	1 (1.1)	1	0.8
Acute kidney injury									
<30	0			0			0		
30-<35	0			0			0		
35-<40	2 (2.0)	2	1.5	2 (1.9)	2	1.4	2 (2.1)	2	1.5
>=40	0			1 (1.1)	2	1.6	0		
Renal cyst									
<30	0			0			3 (3.9)	3	3.1
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	2 (2.2)	2	1.6	0		
Chronic kidney disease									

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Renal impairment									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Hydronephrosis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Kidney fibrosis									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Urolithiases									
<30	1 (1.5)	1	1.2	0			1 (1.3)	1	1.0
30-<35	3 (1.8)	3	1.4	1 (0.7)	1	0.6	2 (1.5)	2	1.1
35-<40	1 (1.0)	2	1.5	2 (1.9)	2	1.4	1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	2 (2.2)	2	1.6
Nephrolithiasis									
<30	1 (1.5)	1	1.2	0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	3 (1.8)	3	1.4	0			2 (1.5)	2	1.1
35-<40	1 (1.0)	2	1.5	1 (1.0)	1	0.7	0		
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	2 (2.2)	2	1.6
Calculus urinary									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Stag horn calculus									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Ureterolithiasis									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			0			0		
Bladder and bladder neck disorders (excl calculi)									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			1 (1.1)	1	0.8
Hypertonic bladder									
<30	0			1 (1.5)	1	1.1	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Bladder outlet obstruction									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Bladder hypertrophy									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Psychiatric disorders									
<30	4 (6.1)	4	4.8	4 (5.9)	5	5.5	4 (5.2)	4	4.1
30-<35	5 (3.1)	5	2.3	4 (2.9)	5	2.8	5 (3.7)	5	2.8
35-<40	4 (4.0)	6	4.6	9 (8.7)	10	7.1	3 (3.1)	3	2.3
>=40	10 (13.5)	13	12.7	7 (7.5)	9	7.2	3 (3.2)	4	3.3
Sleep disorders and disturbances									
<30	2 (3.0)	2	2.4	2 (2.9)	2	2.2	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	0			3 (2.9)	3	2.1	1 (1.0)	1	0.8
>=40	3 (4.1)	3	2.9	3 (3.2)	3	2.4	1 (1.1)	1	0.8
Insomnia									
<30	2 (3.0)	2	2.4	1 (1.5)	1	1.1	1 (1.3)	1	1.0

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	0			2 (1.9)	2	1.4	1 (1.0)	1	0.8
>=40	3 (4.1)	3	2.9	2 (2.2)	2	1.6	1 (1.1)	1	0.8
Sleep disorder									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Abnormal dreams									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Middle insomnia									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Depressed mood disorders and disturbances									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	2 (1.2)	2	0.9	2 (1.4)	2	1.1	2 (1.5)	2	1.1
35-<40	1 (1.0)	1	0.8	3 (2.9)	3	2.1	1 (1.0)	1	0.8
>=40	2 (2.7)	2	2.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
Depressed mood									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	0		
35-<40	0			2 (1.9)	2	1.4	0		
>=40	2 (2.7)	2	2.0	0			0		
Depression									
<30	0			0			1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	0			2 (1.5)	2	1.1
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			1 (1.1)	1	0.8	1 (1.1)	1	0.8
Anhedonia									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Major depression									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Anxiety disorders and symptoms									
<30	1 (1.5)	1	1.2	0			1 (1.3)	1	1.0
30-<35	0			1 (0.7)	1	0.6	2 (1.5)	2	1.1
35-<40	3 (3.0)	3	2.3	2 (1.9)	2	1.4	1 (1.0)	1	0.8
>=40	6 (8.1)	7	6.9	2 (2.2)	2	1.6	2 (2.2)	2	1.6
Anxiety									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	1 (0.7)	1	0.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	2 (2.0)	2	1.5	1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	5 (6.8)	6	5.9	1 (1.1)	1	0.8	2 (2.2)	2	1.6
Anxiety disorder due to a general medical condition									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Stress									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		
Generalised anxiety disorder									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Nervousness									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Post-traumatic stress disorder									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			0			0		
>=40	0			0			0		
Mood disorders and disturbances NEC									
<30	0			1 (1.5)	2	2.2	1 (1.3)	1	1.0
30-<35	2 (1.2)	2	0.9	0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Mood altered									
<30	0			1 (1.5)	2	2.2	1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Irritability									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Mood swings									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Adjustment disorders (incl subtypes)									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	0		
Adjustment disorder with depressed mood									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	0		
Grief reaction									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	1 (1.0)	1	0.7	0		
>=40	0			0			0		
Suicidal and self-injurious behaviours NEC									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Suicidal ideation									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Changes in physical activity									
<30	0			0			0		
30-<35	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
35-<40	0				1	(1.0)	1	0.7	0			
>=40	0				0				0			
Restlessness												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				1	(1.0)	1	0.7	0			
>=40	0				0				0			
Psychiatric disorders NEC												
<30	1	(1.5)	1	1.2	0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				0			
Mental status changes												
<30	1	(1.5)	1	1.2	0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	0				0				0			
Sexual dysfunctions, disturbances and gender identity disorders												
<30	0				0				0			
30-<35	0				0				0			
35-<40	1	(1.0)	1	0.8	0				0			
>=40	0				0				0			
Libido decreased												
<30	0				0				0			
30-<35	0				0				0			

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Vascular disorders									
<30	3 (4.5)	3	3.6	3 (4.4)	4	4.4	5 (6.5)	5	5.1
30-<35	8 (4.9)	8	3.7	8 (5.8)	8	4.5	7 (5.2)	7	3.9
35-<40	4 (4.0)	5	3.8	6 (5.8)	6	4.3	9 (9.3)	10	7.7
>=40	7 (9.5)	7	6.9	7 (7.5)	8	6.4	9 (9.7)	10	8.2
Vascular hypertensive disorders									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	3 (3.9)	3	3.1
30-<35	4 (2.5)	4	1.9	5 (3.6)	5	2.8	2 (1.5)	2	1.1
35-<40	0			3 (2.9)	3	2.1	7 (7.2)	8	6.2
>=40	4 (5.4)	4	3.9	1 (1.1)	2	1.6	3 (3.2)	3	2.5
Hypertension									
<30	1 (1.5)	1	1.2	1 (1.5)	1	1.1	2 (2.6)	2	2.0
30-<35	4 (2.5)	4	1.9	5 (3.6)	5	2.8	1 (0.7)	1	0.6
35-<40	0			3 (2.9)	3	2.1	6 (6.2)	6	4.6
>=40	4 (5.4)	4	3.9	1 (1.1)	2	1.6	3 (3.2)	3	2.5
Hypertensive crisis									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			2 (2.1)	2	1.5
>=40	0			0			0		
Hypertensive urgency									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			0			0		
>=40	0			0			0		
Decreased and nonspecific blood pressure disorders and shock									
<30	0			2 (2.9)	3	3.3	2 (2.6)	2	2.0
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	2 (2.0)	3	2.3	1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	2 (2.7)	2	2.0	1 (1.1)	1	0.8	1 (1.1)	1	0.8
Hypotension									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	2 (2.0)	3	2.3	0			1 (1.0)	1	0.8
>=40	2 (2.7)	2	2.0	1 (1.1)	1	0.8	0		
Orthostatic hypotension									
<30	0			1 (1.5)	2	2.2	2 (2.6)	2	2.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Blood pressure inadequately controlled									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			1 (1.1)	1	0.8
Shock									
<30	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Vascular disorders NEC									
<30	0			0			0		
30-<35	0			0			2 (1.5)	2	1.1
35-<40	0			1 (1.0)	1	0.7	0		
>=40	1 (1.4)	1	1.0	2 (2.2)	2	1.6	0		
Aortic dilatation									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Aortic rupture									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Hot flush									
<30	0			0			0		
30-<35	0			0			2 (1.5)	2	1.1
35-<40	0			1 (1.0)	1	0.7	0		
>=40	1 (1.4)	1	1.0	0			0		
Vascular haemorrhagic disorders									
<30	0			0			0		
30-<35	0			2 (1.4)	2	1.1	0		

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			0			0		
Haematoma									
<30	0			0			0		
30-<35	0			2 (1.4)	2	1.1	0		
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	1	0.8
>=40	0			0			0		
Aneurysms and artery dissections									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Aortic aneurysm									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1 (1.1)	1	0.8	0		
Arteriosclerosis, stenosis, vascular insufficiency and necrosis									
<30	2 (3.0)	2	2.4	0			0		
30-<35	3 (1.8)	3	1.4	0			2 (1.5)	2	1.1
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			1 (1.1)	1	0.8	3 (3.2)	4	3.3
Aortic arteriosclerosis									
<30	1 (1.5)	1	1.2	0			0		
30-<35	2 (1.2)	2	0.9	0			0		

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Arteriosclerosis									
<30	1	(1.5)	1 1.2	0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Peripheral arterial occlusive disease									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			1	(1.1)	1 0.8
Peripheral artery stenosis									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
Peripheral coldness									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			0			0		
Peripheral venous disease									
<30	0			0			0		
30-<35	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
35-<40	0			0			0		
>=40	0			0			2	(2.2)	3 2.5
Embolism and thrombosis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	1	(1.1)	1 0.8
Post thrombotic syndrome									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			1	(1.1)	1 0.8	0		
Deep vein thrombosis									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1	(1.1)	1 0.8
Vascular infections and inflammations									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Temporal arteritis									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	0		
35-<40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	0			0			0		
Lymphatic vessel disorders									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Lymphoedema									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			1 (1.1)	1	0.8
Venous varices									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Varicose vein									
<30	0			0			0		
30-<35	0			0			1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Ear and labyrinth disorders									
<30	0			5 (7.4)	5	5.5	2 (2.6)	2	2.0
30-<35	6 (3.7)	8	3.7	4 (2.9)	4	2.3	3 (2.2)	4	2.2
35-<40	2 (2.0)	3	2.3	5 (4.9)	5	3.6	4 (4.1)	4	3.1

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	3 (4.1)	3	2.9	6 (6.5)	6	4.8	3 (3.2)	4	3.3
Inner ear and VIIIth cranial nerve disorders									
<30	0			2 (2.9)	2	2.2	1 (1.3)	1	1.0
30-<35	4 (2.5)	6	2.8	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	1 (1.0)	2	1.5	2 (1.9)	2	1.4	4 (4.1)	4	3.1
>=40	3 (4.1)	3	2.9	4 (4.3)	4	3.2	2 (2.2)	3	2.5
Vertigo									
<30	0			2 (2.9)	2	2.2	1 (1.3)	1	1.0
30-<35	3 (1.8)	5	2.3	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			2 (1.9)	2	1.4	2 (2.1)	2	1.5
>=40	0			2 (2.2)	2	1.6	2 (2.2)	3	2.5
Vertigo positional									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			1 (1.0)	1	0.8
>=40	0			2 (2.2)	2	1.6	0		
Motion sickness									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	1 (1.0)	2	1.5	0			0		
>=40	0			0			0		
Tinnitus									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	1	0.8

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Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
>=40	3 (4.1)	3	2.9	0			0		
Aural disorders NEC									
<30	0			1 (1.5)	1	1.1	1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			2 (1.9)	2	1.4	0		
>=40	0			2 (2.2)	2	1.6	1 (1.1)	1	0.8
Ear pain									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			2 (1.9)	2	1.4	0		
>=40	0			2 (2.2)	2	1.6	1 (1.1)	1	0.8
Ear pruritus									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Ear discomfort									
<30	0			0			1 (1.3)	1	1.0
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Hearing disorders									
<30	0			2 (2.9)	2	2.2	0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E R	N	(%)	E R	N	(%)	E R
Hypoacusis									
<30	0			1	(1.5)	1 1.1	0		
30-<35	0			0			0		
35-<40	0			1	(1.0)	1 0.7	0		
>=40	0			0			0		
Deafness bilateral									
<30	0			1	(1.5)	1 1.1	0		
30-<35	0			0			0		
35-<40	0			0			0		
>=40	0			0			0		
Deafness unilateral									
<30	0			0			0		
30-<35	1	(0.6)	1 0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Mixed deafness									
<30	0			0			0		
30-<35	0			0			1	(0.7)	1 0.6
35-<40	0			0			0		
>=40	0			0			0		
External ear disorders (excl congenital)									
<30	0			0			0		
30-<35	0			1	(0.7)	1 0.6	1	(0.7)	1 0.6
35-<40	1	(1.0)	1 0.8	0			0		
>=40	0			0			0		

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
Cerumen impaction									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			0			0		
Excessive cerumen production									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			0			0		
Cardiac disorders									
<30	3 (4.5)	3	3.6	3 (4.4)	3	3.3	2 (2.6)	3	3.1
30-<35	10 (6.1)	13	6.1	9 (6.5)	14	7.9	4 (3.0)	4	2.2
35-<40	3 (3.0)	3	2.3	3 (2.9)	3	2.1	4 (4.1)	7	5.4
>=40	4 (5.4)	5	4.9	7 (7.5)	8	6.4	3 (3.2)	3	2.5
Cardiac arrhythmias									
<30	2 (3.0)	2	2.4	2 (2.9)	2	2.2	1 (1.3)	1	1.0
30-<35	6 (3.7)	7	3.3	4 (2.9)	6	3.4	1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	1 (1.0)	2	1.5
>=40	2 (2.7)	3	2.9	6 (6.5)	7	5.6	1 (1.1)	1	0.8
Atrial fibrillation									
<30	1 (1.5)	1	1.2	0			0		
30-<35	1 (0.6)	1	0.5	2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	0			0			0		
>=40	0			3 (3.2)	3	2.4	1 (1.1)	1	0.8

Adverse events with onset prior to randomisation are not included.
Sorted in descending order by system organ class, high level group term, and preferred term based on the proportion of subjects experiencing at least one event.
BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Supraventricular extrasystoles												
<30	0				2	(2.9)	2	2.2	0			
30-<35	0				1	(0.7)	1	0.6	0			
35-<40	0				1	(1.0)	1	0.7	0			
>=40	0				0				0			
Tachycardia												
<30	0				0				0			
30-<35	1	(0.6)	1	0.5	0				0			
35-<40	0				0				0			
>=40	0				2	(2.2)	2	1.6	0			
Atrioventricular block first degree												
<30	0				0				0			
30-<35	1	(0.6)	1	0.5	0				0			
35-<40	0				0				0			
>=40	0				1	(1.1)	1	0.8	0			
Supraventricular tachycardia												
<30	0				0				0			
30-<35	0				0				0			
35-<40	0				0				0			
>=40	1	(1.4)	1	1.0	1	(1.1)	1	0.8	0			
Bundle branch block right												
<30	0				0				0			
30-<35	1	(0.6)	1	0.5	1	(0.7)	1	0.6	0			
35-<40	0				0				0			
>=40	0				0				0			
Sinus tachycardia												

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BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
Subjects are considered on-treatment if any dose of trial product has been administered within the prior 49 days.
MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
<30	0			0			1 (1.3)	1	1.0
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Ventricular extrasystoles									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Atrial flutter									
<30	0			0			0		
30-<35	0			0			0		
35-<40	0			0			1 (1.0)	2	1.5
>=40	0			0			0		
Bradycardia									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Bundle branch block left									
<30	1 (1.5)	1	1.2	0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	1 (1.4)	1	1.0	0			0		
Coronary artery disorders									
<30	0			1 (1.5)	1	1.1	0		

Adverse events with onset prior to randomisation are not included.
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BMI: Body mass index (kg/m^2)
Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
Subjects with events: N: Number of subjects experiencing at least one event, %: Percentage of subjects experiencing at least one event, E: Number of events, R: Event rate per 100 patient-years of exposure.
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MedDRA version 22.1

Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
30-<35	4 (2.5)	4	1.9	3 (2.2)	3	1.7	1 (0.7)	1	0.6
35-<40	2 (2.0)	2	1.5	2 (1.9)	2	1.4	1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	1 (1.1)	1	0.8	2 (2.2)	2	1.6
Angina pectoris									
<30	0			1 (1.5)	1	1.1	0		
30-<35	0			1 (0.7)	1	0.6	0		
35-<40	1 (1.0)	1	0.8	0			1 (1.0)	1	0.8
>=40	0			0			1 (1.1)	1	0.8
Myocardial infarction									
<30	0			0			0		
30-<35	0			0			0		
35-<40	1 (1.0)	1	0.8	0			0		
>=40	0			1 (1.1)	1	0.8	0		
Acute myocardial infarction									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			1 (0.7)	1	0.6
35-<40	0			1 (1.0)	1	0.7	0		
>=40	1 (1.4)	1	1.0	0			0		
Myocardial ischaemia									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			1 (1.0)	1	0.7	0		
>=40	0			0			1 (1.1)	1	0.8
Angina unstable									
<30	0			0			0		
30-<35	0			1 (0.7)	1	0.6	0		

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Subjects and exposure: N: Number of subjects, PYE: Patient-years of exposure
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Adverse events by BMI at baseline, system organ class, high level group term and preferred term - on-treatment - safety analysis set - STEP 2

	Sema 1.0 mg			Sema 2.4 mg			Placebo		
Subjects with events	N (%)	E	R	N (%)	E	R	N (%)	E	R
35-<40	0			0			0		
>=40	0			0			0		
Coronary artery disease									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	1 (0.7)	1	0.6	0		
35-<40	0			0			0		
>=40	0			0			0		
Arteriosclerosis coronary artery									
<30	0			0			0		
30-<35	1 (0.6)	1	0.5	0			0		
35-<40	0			0			0		
>=40	0			0			0		
Cardiac disorders, signs and symptoms NEC									
<30	1 (1.5)	1	1.2	0			1 (1.3)	1	1.0
30-<35	0			3 (2.2)	4	2.3	1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	0			2 (2.1)	2	1.5
>=40	1 (1.4)	1	1.0	0			0		
Palpitations									
<30	1 (1.5)	1	1.2	0			0		
30-<35	0			2 (1.4)	2	1.1	1 (0.7)	1	0.6
35-<40	1 (1.0)	1	0.8	0			1 (1.0)	1	0.8
>=40	1 (1.4)	1	1.0	0			0		
Cardiovascular disorder									
<30	0			0			0		
30-<35	0			1 (0.7)	2	1.1	0		

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