2.7.6.22 NN9535-3625

2.7.6.22.1 臨床試験概要

治験依頼者名： Novo Nordisk A/S, Novo Allé, DK-2880 Bagsvaerd, Denmark	
有効成分名： セマグルチド	
Trial Registration ID-number： NCT02128932	UTN：U1111-1146-0211 IND number：79,754 EudraCT number：2013-004392-12 Japanese registration number：該当なし
治験の標題： SUSTAIN 4：メトホルミン単独療法又はメトホルミンとスルホニルウレア薬の併用療法実施中のインスリン治療歴のない 2 型糖尿病患者を対象とした、セマグルチドの週 1 回投与とインスリン グラルギンの 1 日 1 回投与による有効性及び安全性の比較検討	
治験責任医師名： 治験実施施設（全 196 施設）ごとに 1 名の治験責任医師が任命された。以下の治験責任医師が治験総括報告書の内容を確認し、署名する「治験総括報告書への署名責任を有する医師（signatory investigator）」に指名された。 [redacted]	
治験実施施設： 本試験は以下の 14 ヵ国 196 施設において被験者の無作為割り付けが実施された：アルゼンチン（3 施設）、クロアチア（3 施設）、フランス（5 施設）、ドイツ（11 施設）、インド（12 施設）、マケドニア（3 施設）、メキシコ（3 施設）、オランダ（3 施設）、ルーマニア（5 施設）、スロバキア（5 施設）、スロベニア（3 施設）、南アフリカ（4 施設）英国（13 施設）及び米国（123 施設）	
公表文献（引用文献）： 本臨床試験概要作成時点での公表文献はなし	
治験期間： 開始日：2014 年 8 月 4 日 終了日：2015 年 9 月 3 日	**開発のフェーズ**： 第 3a 相
Cut-off date： ここに提示する結果は、2015 年 10 月 23 日の時点での臨床データベースに基づいている。	
報告書作成日： 2016 年 7 月 20 日	
目的： 主要目的： • インスリン治療歴のない2型糖尿病患者を対象とし、投与後30週の血糖コントロールについて、セマグルチド（2用量、週1回投与）の有効性をインスリン グラルギン（IGlar）（1日1回投与）と比較検討する。 副次的目的： • 投与後30週の以下の項目に対するセマグルチド（2用量、週1回投与）の有効性を、IGlar（1日1回投	

与）と比較検討する。
- 体重減少の誘導及び維持
- 有効性、安全性及び忍容性ならびに患者報告アウトカムに関するその他のパラメータ

治験方法：

本試験は、セマグルチド（2 用量：0.5 mg 及び 1.0 mg、週 1 回投与）と IGlar（1 日 1 回投与）を比較する無作為割り付け、非盲検、実薬対照、並行群、多施設、多国籍、3 群試験であった。被験者は、男性及び女性の成人 2 型糖尿病患者であった。

本試験は 2 週間のスクリーニング期間、30 週間の無作為割り付けされた治験薬の投与期間及び実際の最終投与来院日から 5 週間後の事後調査来院で構成された。スクリーニング来院後、適格例は無作為割り付けを受けるために来院し、セマグルチド 0.5 mg 又はセマグルチド 1.0 mg を週 1 回 30 週間投与あるいは IGlar を 1 日 1 回 30 週間投与のいずれかに 1:1:1 の割合で無作為割り付けされた。

無作為割り付け後、セマグルチド投与に割り付けられた被験者は規定された用量漸増法に従って用量を増加した。セマグルチド 0.5 mg 群では、0.25 mg を 4 回（4 週間）投与した後に 0.5 mg の維持用量へ増量した。セマグルチド 1.0 mg 群では、0.25 mg を 4 回（4 週間）、続いて 0.5 mg を 4 回（4 週間）投与した後、1.0 mg の維持用量へ増量した。維持用量に到達した後、残りの試験期間中において用量変更は行わないこととした。

IGlar 群では、10 単位の 1 日 1 回皮下投与から開始した。投与時刻は被験者ごとに決めることとしたが、毎日一定とした。投与期間中の IGlar の投与量は、来院及び電話コンタクト前 3 日間に測定した朝食前血糖値（血糖自己測定）の最低値に基づき、治験責任医師が調節することとした。IGlar の投与量の調節は、治験責任医師の判断により来院と来院の間にも行うことが可能であった。

治験薬に起因すると疑われる安全性の理由により必要に応じて投与を中止できることとし、その場合には投与を再開しないこととした。治験薬の投与は投与後 30 週である来院 16 まで継続した。各被験者の最終予定来院は、実際の最終投与来院日から 5 週間後の事後調査来院であった。

ノボ ノルディスク社は、盲検化された安全性データの継続的な安全性審査を行う、社内のセマグルチド安全性委員会を設置した。このセマグルチド安全性委員会は、本試験の全体的な安全性審査の責任を負った。

進行中のセマグルチドの心血管系アウトカム試験（NN9535-3744）から得られる非盲検化された安全性データを独立して確認し、評価するために設立された外部データモニタリング委員会（DMC）が、本試験で認められたすべての主要な心血管イベント（MACE）を評価した。

また、特定の事象の継続的な判定、標準化及び評価を行うため、独立した外部のイベント判定委員会が設立された。当該判定は、独立した外部の医学専門家が統一基準に基づいて一貫性を持って事象を確認することを目的とした。

計画及び解析された被験者数：

無作為割り付けする予定症例数を 1047 例とした；実際には 1610 例がスクリーニングを受け、うち 1089 例が無作為割り付けされた。

	Sema 0.5 mg N (%)	Sema 1.0 mg N (%)	IGlar N (%)	Total N (%)
Screened				1610
Screening failures				521 (32.4)
Randomised	362	362	365	1089
Exposed/FAS/SAS	362 (100)	360 (99.4)	360 (98.6)	1082 (99.4)
Treatment completers [1]	313 (86.5)	305 (84.7)	334 (92.8)	952 (88.0)
Trial completers [3]	335 (92.5)	342 (94.5)	343 (94.0)	1020 (93.7)
Premature treatment discontinuers- primary reason [2]	49 (13.5)	55 (15.3)	26 (7.2)	130 (12.0)
Pregnancy		1 (0.3)	1 (0.3)	2 (0.2)
Protocol violation	12 (3.3)	13 (3.6)	2 (0.6)	27 (2.5)
Adverse event	19 (5.2)	27 (7.5)	5 (1.4)	51 (4.7)

IGlar: Insulin glargine, N: Number of subjects, %: For treatment completers and treatment non-completers percentages are based on exposed subjects. For trial completers and withdrawals percentages are based on randomised subjects.

[1]: Completion of treatment according to end-of-trial form. [2]: Subjects with a follow-up visit. [3]: Includes only exposed subjects.
診断及び主要な組入れ基準： **主な選択基準**： 性別不問、年齢 18 歳以上（同意取得時点）、スクリーニングの 90 日以上前からメトホルミンの単独療法、もしくはメトホルミンとスルホニルウレア薬（SU）の併用療法〔メトホルミン：1500 mg 以上又は最大耐用量、SU：各国の承認最大用量の半量以上〕による安定した糖尿病治療を受けている、HbA1c 7.0%以上 10.0%以下（53～86 mmol/mol）の 2 型糖尿病患者。 **主な除外基準**： 妊婦、授乳婦、妊娠を希望している、又は妊娠する可能性のある女性被験者で 5 週間の事後調査期間を含めた試験期間中に適切な避妊法（各国の規制又は慣習に基づく）を受け入れられない被験者、被験者の安全を脅かしたり、治験実施計画書の遵守を困難にしたりする可能性があると治験責任医師により判断された何らかの疾患を有する被験者、スクリーニング前 90 日以内に選択基準に示された糖尿病治療薬以外の血糖降下薬の投与を受けた被験者〔ただし、併発疾患のための短期間（合計で 7 日以内）のインスリン投与は除く〕、慢性又は特発性急性膵炎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濃度 50 ng/L 以上の被験者、甲状腺髄様癌又は多発性内分泌腫瘍症候群 2 型の既往歴又は家族歴を有する被験者、重度の腎機能障害〔推算糸球体濾過量（eGFR）30 mL/min/1.73 m^2 未満と定義〕を有する被験者、無作為割り付け前 90 日以内に急性冠動脈疾患又は脳血管疾患を発現した被験者、心不全（NYHA 分類クラス IV）を有する被験者、緊急の処置を要する増殖網膜症又は黄斑症を有する被験者（治験責任医師の判断による）、過去 5 年以内に悪性腫瘍（ただし皮膚の基底細胞癌又は有棘細胞癌を除く）の診断を受けた被験者、意思決定能力がない、協力する意思がない又は治験手順の適切な理解と遵守を妨げる言語上の問題を有する被験者。 **主な投与中止基準**： 治験薬との関連が疑われる安全性の懸念がある場合、又は治験薬投与に受け入れがたい非忍容性が認められる場合。 **中止・脱落基準**： 被験者は同意を撤回することにより、いつでも自由意思で試験を中止することができた。
被験薬、用量及び投与方法、ロット番号： セマグルチド注射液（1.34 mg/mL）〔PDS290 ペン型注入器（1.5 mL）と一体化したプレフィルド製剤〕を、食事時間に関係なく 1 日のいずれかの時点において 0.5 mg 又は 1.0 mg を大腿部、腹部又は上腕部のいずれかに週 1 回皮下投与した。セマグルチドのロット番号（有効期限）：CV40235（2016 年 2 月 21 日）、DV40009（2016 年 4 月 10 日）及び DV40092（2016 年 5 月 7 日）。
投与期間： 30 週間
対照薬、用量及び投与方法、ロット番号： IGlar（Lantus®）注射液（100 単位/mL）〔SoloStar®（3 mL）ペン型注入器と一体化したプレフィルド製剤〕の投与は 10 単位から開始し、食事時間に関係なく 1 日のいずれかの時点において大腿部、腹部又は上腕部のいずれかに 1 日 1 回皮下投与した。IGlar のロット番号（有効期限）：3F205A（2016 年 1 月 31 日）、3F256A（2016 年 2 月 29 日）、4F720A（2016 年 9 月 30 日）及び 4F266A（2017 年 2 月 17 日）。
評価基準：**有効性** HbA1c、体重、空腹時血糖値、収縮期及び拡張期血圧ならびに患者報告アウトカム質問票（SF-36v2 及び DTSQ）
評価基準：**安全性** 治験薬投与下で発現した有害事象〔（Treatment Emergent Adverse Event、以下、有害事象とする）：これには、独立した外部のイベント判定委員会により判定される事前に規定した特に注目すべき医学的事象が含まれる〕、低血糖、脈拍数及び安全性に関する臨床検査項目。

統計手法：

検出力の算出

被験者数は、プライマリーエンドポイント及び検証的セカンダリーエンドポイントに基づいて算出した。仮説検定は互いに独立と仮定し、それぞれの仮説に関し、検出力の算出は有意水準 2.5%の片側検定を仮定した t-統計量に基づいた。非劣性マージン 0.3%を用い、HbA1c の真の群間差（セマグルチドーIGlar）を 0%、SD を 1.1%と仮定すると、治験実施計画書に適合した対象集団〔per protocol（PP） anasysis set〕における各投与群の被験者数が 279 例であれば、セマグルチドの各用量と IGlar の比較で HbA1c に関する非劣性を結論付けるための検出力は 90%となる。セマグルチドの 2 用量に HbA1c に対する同程度の効果を仮定すると、HbA1c に関するセマグルチドの 2 用量の IGlar に対する非劣性及び体重に関するセマグルチド 1.0 mg の IGlar に対する優越性を同時に検証するための全体の検出力は 80%となる。全体として 1047 例を 1:1:1 の割合（各投与群に 349 例ずつ）で無作為割り付けすることとした。無作為割り付けされた治療を中止する被験者の割合の予想が 20%であることを考慮し、さらにこれらの被験者が PP analysis set から除外されると仮定し、各投与群で 279 例ずつが PP analysis set に含まれると予測された。

解析対象集団の定義

最大の解析対象集団〔full analysis set（FAS）〕及び安全性解析対象集団〔safety analysis set（SAS）〕の両集団には、無作為割り付けされてセマグルチド又は IGlar の投与を少なくとも 1 回受けたすべての被験者が含まれた。FAS の被験者は「無作為割り付けされたとおり（as randomised）」の評価に寄与した。PP analysis set には、FAS の被験者のうち、選択基準違反／除外基準抵触がなく、スクリーニング又は無作為割り付け時に HbA1c の測定値を有し、投与期間が少なくとも 23 週であり、23 週の投与以降に少なくとも 1 つの HbA1c の測定値を有するすべての被験者が含まれた。PP analysis set の被験者は「治療されたとおり（as treated）」の評価に寄与した。選択基準違反／除外基準抵触は、選択基準及び除外基準のフォームに記録された情報に基づき評価された。5 つの基準すべてを評価するが、上述の PP analysis set に対する基準の違反が 2 つ以上あった場合、PP analysis set から除外された症例の一覧では除外理由は 1 つのみ表示した。

観察期間

In-trial 期間：被験者が試験参加者とみなされ、データが系統的に収集される、無作為割り付け後の観察期間。この期間は有効性及び安全性の補足的解析に用いられた。

On-treatment 期間：In-trial 期間の一部であり、被験者が投与を受け治験薬に曝露されていると考えられる観察期間。この期間は、判定されたイベント、心電図及び低血糖を含む有害事象等、安全性エンドポイントの評価における主要観察期間であった。

レスキュー治療を伴わない on-treatment 期間：糖尿病治療薬によるレスキュー後に収集された情報をこの観察期間から除外した。具体的には、治験薬の初回投与日以降に記録され、on-treatment 期間の終了日とレスキュー治療の開始日のうち早い日付までに記録された観測値を含めた。この期間は有効性エンドポイントの評価における主要観察期間であった。

統計解析

プライマリーエンドポイント：ベースラインから投与後 30 週までの HbA1c の変化量

解析は、FAS に基づきレスキュー治療期間を除く on-treatment 期間から得られたデータを用いて行った。プライマリーエンドポイントは標準的な繰り返し測定に対する混合モデル（MMRM）により解析した。無作為割り付けされた治療の中止、又はレスキュー治療薬の投与開始前までの予定来院時に得られたすべてのベースライン後の HbA1c の測定値を目的変数として含めた。モデルには、治療、国、スクリーニング時に被験者が使用していた前治療の経口糖尿病薬（メトホルミン又はメトホルミンと SU）を固定効果、ベースライン時の HbA1c を共変量として含め、すべてについて来院内で入れ子にした。同一被験者の HbA1c の測定値に対し、無構造共分散行列を仮定した。欠測データは missing at random（MAR）に従うと仮定した。

検証的セカンダリーエンドポイント：ベースラインから投与後 30 週までの体重の変化量

このエンドポイントは、プライマリーエンドポイントと同様のモデルを用いて解析したが、共変量として

ベースラインの体重を含めた。

仮説

検定全体の第一種の過誤を制御するため、投与後 30 週における IGlar に対するセマグルチドの各用量の非劣性及び優越性の検定を階層的に実施した：

- HbA1cの変化量におけるセマグルチド1.0 mgのIGlarに対する非劣性
- 体重の変化量におけるセマグルチド1.0 mgのIGlarに対する優越性
- HbA1cの変化量におけるセマグルチド0.5 mgのIGlarに対する非劣性
- HbA1cの変化量におけるセマグルチド1.0 mgのIGlarに対する優越性
- 体重の変化量におけるセマグルチド0.5 mgのIGlarに対する優越性
- HbA1cの変化量におけるセマグルチド0.5 mgのIGlarに対する優越性

HbA1c の変化量において、セマグルチドと IGlar の群間差の両側 95%信頼区間の上限が 0.3%未満の場合に非劣性と結論づけることとした。HbA1c 又は体重の変化量において、群間差の両側 95%信頼区間の上限がそれぞれ 0%又は 0 kg 未満の場合に優越性と結論づけることとした。

感度分析

主要解析の安定性（例えば欠測データに関して）を検討するため、プライマリーエンドポイント及び検証的セカンダリーエンドポイントについて、それぞれ 6 つ及び 4 つの感度分析を実施した。

有効性に関する主な補足的セカンダリーエンドポイント

1. 投与後30週に米国臨床内分泌学会（AACE）によるHbA1cの目標値である6.5%以下（48 mmol/mol）を達成した被験者の割合
2. ベースラインから投与後30週までの空腹時血糖値の変化量
3. ベースラインから投与後30週までの収縮期及び拡張期血圧の変化量
4. ベースラインから投与後30週までのSF-36v2スコアの変化量
5. ベースラインから投与後30週までのDTSQスコアの変化量

すべての有効性エンドポイントは FAS を用いて要約して評価した。補足的エンドポイントの 1 は、治療、国、スクリーニング時に被験者が使用していた前治療の経口糖尿病薬を固定効果として含むロジスティック回帰モデルを用いて解析した。補足的エンドポイントの 2、3、4 及び 5 は、プライマリーエンドポイントと同様のモデルで解析したが、共変量として対応するベースライン値を含めた。

安全性に関する補足的セカンダリーエンドポイント

すべての安全性エンドポイントを、SAS を用いて要約して評価した。

治験薬投与下で発現した有害事象は記述的に要約した。事前に規定した注目すべき安全性領域については、特定の事象に対する外部のイベント判定及び事前に規定した MedDRA 検索（以降、MedDRA 検索）に基づき評価した。注目すべき安全性領域はノボ ノルディスク社 Global Safety により定義された。

低血糖は、ノボ ノルディスク社 及び米国糖尿病学会（ADA）の低血糖の分類に基づいて分類した。30 週間の投与期間中に発現した低血糖は、対数リンク関数を仮定し、無作為割り付けから低血糖の発現が治験薬投与下と考えられる期間の対数をオフセット項とする負の二項分布回帰モデルを用いて解析した。モデルには、治療、国、スクリーニング時に被験者が使用していた前治療の経口糖尿病薬を固定効果、ベースライン時の HbA1c を共変量として含めた。脈拍は、プライマリーエンドポイントと同様の方法により、ベースライン時の脈拍を共変量として解析した。すべての臨床検査項目を、SAS を用いて記述統計量により要約して評価した。

被験者背景：

	Sema 0.5 mg N	%	Sema 1.0 mg N	%	IGlar N	%	Total N	%
Number of subjects	362		360		360		1082	
Sex								
N	362	(100.0)	360	(100.0)	360	(100.0)	1082	(100.0)
Female	165	(45.6)	178	(49.4)	165	(45.8)	508	(47.0)
Male	197	(54.4)	182	(50.6)	195	(54.2)	574	(53.0)

Age (years)				
Mean (SD)	56.5 (10.3)	56.7 (10.4)	56.2 (10.6)	56.5 (10.4)
Race				
American Indian or Alaska Native	1 (0.3)	0 (0.0)	1 (0.3)	2 (0.2)
Asian	42 (11.6)	39 (10.8)	38 (10.6)	119 (11.0)
Black or African American	32 (8.8)	34 (9.4)	33 (9.2)	99 (9.1)
Native Hawaiian/Other Pacific Island	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
White	279 (77.1)	279 (77.5)	276 (76.7)	834 (77.1)
Other	3 (0.8)	3 (0.8)	5 (1.4)	11 (1.0)
NA	5 (1.4)	5 (1.4)	7 (1.9)	17 (1.6)
HbA1c (%)				
N	362	360	360	1082
Mean (SD)	8.13 (0.85)	8.25 (0.94)	8.13 (0.88)	8.17 (0.89)
HbA1c (mmol/mol)				
N	362	360	360	1082
Mean (SD)	65.36 (9.28)	66.63 (10.30)	65.39 (9.58)	65.79 (9.74)
Fasting plasma glucose (mmol/L)				
N	356	356	357	1069
Mean (SD)	9.56 (2.80)	9.95 (2.98)	9.67 (2.72)	9.73 (2.84)
Duration of Diabetes (years)				
N	362	360	360	1082
Mean (SD)	7.77 (5.14)	9.34 (7.17)	8.61 (6.29)	8.57 (6.28)
Body weight (kg)				
Mean (SD)	93.73 (21.39)	94.00 (22.48)	92.61 (21.52)	93.45 (21.79)
Body mass index (kg/m2)				
Mean (SD)	33.11 (6.45)	32.96 (6.51)	32.95 (6.51)	33.01 (6.49)
MDRD GFR 'estimated' (mL/min/1.73 m^2)				
N	362	360	360	1082
Mean (SD)	97.89 (25.94)	97.95 (27.55)	99.66 (26.46)	98.50 (26.64)
Smoker status				
N	362 (100.0)	360 (100.0)	360 (100.0)	1082 (100.0)
Current smoker	50 (13.8)	50 (13.9)	60 (16.7)	160 (14.8)
Never smoked	213 (58.8)	217 (60.3)	222 (61.7)	652 (60.3)
Previous smoker	99 (27.3)	93 (25.8)	78 (21.7)	270 (25.0)
Renal function				
N	362 (100.0)	360 (100.0)	360 (100.0)	1082 (100.0)
Normal	210 (58.0)	221 (61.4)	221 (61.4)	652 (60.3)
Mild Renal Impairment	138 (38.1)	117 (32.5)	123 (34.2)	378 (34.9)
Moderate Renal Impairment	14 (3.9)	22 (6.1)	16 (4.4)	52 (4.8)
Severe Renal Impairment	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
End stage Renal Impairment	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

IGlar: Insulin glargine, N: Number of subjects, SD: Standard deviation, CV: Coefficient of variation, MDRD: Modification of diet in renal disease, eGFR: estimated glomerular filtration rate.
The baseline value is defined as the latest pre-dosing value.
Body mass index is calculated based on baseline measurement of body weight and height.

有効性の結果：

本試験はプライマリーエンドポイントを達成し、検証的セカンダリーエンドポイントを満たした。

<u>プライマリーエンドポイント：HbA1c の変化量</u>

ベースラインから投与後 30 週までの HbA1c の変化量について、セマグルチド 0.5 mg 群（-1.21%）及びセマグルチド 1.0 mg 群（-1.64%）の IGlar 群（-0.83%）に対する優越性が検証された；IGlar 群との群差の推定値は、セマグルチド 0.5 mg 群で-0.38%（95%信頼区間：-0.52; -0.24）、セマグルチド 1.0 mg 群で-0.81%（95%信頼区間：-0.96; -0.67）であった。

<u>検証的セカンダリーエンドポイント：体重の変化量</u>

ベースラインから投与後 30 週までの体重の変化量について、セマグルチド 0.5 mg 群（-3.47 kg、-3.82%）及びセマグルチド 1.0 mg 群（-5.17 kg、-5.46%）の IGlar 群（+1.15 kg、1.41%）に対する優越性が検証された；IGlar 群との群差の推定値は、セマグルチド 0.5 mg 群で-4.62 kg（95%信頼区間：-5.27; -3.96）、セマグルチド 1.0 mg 群で -6.33 kg（95%信頼区間：-6.99; -5.67）であった。

プライマリーエンドポイント及び検証的セカンダリーエンドポイントについて、すべての感度分析で有意差が認められ、群差の推定値が主要解析の結果と同程度であったことにより、主要解析の安定性が裏付けられた。

有効性に関する主な補足的セカンダリーエンドポイント

- HbA1c 6.5%（48 mmol/mol）以下（AACEの目標値）を達成した被験者の割合は、IGlar群（17.5%）と比較してセマグルチド0.5 mg群（37.3%）及びセマグルチド1.0 mg群（54.2%）で高かった。IGlar群とのオッズ比の推定値は、セマグルチド0.5 mg群で3.02（95%信頼区間：2.11; 4.33）、セマグルチド1.0 mg群で6.86（95%信頼区間：4.76; 9.89）であった。
- 投与後30週の空腹時血糖値は、IGlar群と比較してセマグルチド1.0 mg群で有意に低下した。ベースラインからの平均変化量は、セマグルチド1.0 mg群で -2.73 mmol/L（-49.21 mg/dL）及びIGlar群で-2.12 mmol/L（-38.18 mg/dL）であった。セマグルチド1.0 mg群とIGlar群の群差の推定値は-0.61 mmol/L（95%信頼区間：0.93; -0.29）、-11.02 mg/dL（95%信頼区間：-16.85; -5.20）であった。
- 投与後30週の収縮期血圧は、IGlar群と比較してセマグルチド両用量群で有意に低下した。ベースラインからの平均変化量は、セマグルチド0.5 mg群で-4.60 mmHg、セマグルチド1.0 mg群で-5.17 mmHg及びIGlar群で-1.68 mmHgであった。IGlar群との群差の推定値は、セマグルチド0.5 mg群で-2.93 mmHg（95%信頼区間：-4.87; -0.98）及び セマグルチド1.0 mg群で-3.50 mmHg（95%信頼区間：-5.46; -1.54）であった。
- 投与後30週のSF-36v2質問票の2つのドメインにおいて、セマグルチド1.0 mg群とIGlar群の間で有意差が認められた：「全体的健康感」における群差の推定値は、1.15（95%信頼区間：0.12; 2.18）であった。「日常役割機能（精神）」における群差の推定値は1.67（95%信頼区間：0.20; 3.14）であった。
- 投与後30週のDTSQの約半分のドメインにおいて、IGlar群と比較してセマグルチド両用量群で有意な改善が認められた。治療満足度に関するサマリードメインスコアにおけるIGlar群との群差の推定値はセマグルチド0.5 mg群で0.87（95%信頼区間：0.11; 1.63）、セマグルチド1.0 mg群で1.38（95%信頼区間：0.60; 2.15）であった。

安全性の結果：

30 週間の投与期間において、セマグルチド及び IGlar は全般的に安全で忍容性も良好であった。安全性に関する所見は、有害事象及び関連する結果に基づき以下に要約した。

有害事象

- 本試験中、死亡に至った事象が6件発現した：セマグルチド0.5 mg群で4件及びIGlar群で2件。
- On-treatment期間において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、IGlar群（65.3%、316.7件／100人･年）と比較してセマグルチド0.5 mg群（69.9%、455.9件／100人･年）及びセマグルチド1.0 mg群（73.3%、525.2件／100人･年）で多かった。
- 最も高頻度で報告された有害事象は、セマグルチド両用量群では器官別大分類の胃腸障害に分類される有害事象であったのに対し、IGlar群では器官別大分類の感染症および寄生虫症に分類される有害事象であった。
  - セマグルチドの両用量群において被験者の5%以上で認められた有害事象の大部分は、器官別大分類の胃腸障害に分類される有害事象であり、基本語の悪心、下痢、嘔吐、消化不良及び胃食道逆流性疾患で構成された。
- すべての投与群において、報告された有害事象の大部分は軽度又は中等度であった；重度の有害事象を発現した被験者の割合は、セマグルチド0.5 mg群、セマグルチド1.0 mg群及びIGlar群でそれぞれ7.5%、5.6%及び2.8%であった。
  - 有害事象の転帰が「回復」であった被験者の割合は、セマグルチド0.5 mg群、セマグルチド1.0 mg群及びIGlar群でそれぞれ63.0%、70.0%及び57.2%であった。
- 投与群を通じて、有害事象の大部分（50%以上）は治験責任医師により治験薬との因果関係が「なし」と判定された。
  - セマグルチド両用量群で、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うち、最も多く報告された事象は、胃腸障害の有害事象（セマグルチド0.5 mg群及びセ

マグルチド1.0 mg群でそれぞれ被験者の31.8%及び34.7%）及び器官別大分類の臨床検査に分類される有害事象（セマグルチド0.5 mg群及びセマグルチド1.0 mg群でそれぞれ被験者の10.2%及び10.3%）であった。
  - IGlar群で、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のうち、最も多く報告された事象は、器官別大分類の胃腸障害に分類される有害事象（被験者の2.8%）、器官別大分類の臨床検査に分類される有害事象（被験者の3.1%）及び器官別大分類の皮膚および皮下組織障害に分類される有害事象（被験者の2.5%）であった。
- 重篤な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（セマグルチド0.5 mg群、セマグルチド1.0 mg群及びIGlar群でそれぞれ被験者の6.1%、4.7%及び5.0%）。本試験中、計6件の重篤な有害事象の転帰が「死亡」であった：セマグルチド0.5 mgで4件及びIGlar群で2件。
- 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低く、セマグルチド両用量群で同程度であったが（セマグルチド0.5 mg群及びセマグルチド1.0 mg群でそれぞれ5.5%及び7.5%）、IGlar群（1.1%）と比較するとその割合は高かった。これは、セマグルチド両用量群の被験者では投与の中止に至った胃腸障害の有害事象の発現頻度が高かったことを反映していた。
- 有害事象の発現件数は、on-treatment期間と比較してin-trial期間でわずかに多かった；しかし、2つの観察期間で認められた違いは、臨床的に問題となるとは考えられなかった。
- 全般的に、セマグルチド及びIGlarの忍容性は良好であった。

<u>低血糖</u>

- 重大な低血糖はセマグルチド0.5 mg群で2例、セマグルチド1.0 mg群で5例及びIGlar群で5例報告された。
- 重大な又は血糖値確定症候性低血糖を発現した被験者の割合は低かった。また、低血糖はSUを併用した被験者で多く報告された。

<u>注目すべき安全性領域</u>

- 胃腸障害の有害事象
  - 胃腸障害の有害事象は、本試験においてセマグルチドの投与後に最も高頻度で報告された有害事象である。最も高頻度（5%以上）で報告された胃腸障害の有害事象は、悪心、下痢、嘔吐、消化不良及び胃食道逆流性疾患であり、これらの有害事象はIGlar群と比較してセマグルチド両用量群で単位時間あたりの発現件数が多く、発現した被験者の割合も高かった。
  - 事象の大部分は、投与開始後12～18週間以内に発現し、胃腸障害の有害事象である悪心、下痢、嘔吐及び消化不良は一時的なもので、発現期間の中央値はいずれの投与群でも1～5日であった。
  - 5例（セマグルチド0.5 mg群で3例及びIGlar群で2例）から、重篤な胃腸障害の有害事象が報告された。
- 心血管系事象
  - イベント判定委員会により、10例11件の心血管系事象が確認された（セマグルチド0.5 mg群、セマグルチド1.0 mg群及びIGlar群でそれぞれ3件、4件及び4件）。11件のうち5件の転帰が「死亡」であった〔セマグルチド0.5 mg群で3例（心筋炎、脳血管発作及び虚血性脳卒中）、IGlar群で2例（冠動脈硬化症及び原因不明の死亡）〕。残りの6件の有害事象の転帰は「回復」であった。
  - MedDRA検索により、92件の心血管系事象が特定され、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を通じて同様であった。セマグルチド0.5 mg群で2件（急性呼吸不全及び呼吸困難）が治験薬の投与の中止に至った。
  - ベースラインから投与終了までの脈拍数は、IGlar群と比較してセマグルチド両用量群で統計的に有意に増加した。脈拍数の平均増加量（推定値）は、セマグルチド0.5 mg群で2.31、セマグルチド1.0 mg群で3.14及びIGlar群で–0.05であった。
  - ベースライン及び投与後30週において、いずれの投与群でも心電図測定結果の大部分は「正常」又は「異常、臨床的に問題なし」であった。
- 膵炎

- 判定されたイベント7件のうち2件（いずれもセマグルチド0.5 mg群）が、イベント判定委員会により膵炎と確認された。2件がMedDRA検索により特定された（イベント判定委員会により確認された1件を含む）。MedDRA検索により特定されたうちの1件は、リパーゼの異常な増加による膵炎の疑いであった。本事象により治験薬の投与が一時中断された。
- リパーゼ及びアミラーゼの平均増加量は、IGlar群と比較してセマグルチド両用量群で有意に大きかった。被験者の大部分は試験期間を通じて酵素値が基準範囲上限2倍未満であり、リパーゼが基準範囲上限5倍超又はアミラーゼが基準範囲上限2倍超を示した被験者のほとんどが、外れ値を示したのは1回のみであった。

- 肝胆道系障害
  - MedDRA検索により、9例11件の胆嚢に関連する有害事象が特定された；セマグルチド0.5 mg群、セマグルチド1.0 mg群及びIGlar群でそれぞれ4件、6件及び1 件。胆石症、慢性胆嚢炎、胆嚢障害及び陶器様胆嚢を発現したすべての被験者において、試験終了時のこれらの事象の転帰は「未回復」であった。いずれの事象も、投与の中止には至らなかった。
  - 本試験中、肝機能検査値の平均は減少が認められた。7例でアラニンアミノトランスフェラーゼ（ALT）及び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5倍超、1例で総ビリルビンが基準範囲上限3倍超を示したが、アルカリフォスファターゼ（ALP）の外れ値は認められなかった。4つのパラメータのベースラインからの平均変化量は、セマグルチド両用量群とIGlar群で同程度であり臨床的に問題のある変化とは考えられなかった。
  - 2例が血液生化学的検査でHy's lawの定義を満たした。1例はB型肝炎に関連する酵素増加で、有害事象のB型肝炎からの回復が確認された時点で正常化していた（治験薬の投与を継続しながら被験者は回復）。もう1例はアルコール乱用に起因し、治験薬の投与期間中に酵素値は試験開始前の値まで正常化した。
- 新生物
  - イベント判定委員会により、13例19件の新生物が確認された：セマグルチド0.5 mg群、セマグルチド1.0 mg群及びIGlar群でそれぞれ9件、5件及び5件であった。ここで確認された事象は、MedDRA検索により特定された新生物と一致していた。
  - イベント判定委員会により確認された新生物の大部分は1例1件の発現であり、原発組織又は臓器及びクラス（良性及び悪性）の分布は、すべての投与群間で同様であった。
  - イベント判定員会により確認された甲状腺新生物はなかった。
- 甲状腺障害
  - イベント判定委員会により確認された甲状腺切除を必要とする甲状腺疾患又は甲状腺新生物はなかった。MedDRA検索により、5件の非重篤かつ軽度又は中等度のカルシトニンの増加に関連する事象（血中カルシトニン増加）が特定された。
  - 全般的に、平均及び個々のカルシトニン値について、投与期間を通じて投与群内又は投与群間で臨床的に問題となる変化は認められなかった。
- 腎障害
  - 本試験中、急性腎不全に関連する有害事象の全体的な発現頻度は低かった（セマグルチド0.5 mg群、セマグルチド1.0 mg群及びIGlar群でそれぞれ7件、9件及び1件）。事象の大部分は、非重篤かつ軽度又は中等度であり、2件の重篤な有害事象（急性腎不全及び腎不全）がセマグルチド1.0 mg群で報告された。1件（腎機能障害）が投与の中止に至った。
  - セマグルチド0.5 mg群の1例が、投与後30週においてクレアチニンの外れ値の基準（少なくとも1回の基準範囲上限の6倍超又はベースライン値の3倍超を示す）を満たした。本被験者において1件の有害事象（血中クレアチニン増加）が報告された。当該事象は、軽度かつ非重篤で、治験薬との因果関係は「なし」と判定された。また、本事象による治験薬投与の中断はなく、発現から4日後に本事象からの回復が確認された。
  - その他の腎機能に関連する臨床検査項目又は尿検査の結果には、投与群内及び投与群間で臨床的に問題となる経時的変化は認められなかった。
- 免疫原性に関連する有害事象及び注射部位反応

- 32例34件の皮膚、呼吸、眼、免疫系及び血管障害に関連するアレルギー反応が報告された（セマグルチド0.5 mg群、セマグルチド1.0 mg群及びIGlar群でそれぞれ18件、9件及び7件）。IGlar群で報告された2件（蕁麻疹及び'全身性皮疹）については、治験薬との因果関係が「あり」と判定され、当該事象の発現により治験薬の投与を中止した。
- 来院2（ベースライン）においてセマグルチドの投与を開始する前に、2例が抗セマグルチド抗体及びGLP-1に対する交叉抗体が陽性であった。いずれの被験者も以降の来院では抗体陰性を示し、投与に関連する抗セマグルチド抗体の産生は認められなかった。また、事後調査来院では抗体陽性でなかったため*in vitro*での中和作用は評価されなかった。
- 11例12件の免疫複合体疾患が報告された（セマグルチド0.5 mg群で2件、セマグルチド1.0 mg群で4件及びIGlar群で6件）。報告された事象の種類及び分布に明らかな傾向は認められず、いずれの事象も投与の中止には至らなかった。
- 計11件の注射部位反応が報告された。セマグルチド0.5 mg群で3例3件、セマグルチド1.0 mg群で2例2件及びIGlar群で6例6件：いずれの事象も非重篤で、投与の中止には至らなかった。

- 投薬過誤
  - 本試験のon-treatment期間中において、2件の投薬過誤が報告された：セマグルチド1.0 mg群の1例で偶発的過量投与（治験薬を週に2回投与した）及びIGlar群の1例で誤用量投与。いずれも非重篤かつ軽度であり、関連症状の発現は認められず、投与の中断又は投与の中止には至らなかった。
- 稀な事象
  - 事前に規定した検索により、計12件の薬剤誘発性の疑いのある稀な事象が特定された：セマグルチド0.5 mg群で5例5件、セマグルチド1.0 mg群で3例3件及びIGlar群で4例4件。すべての事象が非重篤かつ軽度又は中等度で、治験薬との因果関係は「なし」と判定され、治験薬の投与中止又は用量変更には至らなかった。また、10例のうち2例のみが、試験終了時に回復が確認された。

<u>その他の臨床検査項目、身体所見及び妊娠</u>

- 注目すべき安全性領域に記載されていない血液生化学的検査又は血液学的検査に関するパラメータについて、臨床的に問題となる変化は認められなかった。
- 身体所見について、投与群間に臨床的に問題となる違いは認められなかった。
- 本試験中に2件の妊娠（セマグルチド1.0 mg群で1件及びIGlar群で1件）が報告され、両被験者ともに投与を中止した。いずれも妊娠は正常で、妊娠満期で先天性異常のない健康児を出産した。

全体の結論：

- ベースラインから投与後30週までのHbA1c及び体重の変化量について、セマグルチドのIGlar対する優越性が検証された。
- HbA1cの目標達成（6.5%以下又は7.0%未満）及び体重減少（5%以下又は10%以下）に関するオッズは、IGlarと比較してセマグルチドで有意に高かった。
- セマグルチドの投与により、空腹時血糖値、収縮期及び拡張期血圧ならびに患者報告アウトカムの有意な改善が認められた。
- セマグルチド及びIGlarの投与は忍容性が良好で、予期しない安全性の問題は認められなかった。
  - 全体的な有害事象の単位時間あたりの発現件数は、IGlarと比較してセマグルチドで多かった；重篤な有害事象を発現した被験者の割合は、投与群を通じて同程度であった。
  - 最も高頻度で報告された有害事象は、セマグルチドでは胃腸障害の有害事象であり、IGlarでは感染症および寄生虫症の有害事象であった；胃腸障害の有害事象の大部分は、軽度又は中等度であり、その発現頻度は経時的に低下した。
  - 有害事象により投与を中止した被験者の割合は低かったが、IGlarと比較するとセマグルチドで高かった。
  - 重大な又は血糖値確定症候性低血糖を発現した被験者の割合は、IGlarと比較してセマグルチド両用量で低かった。また、低血糖はSUを併用した被験者で多く報告された。

本試験は、ヘルシンキ宣言の精神及び ICH-GCP を遵守して実施された。

2.7.6.23 NN9535-4091

2.7.6.23.1 臨床試験概要

治験依頼者名： Novo Nordisk Pharma Ltd, 2-1-1, Marunouchi, Chiyoda-ku Tokyo, Japan	
有効成分名： セマグルチド	
Trial Registration ID-number： NCT02207374	UTN：U1111-1140-3081 IND number：該当なし EudraCT number：該当なし Japanese registration number：JapicCTI-142640
治験の標題： 食事・運動療法又は経口糖尿病薬単剤による治療で十分な血糖コントロールが得られていない日本人 2 型糖尿病患者を対象とした、セマグルチド（週 1 回投与）の単独療法及び経口糖尿病薬との併用療法の安全性及び有効性の検討	
治験責任医師名： 治験実施施設（全 41 施設）ごとに 1 名の治験責任医師が任命された。以下の治験責任医師が治験総括報告書の内容を確認し、署名する「治験総括報告書への署名責任を有する医師（signatory investigator）」に指名された。 [redacted]	
治験実施施設： 本試験は日本国内で実施された。41 施設においてスクリーニングと無作為割り付けを実施した。	
公表文献（引用文献）： 本臨床試験概要作成時点での公表文献はなし	
治験期間： 開始日：2014 年 8 月 4 日 終了日：2016 年 2 月 27 日	**開発のフェーズ**： 第 3a 相
Cut-off date： ここに提示する結果は、2016 年 4 月 18 日の時点での臨床データベースに基づいている。	
報告書作成日： 2016 年 9 月 12 日	
目的： <u>主要目的</u>： 食事・運動療法又は経口糖尿病薬単剤〔スルホニルウレア薬（SU）、グリニド、α-グルコシダーゼ阻害薬（α-GI）又はチアゾリジン薬（TZD）のいずれか〕による治療で十分な血糖コントロールが得られていない日本人 2 型糖尿病患者を対象とし、セマグルチド（0.5 mg 及び 1.0 mg、週 1 回投与）の単独療法及び経口糖尿病薬単剤（SU、グリニド、α-GI 又は TZD のいずれか）との併用療法の 56 週間の安全性を、経口糖尿病薬療法と比較検討する。 <u>副次的目的</u>： 投与後 56 週の以下の項目に対するセマグルチド（0.5 mg 及び 1.0 mg、週 1 回投与）の単独療法及び経口糖尿病薬単剤（SU、グリニド、α-GI 又は TZD のいずれか）との併用療法の有効性を、経口糖尿病薬療法と比較検討する。 ● 血糖コントロール	

- 体重減少の誘導及び維持
- 有効性に関するその他のパラメータ

治験方法：

本試験は、日本人 2 型糖尿病患者を対象とした、セマグルチド（0.5 mg 及び 1.0 mg、週 1 回皮下投与）の単独療法及び経口糖尿病薬単剤（SU、グリニド、α-GI 又は TZD のいずれか）との併用療法の安全性及び有効性を評価する、1 ヵ国（日本）、多施設共同、56 週間投与、無作為割り付け、非盲検、実薬対照、並行群間比較（3 群）試験であった。被験者は、性別不問、年齢 20 歳以上の、2 型糖尿病と診断され安定した治療（薬剤及び用量を変更していない治療と規定）を受けている日本人患者であった。被験者は以下のいずれかの前治療に関する基準を満たすものとした。

- 来院1（-2週）の30日以上前から、食事・運動療法を受けている
- 来院1（-2週）の60日以上前から、食事・運動療法に加え、日本で承認されている用法・用量の範囲内での経口糖尿病薬単剤（SU、グリニド、α-GI又はTZDのいずれか）による治療を受けている

本試験は、スクリーニング期間（-2 週～0 週）、治療期間（0 週～投与後 56 週）及び事後調査期間（投与後 56 週～61 週）で構成された。各被験者の試験参加期間は、計 63 週間（-2 週～投与後 61 週）であった。すべての被験者は、スクリーニング時の前治療（食事・運動療法又は食事・運動療法に加えて経口糖尿病薬単剤を追加）を試験期間中も継続することとした。治療期間中（0 週～投与後 56 週）、被験者は前治療に加えて、被験薬（セマグルチド 0.5 mg 又は 1.0 mg）又は経口糖尿病薬 1 剤のいずれかを投与することとした。

スクリーニング来院後、適格例は無作為割り付けのために来院し、セマグルチド（0.5 mg 又は 1.0 mg）の週 1 回投与、もしくは追加の 1 剤の経口糖尿病薬投与の 56 週間の治療のいずれかに、2:2:1 の割合で無作為に割り付けられた。セマグルチド両用量群の被験者の治療期間は用量漸増期間及び用量維持期間に分けられた。

無作為割り付け後、被験者は事前に規定された用量漸増法に従い、セマグルチド 0.5 mg 群では、0.25 mg を 4 回（4 週間）投与した後に 0.5 mg の維持用量へ増量した。セマグルチド 1.0 mg 群では、0.25 mg を 4 回（4 週間）、続いて 0.5 mg を 4 回（4 週間）投与した後、1.0 mg の維持用量へ増量した。維持用量に達した後、残りの試験期間中において用量変更を行わないこととした。

追加の経口糖尿病薬の種類及び用量は、日本で承認されている承認事項（併用薬剤、禁忌を含む）の範囲内で、治験責任医師の判断により選択することとした。DPP-4 阻害薬、SU、グリニド、ビグアナイド、α-GI 又は TZD のいずれかを、追加の経口糖尿病薬として選択することとした。前治療として経口糖尿病薬単剤による治療を受けていた被験者は、前治療の経口糖尿病薬とは異なる作用機序を有する経口糖尿病薬を、追加の経口糖尿病薬として用い、用法・用量を選択した。追加の経口糖尿病薬の用量は、日本で承認されている用法・用量の範囲内で、来院 6（投与後 8 週）までに最適となるよう調整することとした。その後は、レスキュー治療薬が必要な場合を除き、来院 18（投与後 56 週）まで用量変更を行わないこととした。試験期間中、追加の経口糖尿病薬の種類は変更不可とした。

治療薬に起因すると疑われる安全性の理由により必要に応じて治療を中止できることとし、その場合には急性膵炎の疑いが否定された場合を除き、投与は再開しないこととした。治験薬の投与は投与後 56 週である来院 18 まで継続した。各被験者の最終予定来院は、実際の最終投与来院日から 5 週間後の事後調査来院であった。

ノボ ノルディスク社は、盲検化された安全性データの継続的な安全性審査を行う、社内のセマグルチド安全性委員会を設置した。このセマグルチド安全性委員会は、本試験の全体的な安全性審査の責任を負った。進行中のセマグルチドの心血管系アウトカム試験（NN9535-3744）から得られる非盲検化された安全性データを独立して確認し、評価するために設立された外部のデータモニタリング委員会（DMC）が、本試験で認められたすべての主要な心血管イベント（MACE）を評価した。

また、特定の事象の継続的な判定、標準化及び評価を行うため、独立した外部のイベント判定委員会が設立された。当該判定は、独立した外部の医学専門家が統一基準に基づいて一貫性を持って事象を確認することを目的とした。

計画及び解析された被験者数：

無作為割り付けする予定症例数を 595 例〔前治療として、食事・運動療法及び SU 単独療法の各層に 170 例ずつ、その他の経口糖尿病薬（グリニド、α-GI 及び TZD）による単独療法の各層に 85 例ずつ〕として、計 700 例のスクリーニングが計画された。実際には、665 例がスクリーニングを受け、うち 601 例が無作為割り付けされた。

	Sema 0.5 mg N (%)	Sema 1.0 mg N (%)	Additional OAD N (%)	Total N (%)
Screened				665
Screening failures				64 (9.6)
Randomised	239	241	121	601
Exposed/FAS/SAS	239 (100.0)	241 (100.0)	120 (99.2)	600 (99.8)
Pre-trial treatment at screening				
N	239 (100.0)	241 (100.0)	120 (100.0)	600 (100.0)
Diet and exercise	68 (28.5)	68 (28.2)	35 (29.2)	171 (28.5)
Sulphonylurea	68 (28.5)	69 (28.6)	33 (27.5)	170 (28.3)
Glinide	34 (14.2)	36 (14.9)	17 (14.2)	87 (14.5)
Alpha-glucosidase inhibitor	35 (14.6)	34 (14.1)	18 (15.0)	87 (14.5)
Thiazolidinediones	34 (14.2)	34 (14.1)	17 (14.2)	85 (14.2)
Treatment completers[1]	224 (93.7)	207 (85.9)	113 (94.2)	544 (90.7)
Trial completers[2]	233 (97.5)	231 (95.9)	115 (95.0)	579 (96.3)
Premature treatment discontinuers	15 (6.3)	34 (14.1)	7 (5.8)	56 (9.3)
Other	1 (0.4)	8 (3.3)	3 (2.5)	12 (2.0)
Pregnancy	0	0	0	0
Protocol violation	0	0	0	0
Due to adverse event	14 (5.9)	26 (10.8)	4 (3.3)	44 (7.3)

Abbreviations: Sema: semaglutide, OAD: Oral anti-diabetic drug. N: Number of subjects, %: Percentages of randomised subjects, FAS: Full Analysis Set, SAS: Safety Analysis Set.
[1] Subjects who completed treatment according to end-of-trial electronic case report form.
[2] Subjects with a follow-up visit

診断及び主要な組入れ基準：

主な選択基準：

性別不問、同意取得時点で年齢 20 歳以上、HbA1c が 7.0%以上 10.5%以下（53～91 mmol/mol）であり、以下の a)又は b)のいずれかの安定した治療（薬剤及び用量を変更していない）を受けていた日本人 2 型糖尿病患者。

a）来院 1（-2 週）の 30 日以上前から、食事・運動療法を受けていた

b）来院 1（-2 週）の 60 日以上前から、食事・運動療法に加え、日本で承認されている用法・用量の範囲内での経口糖尿病薬単剤（SU、グリニド、α-GI 又は TZD のいずれか）による治療を受けていた

主な除外基準：

妊婦、授乳婦、妊娠を希望している、又は妊娠する可能性のある女性で、5 週間の事後調査期間を含めた試験期間中に適切な避妊法を受け入れられない被験者。来院 1（-2 週）の前 60 日以内に、選択基準に示された糖尿病治療薬以外の血糖降下薬の投与を受けた被験者、ならびに来院 1（-2 週）の前 90 日以内に、週 1 回投与のグルカゴン様ペプチド-1（GLP-1）受容体作動薬の投与を受けた被験者〔ただし、併発疾患のための短期間のインスリン投与（合計で 7 日以内）については可とする〕。被験者の安全を脅かしたり、治験実施計画書の遵守を困難にしたりする可能性があると治験責任医師により判断された疾患を有する被験者。慢性又は特発性急性膵炎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濃度 50 ng/L（pg/mL）以上の被験者。甲状腺髄様癌又は多発性内分泌腫瘍症候群 2 型の既往歴又は家族歴を有する被験者。腎機能障害〔4 変数 Modification of Diet in Renal Disease 式による推算糸球体濾過量（eGFR）30 mL/min/1.73 m^2 未満と定義〕を有する被験者。無作為割り付け前 90 日以内に急性冠動脈疾患又は脳血管疾患を発現した被験者。心不全（NYHA 分類クラス IV）を有する被験者。

主な投与中止基準：

治験薬との関連が疑われる安全性の懸念がある場合、又は治験薬投与に受け入れがたい非忍容性が認めら

れる場合。
中止・脱落基準：
被験者は、同意を撤回することにより、いつでも自由意思により試験を中止することができた。

被験薬、用量及び投与方法、ロット番号：
セマグルチド注射液（1.34 mg/mL）〔PDS290 ペン型注入器（1.5 mL）と一体化したプレフィルド製剤〕を、食事時間に関係なく 1 日のいずれかの時点において 0.5 mg 又は 1.0 mg を大腿部、腹部又は上腕部のいずれかに週 1 回皮下投与した。セマグルチドのロット番号（有効期限）：CV40206（2016 年 2 月 19 日）、CV40235（2016 年 2 月 21 日）及び DV40234（2017 年 5 月 7 日）

投与期間：
56 週間

対照薬、用量及び投与方法、ロット番号：
追加の経口糖尿病薬は、治験薬ではなく併用薬剤とみなされ、治験責任医師により処方された（ノボ ノルディスクからは提供されなかった）。

評価基準：有効性
HbA1c、体重、空腹時血糖値、収縮期及び拡張期血圧

評価基準：安全性
治験薬投与下で発現した有害事象〔（Treatment Emergent Adverse Event、以下、有害事象とする）これには、独立した外部のイベント判定委員会 により判定される、事前に規定した特に注目すべき医学的事象が含まれる〕、低血糖、脈拍数及び安全性に関する臨床検査項目。

統計手法：
被験者数の設定
本試験の被験者数は、「経口血糖降下薬の臨床評価方法に関するガイドライン」の要求事項に基づいて設定した。無作為割り付けは、スクリーニング時の前治療（食事・運動療法、SU、グリニド、α-GI 又は TZD）で層別した。食事・運動療法及び SU 単独療法の層にそれぞれ 170 例、その他の経口糖尿病薬の単独療法（グリニド、α-GI 及び TZD）の層にそれぞれ 85 例の被験者を組み入れることとした。無作為割り付けされた治療の中止率を 25%と仮定し、セマグルチドの単独療法及び SU との併用療法でそれぞれ 100 例の完了例、ならびにセマグルチドのグリニド、α-GI 及び TZD との併用療法でそれぞれ 50 例の完了例を確保するように各層の被験者数を設定した。本試験では、合計 601 例の被験者を、セマグルチド 0.5 mg、セマグルチド 1.0 mg 又は追加の経口糖尿病薬投与のいずれかに 2:2:1 の割合で無作為割り付けした。15%のスクリーニング不適格例を仮定し、合計 700 例の被験者を本試験に組み入れることとした。
解析対象集団の定義
最大の解析対象集団〔full analysis set（FAS）〕及び安全性解析対象集団〔safety analysis set（SAS）〕の両集団には、無作為割り付けされたセマグルチド又は追加の経口糖尿病薬の投与を少なくとも 1 回受けたすべての割り付けられた被験者が含まれた。FAS 及び SAS の被験者は、それぞれ「無作為割り付けされたとおり（as randomised）」の評価及び実際の「治療されたとおり（as treated）」の評価に寄与した。
観察期間
In-trial 期間：無作為割り付け後に被験者が試験参加者とみなされ、データが系統的に収集される観察期間。この期間は有効性及び安全性の補足的解析に用いられた。
On-treatment 期間：被験者が、投与を受け無作為割り付けされた治験薬に曝露されていると考えられる観察期間。この期間は、判定されたイベント、心電図及び低血糖を含む有害事象等、安全性エンドポイントの評価における主要観察期間であった。
レスキュー治療を伴わない on-treatment 期間：糖尿病治療薬によるレスキュー後に収集された情報をこの観察期間から除外した。具体的には、無作為割り付けされた治療の開始日以降に記録され、on-treatment 期間の終了日とレスキュー治療の開始日のうち早い日付までに記録された観測値を含めた。この期間は有効性エンドポイントの評価における主要観察期間であった。

統計解析

プライマリーエンドポイント：56 週間の治験薬投与下で発現した有害事象の発現件数

治験薬投与下で発現した有害事象（TEAE）は、他のすべての安全性エンドポイントと同様、SAS を用いて解析した。発現日（又は重症度の悪化）が on treatment 観察期間内である有害事象を TEAE と定義した。TEAE は記述的に要約し、有害事象に関して少なくとも 1 件発現した被験者数（N）、少なくとも 1 件発現した被験者の割合（%）、発現件数（E）及び 100 人・年あたりの発現件数（R）を示した。

有効性に関する主な補足的セカンダリーエンドポイント：ベースラインから投与後 56 週までの以下の項目の変化量

- HbA1c
- 体重
- 空腹時血糖値
- 収縮期及び拡張期血圧

解析は FAS に基づいて行った。有効性に関するエンドポイントは標準的な繰り返し測定に対する混合モデル（MMRM）を用いて解析した。無作為割り付けされた治療の中止又はレスキュー治療の開始前までの予定された来院時に得られたすべてのベースライン後の測定値を目的変数として含めた。モデルには、治療及びスクリーニング時の前治療を固定効果、ベースライン値を共変量として含め、すべてについて来院内で入れ子にした。欠測データに関しては missing at random（MAR）に従うと仮定した。投与後 56 週におけるセマグルチドの各用量群及び追加の経口糖尿病薬群の群間差の推定値及び対応する両側 p 値及び 95%信頼区間を提示した。

感度分析

主要解析の安定性を検討するため、投与後 56 週までの HbA1c 及び体重の変化量について、4 つの異なる補足的な感度分析を、FAS を用いて実施した。これらの 4 つの事前規定した感度分析では、欠測データの影響による結果への感度を検討した。完了例に対して MMRM 法で解析した。糖尿病患者を対象とした過去の臨床試験と比較評価するために last observation carried forward（LOCF）法に基づいて解析を行った。Pattern mixture モデル（PMM）に基づく解析では、セマグルチド両用量群の欠測データの推移が追加の経口糖尿病薬群の推移に従うと仮定して欠測データを補完することにより、セマグルチドの効果が徐々に取り除かれた。この解析では、セマグルチドに好ましくない方向への MAR の仮定からの乖離を検討した。最後に、被験者が治療を受けていたか否か、又はレスキュー治療を受けていたか否かに関わらず、無作為割り付け後に収集されたすべてのデータを用いた in-trial 期間の MMRM 解析を行った。

投与後 56 週までに以下の目標を達成した被験者の割合（はい／いいえ）：

- HbA1c 7.0%（53 mmol/mol）未満：米国糖尿病学会（ADA）目標値
- HbA1c 6.5%（48 mmol/mol）以下：米国臨床内分泌学会（AACE）目標値

これらのエンドポイントのそれぞれについて、同様のロジスティック回帰モデルで解析し、オッズ比及び 95%信頼区間及び p 値を用いて提示した。モデルには、治療、スクリーニング時の前治療及びベースラインの HbA1c を共変量として含めた。投与後 56 週における欠測データは HbA1c の解析に用いた MMRM に基づいて補完した。

安全性に関する主な補足的セカンダリーエンドポイント

- 低血糖の有害事象は、ノボ ノルディスク社及びADAで定める低血糖分類に基づいて分類した。治験薬投与下で発現した低血糖（Treatment Emergent hypoglycaemic episode、以下、低血糖とする）は記述的に要約し、100人・年あたりの発現件数として示した。
- 事前に規定した特に注目すべき有害事象については、MedDRA検索（MedDRA Ver.18.0）に基づき評価した。これはノボ ノルディスク社 Global Safetyにより定義され、事前に規定した基本語で構成された。
- 脈拍は標準的なMMRMを用いて解析した。
- 臨床検査項目を、SASを用いて記述統計量を用いて評価した。

重要なこととして、すべてのエンドポイントに関するデータの提示にあたり、「有意」という表現は統計解析により裏付けられる場合にのみ用いる。

被験者背景：

	Sema 0.5 mg N (%)	Sema 1.0 mg N (%)	Additional OAD N (%)	Total N (%)
Number of subjects	239	241	120	600
Sex				
Female	73 (30.5)	67 (27.8)	31 (25.8)	171 (28.5)
Male	166 (69.5)	174 (72.2)	89 (74.2)	429 (71.5)
Age (years)				
Mean (SD)	58.0 (10.6)	58.7(10.2)	59.2 (10.1)	58.5 (10.3)
Body weight (kg)				
Mean (SD)	71.02 (15.41)	71.71(15.90)	72.17 (14.86)	71.53 (15.48)
Body mass index (kg/m2)				
Mean (SD)	26.25 (4.80)	26.42 (4.71)	26.73 (4.56)	26.41 (4.71)
Race				
Japanese	239 (100.0)	241 (100.0)	120 (100.0)	600 (100.0)
Smoker status				
Current smoker	67 (28.0)	64 (26.6)	28 (23.3)	159 (26.5)
Never smoked	89 (37.2)	95 (39.4)	41 (34.2)	225 (37.5)
Previous smoker	83 (34.7)	82 (34.0)	51 (42.5)	216 (36.0)
Renal function				
Normal	160 (66.9)	164 (68.0)	88 (73.3)	412 (68.7)
Mild Renal Impairment	76 (31.8)	70 (29.0)	30 (25.0)	176 (29.3)
Moderate Renal Impairment	3 (1.3)	7 (2.9)	2 (1.7)	12 (2.0)
Severe Renal Impairment	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
End stage Renal Impairment	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
HbA1c (%)				
Mean (SD)	8.04 (0.89)	8.14 (0.96)	8.10 (0.89)	8.09 (0.92)
Fasting plasma glucose (mmol/L)				
Mean (SD)	8.87 (1.92)	8.90 (2.11)	8.97 (1.93)	8.90 (2.00)
Duration of Diabetes (years)				
Mean (SD)	8.12 (6.01)	9.35 (6.50)	9.27 (6.99)	8.85 (6.43)
MDRD eGFR (mL/min/1.73 m2)				
Mean (SD)	101.4 (21.66)	101.6 (24.04)	102.0 (22.54)	101.6 (22.78)

Abbreviations: N: Number of subjects, %: Percentage of subjects, BMI: Body mass index, MDRD: Modification of diet in renal disease, eGFR: estimated glomerular filtration rate, HbA1c: glycosylated haemoglobin, OAD: Oral anti-diabetic drug, sema: semaglutide, SD: standard deviation

有効性の結果：

ベースラインから投与後 56 週までの HbA1c 及び体重の変化量に関して、追加の経口糖尿病薬と比較して、セマグルチド 0.5 mg 及びセマグルチド 1.0 mg の効果が大きいことが示された。さらに、複数の補足的セカンダリーエンドポイントにおいて、追加の経口糖尿病薬群と比較してセマグルチド両用量群で有意な改善がみられた。

<u>有効性に関する主な補足的セカンダリーエンドポイント：HbA1c の変化量</u>

- ベースラインから投与後56週までのHbA1cについては、追加の経口糖尿病薬群と比較して、セマグルチド両用量群にて有意に大きな低下がみられた。追加の経口糖尿病薬群との群差の推定値は、セマグルチド0.5 mg群で-1.08%（95%信頼区間：-1.24; -0.91）、セマグルチド1.0 mg群で-1.37%（95%信頼区間：-1.53; -1.20）であった。ベースラインから投与後56週までのHbA1cの低下量は、追加の経口糖尿病薬群（-0.67%）と比較してセマグルチド0.5 mg群（-1.74%）及びセマグルチド1.0 mg群（-2.03%）で大きかった。
- 4つの感度分析において、セマグルチド両用量群の血糖コントロールが追加の経口糖尿病薬群と比較して有意に改善しており、MMRM法を用いた主要解析の安定性が裏付けられた。4つの感度分析による追加の経口糖尿病薬群との群差の推定値は同様で、範囲はセマグルチド0.5 mg群：
  -1.00%（95%信頼区間：-1.16; -0.83）～-1.08%（-1.24; -0.91）、セマグルチド1.0 mg群：-1.25%（95%信頼区間：-1.44;-1.06）～-1.31%（-1.47; -1.14）であり、セマグルチドの有意な血糖降下作用が裏付けら

れた。
- 治療と前治療との間に、統計的に有意な交互作用は認められなかった（セマグルチド0.5 mg群：p=0.0820、セマグルチド1.0 mg群：P=0.0503）。いずれの前治療の層でも、投与後56週のHbA1c及び平均低下量（推定値）は、追加の経口糖尿病薬群と比較してセマグルチド両用量群で低かった（大きかった）。

有効性に関する主な補足的セカンダリーエンドポイント：体重の変化量
- ベースラインから投与後56週までの体重について、追加の経口糖尿病薬群と比較して、セマグルチド両用量群で有意に大きな減少がみられた。追加の経口糖尿病薬群との群差の推定値はセマグルチド0.5 mg群：-1.84 kg（95%信頼区間：-2.67; -1.01）、セマグルチド1.0 mg群：-3.59 kg（95%信頼区間：-4.43; -2.75）であった。体重の変化量は、追加の経口糖尿病薬群で+0.41 kg（+0.67%）であるのに対し、セマグルチド0.5 mg群で-1.43 kg（-2.29%）及びセマグルチド1.0 mg群で-3.18 kg（-4.90%）であった。
- 4つの感度分析において、セマグルチド両用量群の体重減少が追加の経口糖尿病薬群と比較して有意に大きいことが確認されたことから、主要解析結果の安定性が裏付けられた。4つの感度分析による追加の経口糖尿病薬群との群差の推定値は同様で、範囲はセマグルチド0.5 mg群：-1.69 kg（95%信頼区間：-2.25; -0.84）～-1.84 kg（95%信頼区間：-2.63; -1.05）、セマグルチド1.0 mg群：-3.15 kg（95%信頼区間：-3.96; -2.33）～-3.35 kg（95%信頼区間：-4.14; -2.56）であり、セマグルチドによる有意な体重減少が裏付けられた。
- 治療と前治療との間に、統計的に有意な交互作用は認められなかった（セマグルチド0.5 mg群：p=0.1686、セマグルチド1.0 mg群：p=0.1092）。グリニド以外のすべての前治療において、投与後56週までの体重の平均低下量は、追加の経口糖尿病薬群と比較して、セマグルチド両用量群で大きかった。

有効性に関する他の補足的セカンダリーエンドポイント
- HbA1cの目標値を達成した被験者の割合は、追加の経口糖尿病薬群と比較してセマグルチドの両用量群で高かった。
  - HbA1c 6.5%以下（AACEの目標値）を達成した被験者の割合は、セマグルチド0.5 mg群で71%、セマグルチド1.0 mg群で80%及び追加の経口糖尿病薬群で15%であり、オッズ比の推定値はセマグルチド0.5 mg群：17.76（95%信頼区間：9.64; 32.72）、セマグルチド1.0 mg群：35.76（95%信頼区間：18.66; 68.50）であった。
  - HbA1c 7.0%未満（ADAの目標値）を達成した被験者の割合は、セマグルチド0.5 mg群で84%、セマグルチド1.0 mg群で91%及び追加の経口糖尿病薬群で42%であり、オッズ比の推定値はセマグルチド0.5 mg群：9.42（95%信頼区間：5.39; 16.46）、セマグルチド1.0 mg群：23.06（95%信頼区間：11.99; 44.36）であった。
- 空腹時血糖値は追加の経口糖尿病薬群と比較してセマグルチド両用量群で有意な低下を示した。追加の経口糖尿病薬群との群差の推定値は、セマグルチド0.5 mg群：-1.66 mmol/L（95%信頼区間：-1.94; -1.38）、セマグルチド1.0 mg群：-2.03 mmol/L（95%信頼区間：-2.32; -1.75）であった。mg/dLで示した場合の群差の推定値は、セマグルチド0.5 mg群： -29.91 mg/dL（95%信頼区間：-35.02; -24.79）、セマグルチド1.0 mg群：-36.63 mg/dL（95%信頼区間：-41.79; -31.46）であった。
- 投与後56週までの収縮期血圧は、追加の経口糖尿病薬群と比較してセマグルチド1.0 mg群において有意な低下を示した。群差の推定値は-3.87 mmHg（95%信頼区間：-6.59; -1.15）であった。一方、セマグルチド0.5 mg群と追加の経口糖尿病薬群の間の違いはみられなかった。
- 投与後56週までの拡張期血圧は、すべての投与群で低下を示したが、セマグルチド両用量群と追加の経口糖尿病薬群の間で有意な違いはみられなかった。

安全性の結果：

プライマリーエンドポイント：有害事象の発現件数
- 2件の死亡が報告された：セマグルチド0.5 mg群で1件（遠隔転移を伴う乳癌；治験薬との因果関係は「なし」）、追加の経口糖尿病薬群で1件（溺死）であった。
- 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（セマグルチド0.5 mg群、セマ

グルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ7.9%、5.0%及び6.7%）。報告された重篤な有害事象について、投与群及び基本語を通じて一定の傾向は認められなかった。

- 有害事象の発現頻度は追加の経口糖尿病薬群と比較してセマグルチド両用量群で高かった（セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ86.2%、335.5件／100人・年、88.0%、371.5件／100人・年及び71.7%、197.9件／100人・年）。この差は主に、胃腸障害、臨床検査、眼障害、代謝および栄養障害、神経系障害、皮膚および皮下組織障害に関連した。
  - いずれの投与群においても有害事象の大部分は軽度又は中等度であり（計2132件中2114件の99.2%）、その内訳はセマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ909件中897件、954件中951件、及び269件中266件であった。全般的にいずれの投与群においても重度の有害事象は少なかった（計2132件中18件）。有害事象を発現した被験者の大部分において試験終了時の転帰が「回復」又は「軽快」であった（セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ909件中720件、954件中764件及び269件中211件）。
  - 最も高頻度で報告された有害事象は、セマグルチド両用量群では器官別大分類の胃腸障害に分類される有害事象であったのに対し、追加の経口糖尿病薬群では器官別大分類の感染症および寄生虫症に分類される有害事象であった。
- 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0.5 mg群（5.9%）と比較してセマグルチド1.0 mg群（10.8%）で高かった。追加の経口糖尿病薬は治験薬とみなさなかったため、追加の経口糖尿病薬との因果関係に関する情報は収集しなかった。セマグルチド1.0 mg群で投与の中止に至った有害事象の件数が多かったことは、主に胃腸障害を理由に投与を中止した被験者の割合が、セマグルチド0.5 mg群と比較して高かったことに起因していた（セマグルチド0.5 mg群で14例中6例、セマグルチド1.0 mg群で26例中15例）。
- セマグルチド1.0 mg群ではセマグルチド0.5 mg群と比較して維持用量が高かったが、高い維持用量の投与群において、全体的な安全性プロファイルの悪化は認められなかった（胃腸障害の有害事象を除く）。

<u>低血糖</u>

- 重大な低血糖（ADA分類による）は報告されなかった。
- 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による）は、セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ3例（1.3%）、6例（2.5%）及び2例（1.7%）報告された。
- 重大な又は血糖値確定症候性低血糖の大部分は、SU薬を併用した被験者から報告された（計14件中13件）。

<u>注目すべき安全性領域</u>

- 胃腸障害の有害事象
  - 胃腸障害の有害事象はセマグルチド投与下で最も高頻度で報告された有害事象であった。最も高頻度（いずれかの群において被験者の5%以上）で報告された有害事象は、多い順に便秘、悪心、下痢、腹部不快感、及び嘔吐であった。便秘、悪心、下痢については、単位時間あたりの発現件数及び被験者の割合が、追加の経口糖尿病薬群と比較してセマグルチド両用量群で高かった。腹部不快感は追加の経口糖尿病薬群では報告されなかった。
  - 胃腸障害の有害事象は、追加の経口糖尿病薬群と比較してセマグルチド両用量群で発現頻度が高かった。胃腸障害の有害事象（基本語別）を発現した被験者の割合は、セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ便秘：18.8%、14.9%及び4.2%、悪心：12.1%、19.1%及び0.8%、下痢：10.0%、15.8%及び6.7%、腹部不快感：6.3%、6.2%及び0.0%、嘔吐：5.4%、5.8%及び1.7%であった。
  - 有害事象の大部分は投与後16週間以内に発現した。胃腸障害の有害事象の発現期間の中央値は、投与群ごと及び事象の種類ごとでばらつきがみられた。
  - 胃腸障害の有害事象の大部分は軽度又は中等度であった。重篤な胃腸障害の有害事象は5例（セ

マグルチド0.5 mg群で3例、セマグルチド1.0 mg群で2例）で報告された。

- 心血管系事象
  - イベント判定委員会により、2件の心血管系事象（セマグルチド0.5 mg群にて心不全1件、セマグルチド1.0 mg群で経皮的冠インターベンション1件）が確認された。本試験では、イベント判定委員会により主要な心血管イベントは確認されなかった。MedDRA検索により、計42例50件（セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ19例23件、16例19件及び7例8件）の心血管系事象が特定された。心血管系事象を発現した被験者の割合及び単位時間あたりの件数は、3つの投与群間で同程度であった。
  - 6例10件（セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ3例6件、1例2件及び2例2件）の重篤な心血管系事象が認められた。これらの重篤な事象のうち、1件（心不全）は、イベント判定委員会で確認された事象（上述の2件のうちの1件）であった。3例4件が投与の中止に至った（いずれもセマグルチド0.5 mg群）。動悸（セマグルチド0.5 mg群で4例、セマグルチド1.0 mgで2例）を除き、重篤な心血管系事象の種類及び発現頻度について投与群間で違いはみられなかった。
  - 投与後56週までの脈拍数の平均値（推定値）は、いずれの投与群においても増加がみられたが、セマグルチド投与群で増加量が大きかった（セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ4.16拍／分、4.94拍／分及び1.58拍／分）。ベースラインから投与終了時にかけて脈拍数は、追加の経口糖尿病薬群と比較してセマグルチド両用量群で有意に増加した〔群差の推定値は、セマグルチド0.5 mg群で2.58拍／分（95%信頼区間：0.70; 4.46）、セマグルチド1.0 mg群で3.36拍／分（95%信頼区間：1.46; 5.26）〕。
  - 全般的に、心電図異常がみられた被験者の割合は、心電図異常のカテゴリーの大部分において投与群間で同様であった。測定結果の大部分は、ベースライン時に「正常」で、投与後30週（94.2～97.0%）及び投与後56週（93.8~98.9%）で変化はなく、投与群間で明らかな差はみられなかった。心電図に関する有害事象が2件、血圧上昇が1件報告された；これらの有害事象はいずれも非重篤で、重症度が軽度であり、治験薬との因果関係は「なし」と判定された。
- 膵炎
  - イベント判定委員会により膵炎は確認されず、MedDRA検索によって特定された事象もなかった。
  - ベースラインから投与終了時（投与後56週）までのリパーゼ及びアミラーゼの平均値は、追加の経口糖尿病薬群と比較してセマグルチド両用量群で有意に増加した（セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病群でそれぞれリパーゼ：32%、39%及び5%、アミラーゼ：18%、21%及び6%の増加）。被験者の大部分において、リパーゼ及びアミラーゼは試験期間を通じて基準範囲上限の2倍未満であり、リパーゼ又はアミラーゼの基準範囲上限のそれぞれ5倍超及び2倍超を示した被験者のほとんどで、外れ値を示したのは1回のみであった。リパーゼが基準範囲の5倍超の被験者及びアミラーゼが基準範囲上限の2倍超の被験者において、それぞれの2例及び3例で胃腸障害の有害事象の併発が報告されたが、肝胆道系事象又は膵炎に関連した有害事象の併発は報告されなかった。
  - 膵酵素増加の有害事象のうち、イベント判定委員会に送付されたものはなかった。また、基本語検索式（PTQ）で特定された事象又は判定が必要と考えられた事象もなかった。
- 肝胆道系障害
  - セマグルチド0.5 mg群で4例（1.7%）及びセマグルチド1.0 mg群で2例（0.8%）の胆嚢に関連する有害事象が報告され、追加の経口糖尿病薬群では報告されなかった。いずれの事象もMedDRA検索で特定されたものであり、器官別大分類の肝胆道系障害に含まれる胆石症（基本語）であった。この6件はいずれも非重篤で、軽度又は中等度であり、投与量の変更に至らず、治験薬との因果関係は「なし」と判定された。また、いずれの被験者も試験終了時の有害事象の転帰が「未回復」であったが、投与の中止に至らなかった。
  - 全般的に、肝機能検査値に変動する傾向がみられたが、平均値の増加は認められなかった。総ビリルビン、アラニンアミノトランスフェラーゼ（ALT）、アスパラギン酸アミノトランスフェラ

ーゼ（AST）及びアルカリホスファターゼ（ALP）の外れ値は認められなかった。これら4つのパラメータについて、ベースラインからの平均変化量はセマグルチド群と追加の経口糖尿病薬群で同程度であり、臨床的に問題となる変化は認められなかった。
  - Hy's lawの定義に合致する被験者は認められなかった。
- 新生物
  - 全般的に、イベント判定委員会に悪性新生物と判定された事象の件数及び発現した被験者の割合は低く（10例10件）、3つの投与群間で同程度であった〔セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ4例（1.7%）、3例（1.2%）及び3例（2.5%）〕。イベント判定委員会により良性と判定された事象を発現した被験者の割合は、追加の経口糖尿病薬群と比較してセマグルチド投与群で高い割合で報告されたものの、全般的にいずれの投与群でも低かった（セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ4.6%、7.9%及び2.5%）。また、イベント判定委員会により前悪性新生物／上皮内新生物のボーダーラインと確認された事象は、セマグルチド1.0 mg群で1件報告されたが、セマグルチド0.5 mg群及び追加の経口糖尿病薬群では認められなかった。
  - 結腸直腸の良性新生物を除き、イベント判定委員会により確認された新生物は主に被験者1例に1件ずつの発現であり、その種類（原発組織又は臓器）の分布は3つの投与群間で概して同様であった。MedDRA検索で特定した事象に関して、新生物の事象を発現した被験者の割合は、追加の経口糖尿病薬群と比較してセマグルチド両用量群で高かった（セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ11.3%、12.9%及び5.0%）。
  - 本試験では、MedDRA検索によりセマグルチド0.5 mg群の1件が甲状腺新生物と特定されたが、イベント判定委員会で甲状腺新生物と確認されたものはなかった。
- 甲状腺障害
  - イベント判定委員会により甲状腺切除を必要とする甲状腺疾患又は甲状腺新生物は確認されなかった。事前に規定したMedDRA検索により特定された甲状腺疾患5件のうち4件は、イベント判定委員会に送られたが、甲状腺疾患とは判定されなかった。セマグルチド0.5 mg群で1件の臨床検査に関する有害事象（CLAE）が報告され（血中カルシトニン増加）、本事象の転帰は「回復」であった。
  - 上述の事象を除き、カルシトニンの平均及び個々のカルシトニン値について、投与期間を通じて投与群内又は投与群間で臨床的に問題となる変化は認められなかった。
- 腎障害
  - 広域のMedDRA標準検索式（acute renal failure；急性腎不全）により、数件の事象が特定された（3群合計4例4件）。これらの事象はいずれも非重篤で軽度であり、事象の転帰は「回復」又は「軽快」であり、投与の中止に至らなかった。いずれの群でもeGFR値の同様な低下がみられた。
  - すべての腎機能に関連する臨床検査項目及び尿検査項目について、投与群内及び投与群間で臨床的に問題となる経時的変化は認められなかった。
- 免疫原性に関連する有害事象及び注射部位反応
  - 計38例46件〔セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ17例（7.1%）、16例（6.6%）及び5例（4.2%）〕のアレルギー反応が報告された。計29例33件の皮膚障害、6例6件の呼吸器、胸郭および縦隔障害及び5例6件の眼障害が報告された。いずれの事象も非重篤であり、軽度又は中等度であった。そのうちセマグルチド1.0 mg群の2件のみが治験薬との因果関係が「可能性あり」と判定された。また、いずれの事象も投与量の変更に至らず、被験者の大部分は試験終了時にそれぞれの事象の転帰が「回復」であった。
  - セマグルチド0.5 mg群で2例、セマグルチド1.0 mg群1例が抗セマグルチド抗体陽性となり、後者1例が内因性GLP-1に対する交叉反応を有していた。事後調査来院時に抗セマグルチド抗体が認められた被験者1例は、セマグルチドに対する中和作用はみられなかった。抗セマグルチド抗体が陽性であった3例の試験期間中のHbA1cの低下量から、抗セマグルチド抗体の存在はセマグルチドの効果に影響を及ぼさないと考えられた。

– 7例7件の免疫複合体疾患が報告された：セマグルチド0.5 mg群、セマグルチド1.0 mg群及び追加の経口糖尿病薬群でそれぞれ4例、2例及び1例であった。この5件はいずれの事象も非重篤で軽度又は中等度であり、1例を除きすべての被験者が事象から回復した。事象からの回復が確認されなかった1例については、当該事象の治験薬との因果関係が「可能性あり」と判定され、投与は中止された。それ以外の事象は投与の中止に至らなかった。
– 2例5件の注射部位反応が報告された：セマグルチド0.5 mg群で1例4件（注射部位疼痛2件、注射部位熱感2件）、セマグルチド1.0 mg群で1例1件（注射部位硬結）であった。いずれの事象も非重篤で軽度であった。また、いずれの事象も治験薬との因果関係が否定されなかったが、投与量の変更及び投与の中止に至らなかった。

その他の臨床検査項目、身体所見及び妊娠

- 注目すべき安全性領域に記載されていない血液生化学的検査又は血液学的検査に関するパラメータについて、臨床的に問題となる変化は認められなかった。
- 身体所見及び眼底検査について、投与群間に臨床的に問題となる違いは認められなかった。
- セマグルチド1.0 mg群で投与完了後に1件の妊娠が報告された。day 406に妊娠嘔吐（つわり）が報告された。この事象は非重篤であり、軽度の事象であり、試験終了時の転帰は「未回復」であった。妊娠中の胎児に関する有害事象は報告されなかった。

全体の結論：

- 日本人2型糖尿病患者において、セマグルチド及び追加の経口糖尿病薬は安全で忍容性が良好であった。
  – 追加の経口糖尿病薬群と比較してセマグルチド両用量群で有害事象の発現頻度は高かった。これは主に胃腸障害の有害事象に起因するものであり、他の臓器では顕著な群間差はなく、特定の事象が多く発現することもなかった。
  – 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。
  – 投与の中止に至った有害事象のうち、セマグルチド両用量群で最も高頻度で報告されたものは胃腸障害の有害事象であった。
- 前治療（食事・運動療法、SU、グリニド、α-GI及びTZD）に関わらず、セマグルチドの一貫した安全性が確認された。
- 追加の経口糖尿病薬群と比較してセマグルチド両用量群の血糖降下作用が有意に大きかった。
- 追加の経口糖尿病薬群と比較してセマグルチド両用量群の体重減少効果が有意に大きかった。
- 前治療に関わらず、セマグルチドのHbA1cと体重に対する一貫した効果が確認された。

本試験は、ヘルシンキ宣言の精神及びGCP-ICHを遵守して実施された。

2.7.6.23.2. 有害事象

表 2.7.6.23.2- 1 有害事象（器官別大分類、高位グループ語及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
Number of subjects	239				241				120				600			
Exposure time (year)	270.9				256.8				135.9				663.6			
Events	206	(86.2)	909	335.5	212	(88.0)	954	371.5	86	(71.7)	269	197.9	504	(84.0)	2132	321.3
感染症および寄生虫症	129	(54.0)	231	85.3	111	(46.1)	184	71.7	59	(49.2)	105	77.2	299	(49.8)	520	78.4
詳細不明な感染体による感染症	116	(48.5)	203	74.9	105	(43.6)	164	63.9	55	(45.8)	91	66.9	276	(46.0)	458	69.0
鼻咽頭炎	81	(33.9)	132	48.7	75	(31.1)	105	40.9	41	(34.2)	60	44.1	197	(32.8)	297	44.8
咽頭炎	12	(5.0)	15	5.5	9	(3.7)	9	3.5	2	(1.7)	3	2.2	23	(3.8)	27	4.1
胃腸炎	15	(6.3)	16	5.9	5	(2.1)	6	2.3	2	(1.7)	2	1.5	22	(3.7)	24	3.6
気管支炎	7	(2.9)	7	2.6	5	(2.1)	6	2.3	4	(3.3)	5	3.7	16	(2.7)	18	2.7
上気道感染	5	(2.1)	6	2.2	7	(2.9)	8	3.1	3	(2.5)	4	2.9	15	(2.5)	18	2.7
膀胱炎	5	(2.1)	5	1.8	2	(0.8)	2	0.8	2	(1.7)	2	1.5	9	(1.5)	9	1.4
結膜炎	5	(2.1)	5	1.8	1	(0.4)	1	0.4	1	(0.8)	1	0.7	7	(1.2)	7	1.1
中耳炎	1	(0.4)	1	0.4	4	(1.7)	4	1.6	1	(0.8)	1	0.7	6	(1.0)	6	0.9
歯肉炎	1	(0.4)	1	0.4	3	(1.2)	3	1.2	1	(0.8)	1	0.7	5	(0.8)	5	0.8
扁桃炎	2	(0.8)	3	1.1	1	(0.4)	1	0.4	2	(1.7)	2	1.5	5	(0.8)	6	0.9
外耳炎	1	(0.4)	1	0.4	1	(0.4)	2	0.8	1	(0.8)	1	0.7	3	(0.5)	4	0.6
歯周炎	1	(0.4)	1	0.4	1	(0.4)	1	0.4	1	(0.8)	1	0.7	3	(0.5)	3	0.5
尿路感染	0				2	(0.8)	2	0.8	1	(0.8)	1	0.7	3	(0.5)	3	0.5
膿痂疹	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
化膿	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
感染性皮膚嚢腫	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
爪囲炎	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
麦粒腫	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
鼻炎	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
副鼻腔炎	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
感染性腸炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
眼瞼感染	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
急性腎盂腎炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
急性中耳炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
腎盂腎炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
精巣上体炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
蓄膿	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
尿道炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
肺炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
肺膿瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
皮膚感染	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
慢性副鼻腔炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
扁桃周囲膿瘍	0				0				1	(0.8)	2	1.5	1	(0.2)	2	0.3
肛門膿瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
鼠径部膿瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
ウイルス感染症	12	(5.0)	12	4.4	11	(4.6)	11	4.3	6	(5.0)	6	4.4	29	(4.8)	29	4.4
インフルエンザ	2	(0.8)	2	0.7	7	(2.9)	7	2.7	3	(2.5)	3	2.2	12	(2.0)	12	1.8
帯状疱疹	5	(2.1)	5	1.8	2	(0.8)	2	0.8	1	(0.8)	1	0.7	8	(1.3)	8	1.2
ウイルス性胃腸炎	2	(0.8)	2	0.7	0				1	(0.8)	1	0.7	3	(0.5)	3	0.5
口腔ヘルペス	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
単純ヘルペス	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
眼部単純ヘルペス	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
細菌感染症	11	(4.6)	12	4.4	4	(1.7)	4	1.6	5	(4.2)	5	3.7	20	(3.3)	21	3.2
ヘリコバクター感染	4	(1.7)	4	1.5	1	(0.4)	1	0.4	0				5	(0.8)	5	0.8
蜂巣炎	1	(0.4)	1	0.4	1	(0.4)	1	0.4	2	(1.7)	2	1.5	4	(0.7)	4	0.6
毛包炎	3	(1.3)	3	1.1	1	(0.4)	1	0.4	0				4	(0.7)	4	0.6
ヘリコバクター性胃炎	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
レンサ球菌感染	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
β溶血性レンサ球菌感染	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
細菌性胃腸炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
細菌性眼感染	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
細菌性膣症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
真菌感染症	4	(1.7)	4	1.5	5	(2.1)	5	1.9	2	(1.7)	2	1.5	11	(1.8)	11	1.7
足部白癬	2	(0.8)	2	0.7	2	(0.8)	2	0.8	1	(0.8)	1	0.7	5	(0.8)	5	0.8
爪真菌症	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
トリコフィトン感染症	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
食道カンジダ症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
体部白癬	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
白癬感染	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
クラミジア感染症	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
クラミジア性肺炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
胃腸障害	129	(54.0)	262	96.7	130	(53.9)	300	116.8	24	(20.0)	40	29.4	283	(47.2)	602	90.7
消化管徴候および症状	66	(27.6)	106	39.1	85	(35.3)	145	56.5	6	(5.0)	7	5.1	157	(26.2)	258	38.9
悪心	29	(12.1)	38	14.0	46	(19.1)	70	27.3	1	(0.8)	1	0.7	76	(12.7)	109	16.4
腹部不快感	15	(6.3)	15	5.5	15	(6.2)	16	6.2	0				30	(5.0)	31	4.7
嘔吐	13	(5.4)	17	6.3	14	(5.8)	21	8.2	2	(1.7)	2	1.5	29	(4.8)	40	6.0
消化不良	7	(2.9)	8	3.0	11	(4.6)	12	4.7	1	(0.8)	1	0.7	19	(3.2)	21	3.2
上腹部痛	10	(4.2)	13	4.8	7	(2.9)	8	3.1	1	(0.8)	1	0.7	18	(3.0)	22	3.3
腹部膨満	6	(2.5)	7	2.6	11	(4.6)	11	4.3	0				17	(2.8)	18	2.7
軟便	3	(1.3)	3	1.1	4	(1.7)	4	1.6	1	(0.8)	1	0.7	8	(1.3)	8	1.2
腹痛	1	(0.4)	1	0.4	2	(0.8)	2	0.8	1	(0.8)	1	0.7	4	(0.7)	4	0.6
おくび	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
心窩部不快感	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
放屁	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
消化管運動および排泄障害	66	(27.6)	88	32.5	72	(29.9)	98	38.2	13	(10.8)	15	11.0	151	(25.2)	201	30.3
便秘	45	(18.8)	50	18.5	36	(14.9)	40	15.6	5	(4.2)	5	3.7	86	(14.3)	95	14.3
下痢	24	(10.0)	33	12.2	38	(15.8)	49	19.1	8	(6.7)	9	6.6	70	(11.7)	91	13.7

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
胃食道逆流性疾患	5	(2.1)	5	1.8	8	(3.3)	8	3.1	1	(0.8)	1	0.7	14	(2.3)	14	2.1
過敏性腸症候群	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
消化管炎症性疾患	19	(7.9)	21	7.8	7	(2.9)	9	3.5	4	(3.3)	4	2.9	30	(5.0)	34	5.1
慢性胃炎	9	(3.8)	9	3.3	4	(1.7)	4	1.6	2	(1.7)	2	1.5	15	(2.5)	15	2.3
胃炎	6	(2.5)	6	2.2	3	(1.2)	3	1.2	1	(0.8)	1	0.7	10	(1.7)	10	1.5
大腸炎	2	(0.8)	4	1.5	2	(0.8)	2	0.8	1	(0.8)	1	0.7	5	(0.8)	7	1.1
小腸炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
腸炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
歯牙および歯肉の状態	12	(5.0)	14	5.2	10	(4.1)	11	4.3	6	(5.0)	8	5.9	28	(4.7)	33	5.0
齲歯	6	(2.5)	6	2.2	5	(2.1)	5	1.9	5	(4.2)	6	4.4	16	(2.7)	17	2.6
歯痛	5	(2.1)	6	2.2	3	(1.2)	3	1.2	1	(0.8)	1	0.7	9	(1.5)	10	1.5
歯周病	1	(0.4)	1	0.4	3	(1.2)	3	1.2	1	(0.8)	1	0.7	5	(0.8)	5	0.8
歯槽骨吸収	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
良性消化管新生物	9	(3.8)	10	3.7	11	(4.6)	14	5.5	2	(1.7)	2	1.5	22	(3.7)	26	3.9
大腸ポリープ	6	(2.5)	6	2.2	6	(2.5)	8	3.1	0				12	(2.0)	14	2.1
胃ポリープ	4	(1.7)	4	1.5	4	(1.7)	4	1.6	2	(1.7)	2	1.5	10	(1.7)	10	1.5
直腸ポリープ	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肛門ポリープ	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
口腔内軟部組織疾患	4	(1.7)	4	1.5	3	(1.2)	5	1.9	1	(0.8)	1	0.7	8	(1.3)	10	1.5
口内炎	4	(1.7)	4	1.5	2	(0.8)	3	1.2	0				6	(1.0)	7	1.1
口唇炎	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
口唇潰瘍	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
消化管の状態ＮＥＣ	4	(1.7)	4	1.5	4	(1.7)	4	1.6	0				8	(1.3)	8	1.2
バレット食道	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
胃障害	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
胃黄色腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
胃酸過多	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
痔瘻	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
食中毒	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
憩室疾患	0				4	(1.7)	4	1.6	2	(1.7)	2	1.5	6	(1.0)	6	0.9
腸憩室	0				4	(1.7)	4	1.6	2	(1.7)	2	1.5	6	(1.0)	6	0.9
消化管潰瘍および穿孔	4	(1.7)	4	1.5	2	(0.8)	2	0.8	0				6	(1.0)	6	0.9
びらん性胃炎	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
胃潰瘍	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
胃十二指腸潰瘍	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
十二指腸潰瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
消化管血行障害	2	(0.8)	2	0.7	2	(0.8)	2	0.8	1	(0.8)	1	0.7	5	(0.8)	5	0.8
痔核	2	(0.8)	2	0.7	2	(0.8)	2	0.8	1	(0.8)	1	0.7	5	(0.8)	5	0.8
消化管出血ＮＥＣ	3	(1.3)	3	1.1	2	(0.8)	2	0.8	0				5	(0.8)	5	0.8
血便排泄	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
メレナ	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肛門出血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
腹部ヘルニアおよびその他の腹壁状態	4	(1.7)	4	1.5	1	(0.4)	1	0.4	0				5	(0.8)	5	0.8
裂孔ヘルニア	3	(1.3)	3	1.1	1	(0.4)	1	0.4	0				4	(0.7)	4	0.6
腰ヘルニア	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
膵外分泌障害	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
膵管拡張	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
膵腫瘤	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
膵嚢胞	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
消化管狭窄および閉塞	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
腸閉塞	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
肛門狭窄	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
臨床検査	40	(16.7)	66	24.4	58	(24.1)	81	31.5	9	(7.5)	11	8.1	107	(17.8)	158	23.8
消化管検査	24	(10.0)	36	13.3	35	(14.5)	52	20.3	3	(2.5)	3	2.2	62	(10.3)	91	13.7
リパーゼ増加	21	(8.8)	25	9.2	33	(13.7)	36	14.0	2	(1.7)	2	1.5	56	(9.3)	63	9.5
アミラーゼ増加	7	(2.9)	8	3.0	13	(5.4)	15	5.8	1	(0.8)	1	0.7	21	(3.5)	24	3.6

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Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
便潜血陽性	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
便潜血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
膵酵素検査異常	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
腎尿路系検査および尿検査	5	(2.1)	5	1.8	6	(2.5)	6	2.3	3	(2.5)	3	2.2	14	(2.3)	14	2.1
尿中血陽性	0				3	(1.2)	3	1.2	2	(1.7)	2	1.5	5	(0.8)	5	0.8
尿中ヘモグロビン陽性	3	(1.3)	3	1.1	0				0				3	(0.5)	3	0.5
血中クレアチニン増加	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
尿中アルブミン／クレアチニン比異常	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
尿中アルブミン陽性	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
尿中血	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
尿中蛋白陽性	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
身体的診察および器官系の状態に関する事項	3	(1.3)	3	1.1	7	(2.9)	7	2.7	0				10	(1.7)	10	1.5
体重減少	3	(1.3)	3	1.1	7	(2.9)	7	2.7	0				10	(1.7)	10	1.5
肝胆道系検査	6	(2.5)	7	2.6	2	(0.8)	2	0.8	1	(0.8)	1	0.7	9	(1.5)	10	1.5
アラニンアミノトランスフェラーゼ増加	5	(2.1)	5	1.8	0				0				5	(0.8)	5	0.8
γ－グルタミルトランスフェラーゼ増加	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
アスパラギン酸アミノトランスフェラーゼ増加	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肝機能検査異常	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
肝酵素上昇	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
酵素検査ＮＥＣ	3	(1.3)	4	1.5	5	(2.1)	5	1.9	1	(0.8)	1	0.7	9	(1.5)	10	1.5
血中クレアチンホスホキナーゼ増加	3	(1.3)	4	1.5	5	(2.1)	5	1.9	1	(0.8)	1	0.7	9	(1.5)	10	1.5
血液学的検査（血液型検査を含む）	3	(1.3)	3	1.1	3	(1.2)	3	1.2	0				6	(1.0)	6	0.9

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
白血球数減少	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
血小板数減少	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
リンパ球形態異常	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
微生物学的および血清学的検査	3	(1.3)	3	1.1	3	(1.2)	3	1.2	0				6	(1.0)	6	0.9
ヘリコバクター検査陽性	3	(1.3)	3	1.1	3	(1.2)	3	1.2	0				6	(1.0)	6	0.9
脂質検査	1	(0.4)	1	0.4	2	(0.8)	2	0.8	1	(0.8)	1	0.7	4	(0.7)	4	0.6
血中トリグリセリド増加	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
低比重リポ蛋白増加	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
心血管系検査（酵素検査を除く）	2	(0.8)	2	0.7	1	(0.4)	1	0.4	1	(0.8)	1	0.7	4	(0.7)	4	0.6
ＱＲＳ軸異常	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
血圧上昇	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
心電図Ｔ波	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
心電図Ｔ波振幅減少	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
代謝、栄養学的および血液ガス検査	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血中ブドウ糖減少	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
蛋白および化学的検査ＮＥＣ	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
Ｃ－反応性蛋白増加	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
内分泌検査（性ホルモン検査を含む）	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血中カルシトニン増加	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
筋骨格系および結合組織障害	35	(14.6)	43	15.9	46	(19.1)	55	21.4	22	(18.3)	26	19.1	103	(17.2)	124	18.7
筋骨格系および結合組織障害ＮＥＣ	17	(7.1)	23	8.5	22	(9.1)	25	9.7	13	(10.8)	15	11.0	52	(8.7)	63	9.5
背部痛	9	(3.8)	10	3.7	13	(5.4)	13	5.1	10	(8.3)	10	7.4	32	(5.3)	33	5.0

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
四肢痛	4	(1.7)	5	1.8	3	(1.2)	3	1.2	1	(0.8)	1	0.7	8	(1.3)	9	1.4
筋骨格痛	1	(0.4)	1	0.4	5	(2.1)	5	1.9	0				6	(1.0)	6	0.9
筋骨格硬直	2	(0.8)	3	1.1	1	(0.4)	2	0.8	1	(0.8)	1	0.7	4	(0.7)	6	0.9
頚部痛	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
筋骨格系胸痛	0				0				2	(1.7)	2	1.5	2	(0.3)	2	0.3
筋骨格不快感	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
筋膜炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
側腹部痛	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
足底筋膜炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
関節障害	16	(6.7)	16	5.9	20	(8.3)	21	8.2	4	(3.3)	4	2.9	40	(6.7)	41	6.2
関節痛	7	(2.9)	7	2.6	11	(4.6)	11	4.3	2	(1.7)	2	1.5	20	(3.3)	20	3.0
関節周囲炎	4	(1.7)	4	1.5	4	(1.7)	4	1.6	2	(1.7)	2	1.5	10	(1.7)	10	1.5
変形性脊椎症	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
肩回旋筋腱板症候群	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
変形性関節症	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
顎関節症候群	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
関節リウマチ	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
関節炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
関節障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
筋障害	0				3	(1.2)	3	1.2	5	(4.2)	5	3.7	8	(1.3)	8	1.2
筋肉痛	0				2	(0.8)	2	0.8	3	(2.5)	3	2.2	5	(0.8)	5	0.8
筋痙縮	0				1	(0.4)	1	0.4	2	(1.7)	2	1.5	3	(0.5)	3	0.5
筋骨格系および結合組織変形（椎間板障害を含む）	2	(0.8)	2	0.7	2	(0.8)	2	0.8	2	(1.7)	2	1.5	6	(1.0)	6	0.9
椎間板突出	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
腰部脊柱管狭窄症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
脊柱管狭窄症	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
椎間板障害	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腱、靭帯および軟骨障害	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
弾発指	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
腱炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
腱鞘炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
滑膜および滑液包障害	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
滑液嚢腫	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
骨障害（先天性障害および骨折を除く）	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
骨粗鬆症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
眼障害	35	(14.6)	49	18.1	36	(14.9)	39	15.2	9	(7.5)	9	6.6	80	(13.3)	97	14.6
網膜、脈絡膜および硝子体の出血および血管障害	15	(6.3)	19	7.0	17	(7.1)	17	6.6	7	(5.8)	7	5.1	39	(6.5)	43	6.5
糖尿病網膜症	11	(4.6)	11	4.1	16	(6.6)	16	6.2	6	(5.0)	6	4.4	33	(5.5)	33	5.0
網膜出血	3	(1.3)	4	1.5	1	(0.4)	1	0.4	1	(0.8)	1	0.7	5	(0.8)	6	0.9
網膜滲出物	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
網膜血管瘤	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
網膜静脈閉塞	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
眼部感染、刺激症状および炎症	6	(2.5)	7	2.6	6	(2.5)	6	2.3	1	(0.8)	1	0.7	13	(2.2)	14	2.1
アレルギー性結膜炎	3	(1.3)	4	1.5	1	(0.4)	1	0.4	0				4	(0.7)	5	0.8
眼瞼炎	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
眼そう痒症	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
眼脂	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
眼充血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
眼瞼浮腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
結膜充血	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
糖尿病性網膜浮腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
眼前方部構造変化、沈着および変性	7	(2.9)	8	3.0	4	(1.7)	4	1.6	1	(0.8)	1	0.7	12	(2.0)	13	2.0
白内障	7	(2.9)	8	3.0	3	(1.2)	3	1.2	1	(0.8)	1	0.7	11	(1.8)	12	1.8
角膜びらん	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
眼部構造変化、沈着および変性ＮＥＣ	4	(1.7)	4	1.5	3	(1.2)	3	1.2	0				7	(1.2)	7	1.1
黄斑症	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
視神経乳頭陥凹	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
硝子体浮遊物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
網膜色素脱失	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
網膜変性	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
眼部障害ＮＥＣ	2	(0.8)	2	0.7	4	(1.7)	4	1.6	0				6	(1.0)	6	0.9
眼乾燥	2	(0.8)	2	0.7	3	(1.2)	3	1.2	0				5	(0.8)	5	0.8
網膜障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
眼球感覚神経障害ＮＥＣ	2	(0.8)	2	0.7	3	(1.2)	3	1.2	0				5	(0.8)	5	0.8
眼精疲労	2	(0.8)	2	0.7	3	(1.2)	3	1.2	0				5	(0.8)	5	0.8
緑内障および高眼圧症	4	(1.7)	4	1.5	1	(0.4)	1	0.4	0				5	(0.8)	5	0.8
緑内障	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
開放隅角緑内障	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
高眼圧症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
眼部出血および血管障害ＮＥＣ	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
結膜出血	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
視覚障害	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
光視症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
複視	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
傷害、中毒および処置合併症	32	(13.4)	33	12.2	28	(11.6)	29	11.3	10	(8.3)	13	9.6	70	(11.7)	75	11.3
損傷ＮＥＣ	21	(8.8)	22	8.1	21	(8.7)	21	8.2	5	(4.2)	5	3.7	47	(7.8)	48	7.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
挫傷	6	(2.5)	6	2.2	4	(1.7)	4	1.6	2	(1.7)	2	1.5	12	(2.0)	12	1.8
靱帯捻挫	5	(2.1)	6	2.2	2	(0.8)	2	0.8	1	(0.8)	1	0.7	8	(1.3)	9	1.4
歯牙破折	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
節足動物咬傷	0				2	(0.8)	2	0.8	1	(0.8)	1	0.7	3	(0.5)	3	0.5
動物咬傷	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
創傷	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
肉離れ	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
腱断裂	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
外傷後頚部症候群	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
筋断裂	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
擦過傷	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
四肢外傷性切断	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
上顎炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
節足動物刺傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
爪損傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
転倒	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
皮膚擦過傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
裂傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
腱損傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
靱帯損傷	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
骨および関節損傷	6	(2.5)	6	2.2	5	(2.1)	5	1.9	5	(4.2)	5	3.7	16	(2.7)	16	2.4
肋骨骨折	1	(0.4)	1	0.4	0				2	(1.7)	2	1.5	3	(0.5)	3	0.5
関節損傷	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
足骨折	0				0				2	(1.7)	2	1.5	2	(0.3)	2	0.3
下肢骨折	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
腰椎骨折	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
手骨折	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
手首関節骨折	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
上腕骨骨折	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
脊椎骨折	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
剥離骨折	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
半月板損傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
尾骨骨折	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
物理的要因による損傷	4	(1.7)	4	1.5	2	(0.8)	2	0.8	3	(2.5)	3	2.2	9	(1.5)	9	1.4
熱中症	2	(0.8)	2	0.7	0				1	(0.8)	1	0.7	3	(0.5)	3	0.5
凍瘡	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
熱射病	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
サンバーン	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
熱傷	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
曝露、化学的損傷および中毒	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
フューム吸引性呼吸障害	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
代謝および栄養障害	24	(10.0)	28	10.3	34	(14.1)	40	15.6	4	(3.3)	4	2.9	62	(10.3)	72	10.8
食欲および総合的栄養摂取障害	18	(7.5)	22	8.1	32	(13.3)	36	14.0	0				50	(8.3)	58	8.7
食欲減退	18	(7.5)	22	8.1	32	(13.3)	36	14.0	0				50	(8.3)	58	8.7
プリンおよびピリミジン代謝障害	3	(1.3)	3	1.1	2	(0.8)	2	0.8	2	(1.7)	2	1.5	7	(1.2)	7	1.1
高尿酸血症	3	(1.3)	3	1.1	1	(0.4)	1	0.4	1	(0.8)	1	0.7	5	(0.8)	5	0.8
痛風	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
脂質代謝障害	2	(0.8)	2	0.7	1	(0.4)	1	0.4	2	(1.7)	2	1.5	5	(0.8)	5	0.8
高脂血症	1	(0.4)	1	0.4	0				2	(1.7)	2	1.5	3	(0.5)	3	0.5
高コレステロール血症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
脂質異常症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
電解質および水分バランス異常	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
脱水	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
低ナトリウム血症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
神経系障害	27	(11.3)	42	15.5	30	(12.4)	44	17.1	4	(3.3)	5	3.7	61	(10.2)	91	13.7
神経学的障害ＮＥＣ	13	(5.4)	14	5.2	14	(5.8)	17	6.6	1	(0.8)	1	0.7	28	(4.7)	32	4.8
浮動性めまい	5	(2.1)	5	1.8	6	(2.5)	7	2.7	0				11	(1.8)	12	1.8
感覚鈍麻	1	(0.4)	1	0.4	4	(1.7)	5	1.9	0				5	(0.8)	6	0.9
体位性めまい	2	(0.8)	2	0.7	2	(0.8)	2	0.8	0				4	(0.7)	4	0.6
味覚異常	1	(0.4)	1	0.4	3	(1.2)	3	1.2	0				4	(0.7)	4	0.6
傾眠	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
意識消失	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
錯感覚	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
神経痛	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
肋間神経痛	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
頭痛	8	(3.3)	16	5.9	11	(4.6)	20	7.8	2	(1.7)	3	2.2	21	(3.5)	39	5.9
頭痛	7	(2.9)	15	5.5	11	(4.6)	20	7.8	1	(0.8)	2	1.5	19	(3.2)	37	5.6
緊張性頭痛	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
片頭痛	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
末梢性ニューロパチー	4	(1.7)	4	1.5	3	(1.2)	3	1.2	1	(0.8)	1	0.7	8	(1.3)	8	1.2
糖尿病性ニューロパチー	2	(0.8)	2	0.7	2	(0.8)	2	0.8	0				4	(0.7)	4	0.6
手根管症候群	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
末梢性ニューロパチー	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
中枢神経系血管障害	2	(0.8)	2	0.7	2	(0.8)	2	0.8	0				4	(0.7)	4	0.6
頚動脈硬化症	2	(0.8)	2	0.7	2	(0.8)	2	0.8	0				4	(0.7)	4	0.6
脊髄および神経根障害	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
頚腕症候群	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
坐骨神経痛	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
脳神経障害（新生物を除く）	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
三叉神経痛	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
第７脳神経麻痺	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
神経筋障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
起立不耐性	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
精神的機能障害	1	(0.4)	3	1.1	0				0				1	(0.2)	3	0.5
注意力障害	1	(0.4)	3	1.1	0				0				1	(0.2)	3	0.5
呼吸器、胸郭および縦隔障害	19	(7.9)	19	7.0	26	(10.8)	34	13.2	9	(7.5)	12	8.8	54	(9.0)	65	9.8
呼吸器系障害ＮＥＣ	8	(3.3)	8	3.0	21	(8.7)	29	11.3	6	(5.0)	6	4.4	35	(5.8)	43	6.5
上気道の炎症	3	(1.3)	3	1.1	11	(4.6)	18	7.0	0				14	(2.3)	21	3.2
咳嗽	3	(1.3)	3	1.1	1	(0.4)	1	0.4	3	(2.5)	3	2.2	7	(1.2)	7	1.1
口腔咽頭痛	1	(0.4)	1	0.4	3	(1.2)	3	1.2	1	(0.8)	1	0.7	5	(0.8)	5	0.8
鼻漏	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
しゃっくり	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
咽喉絞扼感	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
咽喉刺激感	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
喉頭不快感	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
睡眠時無呼吸症候群	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肺腫瘤	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
発声障害	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
鼻閉塞	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
気管支障害（新生物を除く）	4	(1.7)	4	1.5	2	(0.8)	2	0.8	4	(3.3)	5	3.7	10	(1.7)	11	1.7
喘息	2	(0.8)	2	0.7	2	(0.8)	2	0.8	3	(2.5)	4	2.9	7	(1.2)	8	1.2
慢性気管支炎	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
慢性閉塞性肺疾患	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
上気道障害（感染を除く）	6	(2.5)	6	2.2	2	(0.8)	2	0.8	1	(0.8)	1	0.7	9	(1.5)	9	1.4
アレルギー性鼻炎	4	(1.7)	4	1.5	2	(0.8)	2	0.8	0				6	(1.0)	6	0.9
声帯の炎症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
声帯肥厚	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
鼻出血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
下気道障害（閉塞および感染を除く）	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
肺気腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肺嚢胞	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
皮膚および皮下組織障害	25	(10.5)	36	13.3	22	(9.1)	31	12.1	7	(5.8)	8	5.9	54	(9.0)	75	11.3
表皮および皮膚異常	15	(6.3)	21	7.8	18	(7.5)	21	8.2	6	(5.0)	7	5.1	39	(6.5)	49	7.4
湿疹	4	(1.7)	4	1.5	6	(2.5)	7	2.7	2	(1.7)	2	1.5	12	(2.0)	13	2.0
そう痒症	4	(1.7)	5	1.8	2	(0.8)	2	0.8	0				6	(1.0)	7	1.1
脂漏性皮膚炎	2	(0.8)	3	1.1	4	(1.7)	4	1.6	0				6	(1.0)	7	1.1
アレルギー性皮膚炎	2	(0.8)	3	1.1	1	(0.4)	1	0.4	0				3	(0.5)	4	0.6
接触性皮膚炎	0				2	(0.8)	2	0.8	1	(0.8)	1	0.7	3	(0.5)	3	0.5
発疹	0				2	(0.8)	2	0.8	1	(0.8)	1	0.7	3	(0.5)	3	0.5
皮膚炎	0				2	(0.8)	2	0.8	1	(0.8)	1	0.7	3	(0.5)	3	0.5
うっ滞性皮膚炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
アトピー性皮膚炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
貨幣状湿疹	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
紅斑	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
神経皮膚炎	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
皮脂欠乏性湿疹	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
薬疹	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
皮膚付属器状態	4	(1.7)	4	1.5	4	(1.7)	4	1.6	0				8	(1.3)	8	1.2
冷汗	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
線状出血	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
円形脱毛症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
汗疹	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
多汗症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
角化および皮膚異栄養性障害	6	(2.5)	6	2.2	0				0				6	(1.0)	6	0.9
過角化	3	(1.3)	3	1.1	0				0				3	(0.5)	3	0.5
掌蹠角皮症	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
乾皮症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
皮膚血管異常	2	(0.8)	2	0.7	2	(0.8)	4	1.6	1	(0.8)	1	0.7	5	(0.8)	7	1.1
皮下出血	1	(0.4)	1	0.4	2	(0.8)	4	1.6	1	(0.8)	1	0.7	4	(0.7)	6	0.9
点状出血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血管浮腫および蕁麻疹	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
蕁麻疹	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
良性皮膚新生物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
良性皮膚新生物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
皮膚嚢腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
皮膚嚢腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
皮膚および皮下組織障害ＮＥＣ	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
皮膚潰瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
腎および尿路障害	14	(5.9)	14	5.2	19	(7.9)	23	9.0	5	(4.2)	8	5.9	38	(6.3)	45	6.8
尿石症	7	(2.9)	7	2.6	8	(3.3)	10	3.9	2	(1.7)	3	2.2	17	(2.8)	20	3.0
腎結石症	4	(1.7)	4	1.5	5	(2.1)	5	1.9	2	(1.7)	2	1.5	11	(1.8)	11	1.7
尿管結石	1	(0.4)	1	0.4	5	(2.1)	5	1.9	1	(0.8)	1	0.7	7	(1.2)	7	1.1
尿路結石	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
腎障害（腎症を除く）	3	(1.3)	3	1.1	8	(3.3)	8	3.1	2	(1.7)	3	2.2	13	(2.2)	14	2.1
腎嚢胞	3	(1.3)	3	1.1	7	(2.9)	7	2.7	1	(0.8)	1	0.7	11	(1.8)	11	1.7
水腎症	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
腎腫大	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
尿路系徴候および症状	4	(1.7)	4	1.5	5	(2.1)	5	1.9	1	(0.8)	1	0.7	10	(1.7)	10	1.5
頻尿	1	(0.4)	1	0.4	4	(1.7)	4	1.6	0				5	(0.8)	5	0.8

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
夜間頻尿	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
アルブミン尿	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血尿	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
膀胱炎様症状	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
腎症	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
糖尿病性腎症	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
一般・全身障害および投与部位の状態	13	(5.4)	17	6.3	15	(6.2)	15	5.8	6	(5.0)	6	4.4	34	(5.7)	38	5.7
全身障害ＮＥＣ	11	(4.6)	12	4.4	12	(5.0)	12	4.7	4	(3.3)	4	2.9	27	(4.5)	28	4.2
倦怠感	4	(1.7)	4	1.5	4	(1.7)	4	1.6	0				8	(1.3)	8	1.2
疲労	2	(0.8)	2	0.7	3	(1.2)	3	1.2	0				5	(0.8)	5	0.8
末梢性浮腫	1	(0.4)	1	0.4	0				3	(2.5)	3	2.2	4	(0.7)	4	0.6
口渇	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
早期満腹	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
悪寒	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
異常感	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
炎症	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
乾燥症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
胸部不快感	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
無力症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
体温異常	1	(0.4)	1	0.4	2	(0.8)	2	0.8	1	(0.8)	1	0.7	4	(0.7)	4	0.6
発熱	1	(0.4)	1	0.4	2	(0.8)	2	0.8	1	(0.8)	1	0.7	4	(0.7)	4	0.6
投与部位反応	1	(0.4)	4	1.5	1	(0.4)	1	0.4	0				2	(0.3)	5	0.8
注射部位硬結	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
注射部位熱感	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
注射部位疼痛	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
致命的転帰	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
溺死	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	11	(4.6)	11	4.1	9	(3.7)	12	4.7	4	(3.3)	5	3.7	24	(4.0)	28	4.2
良性皮膚新生物	1	(0.4)	1	0.4	2	(0.8)	3	1.2	0				3	(0.5)	4	0.6
良性皮膚新生物	1	(0.4)	1	0.4	2	(0.8)	3	1.2	0				3	(0.5)	4	0.6
皮膚乳頭腫	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
皮膚乳頭腫	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
メラノサイト性母斑	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
メラノサイト性母斑	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
化膿性肉芽腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
化膿性肉芽腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
悪性および詳細不明の消化管新生物	2	(0.8)	2	0.7	3	(1.2)	3	1.2	1	(0.8)	1	0.7	6	(1.0)	6	0.9
遠隔転移を伴う膵癌	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
胃癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
消化管粘膜下腫瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
食道癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
直腸癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
消化器の良性新生物	3	(1.3)	3	1.1	2	(0.8)	2	0.8	0				5	(0.8)	5	0.8
大腸腺腫	3	(1.3)	3	1.1	2	(0.8)	2	0.8	0				5	(0.8)	5	0.8
良性軟部組織新生物	1	(0.4)	1	0.4	0				1	(0.8)	2	1.5	2	(0.3)	3	0.5
血管脂肪腫	0				0				1	(0.8)	2	1.5	1	(0.2)	2	0.3
脂肪腫	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
リンパ腫ＮＥＣ	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
リンパ腫	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
悪性および詳細不明のその他および部位不明新生物	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
腺癌	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
悪性および詳細不明の呼吸器系および縦隔新生物	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
肺腺癌	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
悪性および詳細不明の腎尿路系新生物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
膀胱移行上皮癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
悪性および詳細不明の内分泌新生物	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
甲状腺新生物	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
悪性および詳細不明の乳房新生物（乳頭を含む）	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
遠隔転移を伴う乳癌	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
非ホジキンＢ細胞性リンパ腫	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
びまん性大細胞型Ｂ細胞性リンパ腫	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
良性肝胆道系新生物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肝臓血管腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
良性腎尿路系新生物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
膀胱乳頭腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
良性男性生殖器新生物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
前立腺の良性新生物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
心臓障害	9	(3.8)	10	3.7	11	(4.6)	12	4.7	3	(2.5)	3	2.2	23	(3.8)	25	3.8
不整脈	4	(1.7)	5	1.8	7	(2.9)	8	3.1	2	(1.7)	2	1.5	13	(2.2)	15	2.3
上室性期外収縮	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
右脚ブロック	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
心室性期外収縮	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
心房細動	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
完全房室ブロック	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
脚ブロック	0				1	(0.4)	2	0.8	0				1	(0.2)	2	0.3
第一度房室ブロック	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
第二度房室ブロック	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
不整脈	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
心障害徴候および症状	4	(1.7)	4	1.5	2	(0.8)	2	0.8	0				6	(1.0)	6	0.9
動悸	4	(1.7)	4	1.5	2	(0.8)	2	0.8	0				6	(1.0)	6	0.9
心不全	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
心不全	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
冠動脈障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
冠動脈狭窄	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
心筋障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
左室肥大	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肝胆道系障害	10	(4.2)	12	4.4	8	(3.3)	12	4.7	3	(2.5)	4	2.9	21	(3.5)	28	4.2
肝および肝胆道系障害	6	(2.5)	7	2.6	5	(2.1)	6	2.3	3	(2.5)	4	2.9	14	(2.3)	17	2.6
脂肪肝	3	(1.3)	4	1.5	2	(0.8)	2	0.8	2	(1.7)	3	2.2	7	(1.2)	9	1.4
肝嚢胞	2	(0.8)	2	0.7	4	(1.7)	4	1.6	0				6	(1.0)	6	0.9
肝機能異常	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
胆嚢障害	5	(2.1)	5	1.8	5	(2.1)	6	2.3	0				10	(1.7)	11	1.7
胆石症	4	(1.7)	4	1.5	2	(0.8)	2	0.8	0				6	(1.0)	6	0.9
胆嚢ポリープ	1	(0.4)	1	0.4	4	(1.7)	4	1.6	0				5	(0.8)	5	0.8
血管障害	7	(2.9)	8	3.0	11	(4.6)	11	4.3	2	(1.7)	2	1.5	20	(3.3)	21	3.2
高血圧性血管障害	4	(1.7)	4	1.5	8	(3.3)	8	3.1	2	(1.7)	2	1.5	14	(2.3)	14	2.1
高血圧	4	(1.7)	4	1.5	8	(3.3)	8	3.1	2	(1.7)	2	1.5	14	(2.3)	14	2.1
血管障害ＮＥＣ	3	(1.3)	3	1.1	1	(0.4)	1	0.4	0				4	(0.7)	4	0.6
大動脈石灰化	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
末梢血管障害	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
動脈硬化、狭窄、血流障害および壊死	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
末梢動脈閉塞性疾患	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
末梢冷感	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
瘤および動脈解離	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
大動脈瘤	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
精神障害	6	(2.5)	6	2.2	10	(4.1)	11	4.3	3	(2.5)	3	2.2	19	(3.2)	20	3.0
睡眠障害	4	(1.7)	4	1.5	8	(3.3)	8	3.1	3	(2.5)	3	2.2	15	(2.5)	15	2.3
不眠症	4	(1.7)	4	1.5	8	(3.3)	8	3.1	3	(2.5)	3	2.2	15	(2.5)	15	2.3
不安障害および不安症状	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
ストレス	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
不安	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
不安障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
抑うつ性気分障害	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
うつ病	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
耳および迷路障害	8	(3.3)	9	3.3	8	(3.3)	10	3.9	1	(0.8)	1	0.7	17	(2.8)	20	3.0
内耳および第８脳神経障害	7	(2.9)	7	2.6	7	(2.9)	9	3.5	0				14	(2.3)	16	2.4
回転性めまい	6	(2.5)	6	2.2	2	(0.8)	2	0.8	0				8	(1.3)	8	1.2
耳鳴	1	(0.4)	1	0.4	4	(1.7)	4	1.6	0				5	(0.8)	5	0.8
頭位性回転性めまい	0				2	(0.8)	3	1.2	0				2	(0.3)	3	0.5
耳部障害ＮＥＣ	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
耳そう痒症	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
聴覚障害	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
難聴	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
生殖系および乳房障害	3	(1.3)	4	1.5	6	(2.5)	6	2.3	2	(1.7)	2	1.5	11	(1.8)	12	1.8

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
前立腺障害（感染および炎症を除く）	1	(0.4)	1	0.4	3	(1.2)	3	1.2	0				4	(0.7)	4	0.6
良性前立腺肥大症	0				3	(1.2)	3	1.2	0				3	(0.5)	3	0.5
前立腺石灰化	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
月経周期および子宮出血障害	1	(0.4)	2	0.7	1	(0.4)	1	0.4	1	(0.8)	1	0.7	3	(0.5)	4	0.6
月経困難症	1	(0.4)	2	0.7	0				1	(0.8)	1	0.7	2	(0.3)	3	0.5
不正子宮出血	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
性機能および生殖能障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
勃起不全	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
男性生殖器系感染および炎症	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
前立腺炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
閉経関連症状	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
閉経期障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
卵巣および卵管障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
卵巣嚢胞	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
外科および内科処置	3	(1.3)	4	1.5	1	(0.4)	1	0.4	1	(0.8)	1	0.7	5	(0.8)	6	0.9
血管治療手技	2	(0.8)	3	1.1	1	(0.4)	1	0.4	0				3	(0.5)	4	0.6
経皮的冠インターベンション	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
静脈瘤手術	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
末梢血行再建	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
末梢動脈形成	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
骨および関節治療手技	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
関節形成	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
消化管治療手技	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
痔核手術	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
免疫系障害	2	(0.8)	2	0.7	2	(0.8)	2	0.8	1	(0.8)	1	0.7	5	(0.8)	5	0.8
アレルギー性疾患	2	(0.8)	2	0.7	2	(0.8)	2	0.8	1	(0.8)	1	0.7	5	(0.8)	5	0.8
季節性アレルギー	1	(0.4)	1	0.4	2	(0.8)	2	0.8	1	(0.8)	1	0.7	4	(0.7)	4	0.6
薬物過敏症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
内分泌障害	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
甲状腺障害	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
甲状腺嚢腫	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
甲状腺腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
血液およびリンパ系障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
脾臓、リンパ節および細網内皮系障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
リンパ節症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
妊娠、産褥および周産期の状態	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
妊娠時母体合併症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
妊娠嘔吐	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.23.2- 2　重篤な有害事象（器官別大分類、高位グループ語及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
Number of subjects	239				241				120				600			
Exposure time (year)	270.9				256.8				135.9				663.6			
Events	19	(7.9)	25	9.2	12	(5.0)	13	5.1	8	(6.7)	10	7.4	39	(6.5)	48	7.2
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	5	(2.1)	5	1.8	5	(2.1)	5	1.9	3	(2.5)	3	2.2	13	(2.2)	13	2.0
悪性および詳細不明の消化管新生物	1	(0.4)	1	0.4	3	(1.2)	3	1.2	1	(0.8)	1	0.7	5	(0.8)	5	0.8
遠隔転移を伴う膵癌	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
胃癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
食道癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
直腸癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
リンパ腫ＮＥＣ	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
リンパ腫	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
悪性および詳細不明のその他および部位不明新生物	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
腺癌	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
悪性および詳細不明の呼吸器系および縦隔新生物	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
肺腺癌	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
悪性および詳細不明の腎尿路系新生物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
膀胱移行上皮癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
悪性および詳細不明の乳房新生物（乳頭を含む）	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
遠隔転移を伴う乳癌	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
消化器の良性新生物	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
大腸腺腫	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
非ホジキンＢ細胞性リンパ腫	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
びまん性大細胞型Ｂ細胞性リンパ腫	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
良性男性生殖器新生物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
前立腺の良性新生物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
感染症および寄生虫症	3	(1.3)	3	1.1	2	(0.8)	2	0.8	2	(1.7)	3	2.2	7	(1.2)	8	1.2
詳細不明な感染体による感染症	1	(0.4)	1	0.4	2	(0.8)	2	0.8	1	(0.8)	2	1.5	4	(0.7)	5	0.8
急性腎盂腎炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
腎盂腎炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肺炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
扁桃周囲膿瘍	0				0				1	(0.8)	2	1.5	1	(0.2)	2	0.3
細菌感染症	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
β溶血性レンサ球菌感染	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
蜂巣炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
ウイルス感染症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
帯状疱疹	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
傷害、中毒および処置合併症	4	(1.7)	4	1.5	2	(0.8)	2	0.8	0				6	(1.0)	6	0.9
骨および関節損傷	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
腰椎骨折	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
手首関節骨折	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
上腕骨骨折	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
損傷ＮＥＣ	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
四肢外傷性切断	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
転倒	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
腱断裂	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
胃腸障害	3	(1.3)	3	1.1	2	(0.8)	2	0.8	0				5	(0.8)	5	0.8
良性消化管新生物	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
大腸ポリープ	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
消化管の状態ＮＥＣ	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
痔瘻	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
消化管運動および排泄障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
便秘	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
消化管狭窄および閉塞	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
腸閉塞	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
外科および内科処置	3	(1.3)	4	1.5	1	(0.4)	1	0.4	1	(0.8)	1	0.7	5	(0.8)	6	0.9
血管治療手技	2	(0.8)	3	1.1	1	(0.4)	1	0.4	0				3	(0.5)	4	0.6
経皮的冠インターベンション	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
静脈瘤手術	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
末梢血行再建	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
末梢動脈形成	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
骨および関節治療手技	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
関節形成	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
消化管治療手技	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
痔核手術	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
心臓障害	2	(0.8)	3	1.1	1	(0.4)	1	0.4	2	(1.7)	2	1.5	5	(0.8)	6	0.9
心不全	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
心不全	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
不整脈	1	(0.4)	2	0.7	0				1	(0.8)	1	0.7	2	(0.3)	3	0.5
完全房室ブロック	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
心室性期外収縮	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
心房細動	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
冠動脈障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
冠動脈狭窄	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
一般・全身障害および投与部位の状態	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
致命的転帰	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
溺死	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
血液およびリンパ系障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
脾臓、リンパ節および細網内皮系障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
リンパ節症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血管障害	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
血管障害ＮＥＣ	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
末梢血管障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
動脈硬化、狭窄、血流障害および壊死	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
末梢動脈閉塞性疾患	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.23.2- 3　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（器官別大分類及び基本語別） - on-treatment 期間 - 安全性解析対象集団

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	239				241				120				600			
Exposure time (year)	270.9				256.8				135.9				663.6			
Events	106	(44.4)	261	96.3	138	(57.3)	373	145.3	0				244	(40.7)	634	95.5
胃腸障害	91	(38.1)	157	57.9	103	(42.7)	208	81.0	0				194	(32.3)	365	55.0
便秘	37	(15.5)	40	14.8	35	(14.5)	38	14.8	0				72	(12.0)	78	11.8
悪心	26	(10.9)	33	12.2	44	(18.3)	66	25.7	0				70	(11.7)	99	14.9
下痢	12	(5.0)	16	5.9	24	(10.0)	34	13.2	0				36	(6.0)	50	7.5
腹部不快感	12	(5.0)	12	4.4	14	(5.8)	15	5.8	0				26	(4.3)	27	4.1
嘔吐	11	(4.6)	13	4.8	10	(4.1)	16	6.2	0				21	(3.5)	29	4.4
腹部膨満	6	(2.5)	7	2.6	11	(4.6)	11	4.3	0				17	(2.8)	18	2.7
消化不良	6	(2.5)	7	2.6	9	(3.7)	10	3.9	0				15	(2.5)	17	2.6
上腹部痛	6	(2.5)	9	3.3	2	(0.8)	2	0.8	0				8	(1.3)	11	1.7
胃炎	5	(2.1)	5	1.8	1	(0.4)	1	0.4	0				6	(1.0)	6	0.9
胃食道逆流性疾患	1	(0.4)	1	0.4	3	(1.2)	3	1.2	0				4	(0.7)	4	0.6
軟便	3	(1.3)	3	1.1	1	(0.4)	1	0.4	0				4	(0.7)	4	0.6
大腸ポリープ	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
慢性胃炎	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
おくび	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
胃障害	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
腹痛	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
バレット食道	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
メレナ	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
胃ポリープ	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
胃酸過多	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
胃潰瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. The relationship to the randomised treatment was not collected for comparator treatment as the additional OAD was not considered as trial product in this trial. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
心窩部不快感	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
放屁	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
肛門狭窄	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肛門出血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
臨床検査	26	(10.9)	42	15.5	44	(18.3)	63	24.5	0				70	(11.7)	105	15.8
リパーゼ増加	18	(7.5)	22	8.1	32	(13.3)	35	13.6	0				50	(8.3)	57	8.6
アミラーゼ増加	7	(2.9)	8	3.0	12	(5.0)	14	5.5	0				19	(3.2)	22	3.3
体重減少	3	(1.3)	3	1.1	7	(2.9)	7	2.7	0				10	(1.7)	10	1.5
血中クレアチンホスホキナーゼ増加	2	(0.8)	3	1.1	2	(0.8)	2	0.8	0				4	(0.7)	5	0.8
白血球数減少	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
アラニンアミノトランスフェラーゼ増加	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血小板数減少	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
血中カルシトニン増加	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血中クレアチニン増加	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
血中トリグリセリド増加	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
血中ブドウ糖減少	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
尿中血陽性	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
便潜血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
膵酵素検査異常	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
代謝および栄養障害	15	(6.3)	19	7.0	31	(12.9)	35	13.6	0				46	(7.7)	54	8.1
食欲減退	15	(6.3)	19	7.0	29	(12.0)	33	12.9	0				44	(7.3)	52	7.8
高コレステロール血症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
低ナトリウム血症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. The relationship to the randomised treatment was not collected for comparator treatment as the additional OAD was not considered as trial product in this trial. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
一般・全身障害および投与部位の状態	4	(1.7)	7	2.6	10	(4.1)	10	3.9	0				14	(2.3)	17	2.6
倦怠感	1	(0.4)	1	0.4	4	(1.7)	4	1.6	0				5	(0.8)	5	0.8
疲労	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
早期満腹	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
口渇	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
注射部位硬結	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
注射部位熱感	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
注射部位疼痛	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
無力症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
神経系障害	5	(2.1)	10	3.7	8	(3.3)	8	3.1	0				13	(2.2)	18	2.7
頭痛	2	(0.8)	4	1.5	2	(0.8)	2	0.8	0				4	(0.7)	6	0.9
味覚異常	1	(0.4)	1	0.4	3	(1.2)	3	1.2	0				4	(0.7)	4	0.6
起立不耐性	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
錯感覚	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
注意力障害	1	(0.4)	3	1.1	0				0				1	(0.2)	3	0.5
糖尿病性ニューロパチー	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
浮動性めまい	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
片頭痛	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
眼障害	5	(2.1)	6	2.2	7	(2.9)	7	2.7	0				12	(2.0)	13	2.0
糖尿病網膜症	3	(1.3)	3	1.1	4	(1.7)	4	1.6	0				7	(1.2)	7	1.1
開放隅角緑内障	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
結膜出血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
光視症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
硝子体浮遊物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
糖尿病性網膜浮腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. The relationship to the randomised treatment was not collected for comparator treatment as the additional OAD was not considered as trial product in this trial. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
白内障	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
感染症および寄生虫症	3	(1.3)	3	1.1	6	(2.5)	7	2.7	0				9	(1.5)	10	1.5
胃腸炎	2	(0.8)	2	0.7	4	(1.7)	5	1.9	0				6	(1.0)	7	1.1
外耳炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
急性腎盂腎炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
毛包炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
皮膚および皮下組織障害	2	(0.8)	3	1.1	6	(2.5)	8	3.1	0				8	(1.3)	11	1.7
皮下出血	1	(0.4)	1	0.4	2	(0.8)	4	1.6	0				3	(0.5)	5	0.8
脂漏性皮膚炎	1	(0.4)	2	0.7	1	(0.4)	1	0.4	0				2	(0.3)	3	0.5
湿疹	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
多汗症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
発疹	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
筋骨格系および結合組織障害	1	(0.4)	1	0.4	6	(2.5)	6	2.3	0				7	(1.2)	7	1.1
関節痛	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
四肢痛	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
滑液嚢腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
関節障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
心臓障害	2	(0.8)	2	0.7	5	(2.1)	5	1.9	0				7	(1.2)	7	1.1
動悸	2	(0.8)	2	0.7	2	(0.8)	2	0.8	0				4	(0.7)	4	0.6
冠動脈狭窄	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
心室性期外収縮	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
不整脈	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
腎および尿路障害	2	(0.8)	2	0.7	3	(1.2)	4	1.6	0				5	(0.8)	6	0.9

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. The relationship to the randomised treatment was not collected for comparator treatment as the additional OAD was not considered as trial product in this trial. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
腎結石症	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
頻尿	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
腎嚢胞	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
尿管結石	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	4	(1.7)	4	1.5	1	(0.4)	1	0.4	0				5	(0.8)	5	0.8
大腸腺腫	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
リンパ腫	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
甲状腺新生物	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
食道癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
精神障害	0				4	(1.7)	5	1.9	0				4	(0.7)	5	0.8
不眠症	0				3	(1.2)	3	1.2	0				3	(0.5)	3	0.5
うつ病	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
呼吸器、胸郭および縦隔障害	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
しゃっくり	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
咽喉絞扼感	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
慢性気管支炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
肝胆道系障害	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
肝機能異常	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
脂肪肝	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血管障害	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
高血圧	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. The relationship to the randomised treatment was not collected for comparator treatment as the additional OAD was not considered as trial product in this trial. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
末梢冷感	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
外科および内科処置	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
経皮的冠インターベンション	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
耳および迷路障害	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
回転性めまい	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
難聴	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
生殖系および乳房障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
卵巣嚢胞	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. The relationship to the randomised treatment was not collected for comparator treatment as the additional OAD was not considered as trial product in this trial. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.23.2- 4　重度の有害事象（器官別大分類及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	239				241				120				600			
Exposure time (year)	270.9				256.8				135.9				663.6			
Events	10	(4.2)	12	4.4	3	(1.2)	3	1.2	2	(1.7)	3	2.2	15	(2.5)	18	2.7
感染症および寄生虫症	2	(0.8)	2	0.7	1	(0.4)	1	0.4	1	(0.8)	2	1.5	4	(0.7)	5	0.8
β溶血性レンサ球菌感染	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
急性腎盂腎炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
帯状疱疹	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
扁桃周囲膿瘍	0				0				1	(0.8)	2	1.5	1	(0.2)	2	0.3
傷害、中毒および処置合併症	4	(1.7)	4	1.5	0				0				4	(0.7)	4	0.6
下肢骨折	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
四肢外傷性切断	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
上腕骨骨折	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
転倒	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3	(1.3)	3	1.1	1	(0.4)	1	0.4	0				4	(0.7)	4	0.6
リンパ腫	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
遠隔転移を伴う乳癌	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
肺腺癌	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
膀胱移行上皮癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
胃腸障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
腸閉塞	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
一般・全身障害および投与部位の状態	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
溺死	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
外科および内科処置	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
関節形成	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血液およびリンパ系障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
リンパ節症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
代謝および栄養障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
低ナトリウム血症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.23.2- 5　中等度の有害事象（器官別大分類及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	239				241				120				600			
Exposure time (year)	270.9				256.8				135.9				663.6			
Events	29	(12.1)	46	17.0	29	(12.0)	37	14.4	15	(12.5)	20	14.7	73	(12.2)	103	15.5
胃腸障害	7	(2.9)	11	4.1	8	(3.3)	8	3.1	5	(4.2)	6	4.4	20	(3.3)	25	3.8
悪心	1	(0.4)	1	0.4	3	(1.2)	3	1.2	1	(0.8)	1	0.7	5	(0.8)	5	0.8
下痢	1	(0.4)	1	0.4	1	(0.4)	1	0.4	1	(0.8)	1	0.7	3	(0.5)	3	0.5
歯周病	1	(0.4)	1	0.4	1	(0.4)	1	0.4	1	(0.8)	1	0.7	3	(0.5)	3	0.5
便秘	3	(1.3)	3	1.1	0				0				3	(0.5)	3	0.5
大腸ポリープ	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
嘔吐	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
胃ポリープ	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
胃十二指腸潰瘍	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
消化不良	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
上腹部痛	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
腹痛	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
腹部不快感	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
齲歯	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
感染症および寄生虫症	6	(2.5)	7	2.6	4	(1.7)	4	1.6	2	(1.7)	2	1.5	12	(2.0)	13	2.0
インフルエンザ	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
胃腸炎	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
ヘリコバクター性胃炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
咽頭炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
感染性腸炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
気管支炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
腎盂腎炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肺炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
蜂巣炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
傷害、中毒および処置合併症	5	(2.1)	5	1.8	4	(1.7)	4	1.6	1	(0.8)	1	0.7	10	(1.7)	10	1.5
関節損傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
挫傷	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
手骨折	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
手首関節骨折	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
脊椎骨折	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
動物咬傷	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
剥離骨折	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肋骨骨折	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
腱断裂	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
靭帯捻挫	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
筋骨格系および結合組織障害	3	(1.3)	3	1.1	3	(1.2)	3	1.2	3	(2.5)	3	2.2	9	(1.5)	9	1.4
背部痛	2	(0.8)	2	0.7	0				1	(0.8)	1	0.7	3	(0.5)	3	0.5
関節痛	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
関節リウマチ	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
関節周囲炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
筋骨格痛	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
変形性脊椎症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
臨床検査	2	(0.8)	4	1.5	4	(1.7)	4	1.6	2	(1.7)	2	1.5	8	(1.3)	10	1.5
リパーゼ増加	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
体重減少	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
Ｃ－反応性蛋白増加	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
アミラーゼ増加	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
アラニンアミノトランスフェラーゼ増加	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
肝酵素上昇	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
血小板数減少	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
腎および尿路障害	1	(0.4)	1	0.4	2	(0.8)	3	1.2	1	(0.8)	1	0.7	4	(0.7)	5	0.8
腎結石症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
糖尿病性腎症	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
尿管結石	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
尿路結石	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
頻尿	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2	(0.8)	2	0.7	0				2	(1.7)	2	1.5	4	(0.7)	4	0.6
遠隔転移を伴う膵癌	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
腺癌	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
大腸腺腫	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
外科および内科処置	1	(0.4)	2	0.7	1	(0.4)	1	0.4	1	(0.8)	1	0.7	3	(0.5)	4	0.6
経皮的冠インターベンション	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
痔核手術	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
末梢血行再建	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
末梢動脈形成	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
眼障害	1	(0.4)	1	0.4	1	(0.4)	2	0.8	1	(0.8)	1	0.7	3	(0.5)	4	0.6
糖尿病網膜症	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
黄斑症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
網膜静脈閉塞	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
耳および迷路障害	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
回転性めまい	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
頭位性回転性めまい	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心臓障害	1	(0.4)	1	0.4	1	(0.4)	1	0.4	1	(0.8)	1	0.7	3	(0.5)	3	0.5
心不全	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
冠動脈狭窄	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
代謝および栄養障害	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
食欲減退	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
血管障害	1	(0.4)	2	0.7	1	(0.4)	1	0.4	0				2	(0.3)	3	0.5
高血圧	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
末梢血管障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
末梢動脈閉塞性疾患	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
神経系障害	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
糖尿病性ニューロパチー	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
浮動性めまい	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肝胆道系障害	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
脂肪肝	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
胆石症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
呼吸器、胸郭および縦隔障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
上気道の炎症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
生殖系および乳房障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
卵巣嚢胞	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
皮膚および皮下組織障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
皮膚炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.23.2- 6　軽度の有害事象（器官別大分類及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	239				241				120				600			
Exposure time (year)	270.9				256.8				135.9				663.6			
Events	202	(84.5)	851	314.1	209	(86.7)	914	356.0	80	(66.7)	246	181.0	491	(81.8)	2011	303.0
感染症および寄生虫症	123	(51.5)	222	81.9	109	(45.2)	179	69.7	58	(48.3)	101	74.3	290	(48.3)	502	75.6
鼻咽頭炎	81	(33.9)	132	48.7	75	(31.1)	105	40.9	41	(34.2)	60	44.1	197	(32.8)	297	44.8
咽頭炎	11	(4.6)	14	5.2	9	(3.7)	9	3.5	2	(1.7)	3	2.2	22	(3.7)	26	3.9
胃腸炎	13	(5.4)	14	5.2	5	(2.1)	5	1.9	2	(1.7)	2	1.5	20	(3.3)	21	3.2
気管支炎	6	(2.5)	6	2.2	5	(2.1)	6	2.3	4	(3.3)	5	3.7	15	(2.5)	17	2.6
上気道感染	5	(2.1)	6	2.2	7	(2.9)	8	3.1	3	(2.5)	4	2.9	15	(2.5)	18	2.7
インフルエンザ	1	(0.4)	1	0.4	5	(2.1)	5	1.9	3	(2.5)	3	2.2	9	(1.5)	9	1.4
膀胱炎	5	(2.1)	5	1.8	2	(0.8)	2	0.8	2	(1.7)	2	1.5	9	(1.5)	9	1.4
結膜炎	5	(2.1)	5	1.8	1	(0.4)	1	0.4	1	(0.8)	1	0.7	7	(1.2)	7	1.1
帯状疱疹	4	(1.7)	4	1.5	2	(0.8)	2	0.8	1	(0.8)	1	0.7	7	(1.2)	7	1.1
中耳炎	1	(0.4)	1	0.4	4	(1.7)	4	1.6	1	(0.8)	1	0.7	6	(1.0)	6	0.9
ヘリコバクター感染	4	(1.7)	4	1.5	1	(0.4)	1	0.4	0				5	(0.8)	5	0.8
歯肉炎	1	(0.4)	1	0.4	3	(1.2)	3	1.2	1	(0.8)	1	0.7	5	(0.8)	5	0.8
足部白癬	2	(0.8)	2	0.7	2	(0.8)	2	0.8	1	(0.8)	1	0.7	5	(0.8)	5	0.8
扁桃炎	2	(0.8)	3	1.1	1	(0.4)	1	0.4	2	(1.7)	2	1.5	5	(0.8)	6	0.9
毛包炎	3	(1.3)	3	1.1	1	(0.4)	1	0.4	0				4	(0.7)	4	0.6
ウイルス性胃腸炎	2	(0.8)	2	0.7	0				1	(0.8)	1	0.7	3	(0.5)	3	0.5
外耳炎	1	(0.4)	1	0.4	1	(0.4)	2	0.8	1	(0.8)	1	0.7	3	(0.5)	4	0.6
口腔ヘルペス	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
歯周炎	1	(0.4)	1	0.4	1	(0.4)	1	0.4	1	(0.8)	1	0.7	3	(0.5)	3	0.5
尿路感染	0				2	(0.8)	2	0.8	1	(0.8)	1	0.7	3	(0.5)	3	0.5
膿痂疹	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
蜂巣炎	1	(0.4)	1	0.4	1	(0.4)	1	0.4	1	(0.8)	1	0.7	3	(0.5)	3	0.5
化膿	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
感染性皮膚嚢腫	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
単純ヘルペス	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
爪囲炎	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
爪真菌症	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
麦粒腫	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
鼻炎	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
副鼻腔炎	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
クラミジア性肺炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
トリコフィトン感染症	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
ヘリコバクター性胃炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
レンサ球菌感染	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
眼部単純ヘルペス	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
眼瞼感染	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
急性中耳炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
細菌性胃腸炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
細菌性眼感染	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
細菌性膣症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
食道カンジダ症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
精巣上体炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
体部白癬	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
蓄膿	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
尿道炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
肺膿瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
白癬感染	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
皮膚感染	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
慢性副鼻腔炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
肛門膿瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
鼠径部膿瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
胃腸障害	126	(52.7)	250	92.3	128	(53.1)	292	113.7	20	(16.7)	34	25.0	274	(45.7)	576	86.8

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
便秘	43	(18.0)	47	17.3	36	(14.9)	40	15.6	5	(4.2)	5	3.7	84	(14.0)	92	13.9
悪心	29	(12.1)	37	13.7	44	(18.3)	67	26.1	0				73	(12.2)	104	15.7
下痢	24	(10.0)	32	11.8	37	(15.4)	48	18.7	7	(5.8)	8	5.9	68	(11.3)	88	13.3
腹部不快感	14	(5.9)	14	5.2	15	(6.2)	16	6.2	0				29	(4.8)	30	4.5
嘔吐	13	(5.4)	16	5.9	14	(5.8)	21	8.2	1	(0.8)	1	0.7	28	(4.7)	38	5.7
消化不良	7	(2.9)	8	3.0	10	(4.1)	11	4.3	1	(0.8)	1	0.7	18	(3.0)	20	3.0
上腹部痛	10	(4.2)	13	4.8	7	(2.9)	8	3.1	0				17	(2.8)	21	3.2
腹部膨満	6	(2.5)	7	2.6	11	(4.6)	11	4.3	0				17	(2.8)	18	2.7
慢性胃炎	9	(3.8)	9	3.3	4	(1.7)	4	1.6	2	(1.7)	2	1.5	15	(2.5)	15	2.3
齲歯	6	(2.5)	6	2.2	5	(2.1)	5	1.9	4	(3.3)	5	3.7	15	(2.5)	16	2.4
胃食道逆流性疾患	5	(2.1)	5	1.8	8	(3.3)	8	3.1	1	(0.8)	1	0.7	14	(2.3)	14	2.1
胃炎	6	(2.5)	6	2.2	3	(1.2)	3	1.2	1	(0.8)	1	0.7	10	(1.7)	10	1.5
大腸ポリープ	4	(1.7)	4	1.5	6	(2.5)	8	3.1	0				10	(1.7)	12	1.8
胃ポリープ	3	(1.3)	3	1.1	4	(1.7)	4	1.6	2	(1.7)	2	1.5	9	(1.5)	9	1.4
歯痛	5	(2.1)	6	2.2	3	(1.2)	3	1.2	1	(0.8)	1	0.7	9	(1.5)	10	1.5
軟便	3	(1.3)	3	1.1	4	(1.7)	4	1.6	1	(0.8)	1	0.7	8	(1.3)	8	1.2
口内炎	4	(1.7)	4	1.5	2	(0.8)	3	1.2	0				6	(1.0)	7	1.1
腸憩室	0				4	(1.7)	4	1.6	2	(1.7)	2	1.5	6	(1.0)	6	0.9
痔核	2	(0.8)	2	0.7	2	(0.8)	2	0.8	1	(0.8)	1	0.7	5	(0.8)	5	0.8
大腸炎	2	(0.8)	4	1.5	2	(0.8)	2	0.8	1	(0.8)	1	0.7	5	(0.8)	7	1.1
裂孔ヘルニア	3	(1.3)	3	1.1	1	(0.4)	1	0.4	0				4	(0.7)	4	0.6
血便排泄	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
腹痛	1	(0.4)	1	0.4	1	(0.4)	1	0.4	1	(0.8)	1	0.7	3	(0.5)	3	0.5
おくび	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
びらん性胃炎	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
バレット食道	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
胃障害	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
胃潰瘍	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
口唇炎	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
歯周病	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
メレナ	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
胃黄色腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
胃酸過多	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
過敏性腸症候群	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
口唇潰瘍	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
腰ヘルニア	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
歯槽骨吸収	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
痔瘻	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
十二指腸潰瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
小腸炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
食中毒	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
心窩部不快感	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
腸炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
直腸ポリープ	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
放屁	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
肛門ポリープ	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肛門狭窄	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肛門出血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
膵管拡張	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
膵腫瘤	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
膵嚢胞	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
臨床検査	40	(16.7)	62	22.9	57	(23.7)	77	30.0	7	(5.8)	9	6.6	104	(17.3)	148	22.3
リパーゼ増加	20	(8.4)	23	8.5	32	(13.3)	35	13.6	2	(1.7)	2	1.5	54	(9.0)	60	9.0
アミラーゼ増加	7	(2.9)	7	2.6	13	(5.4)	15	5.8	1	(0.8)	1	0.7	21	(3.5)	23	3.5
血中クレアチンホスホキナーゼ増加	3	(1.3)	4	1.5	5	(2.1)	5	1.9	1	(0.8)	1	0.7	9	(1.5)	10	1.5
体重減少	3	(1.3)	3	1.1	5	(2.1)	5	1.9	0				8	(1.3)	8	1.2
ヘリコバクター検査陽性	3	(1.3)	3	1.1	3	(1.2)	3	1.2	0				6	(1.0)	6	0.9
尿中血陽性	0				3	(1.2)	3	1.2	2	(1.7)	2	1.5	5	(0.8)	5	0.8

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
アラニンアミノトランスフェラーゼ増加	4	(1.7)	4	1.5	0				0				4	(0.7)	4	0.6
血中トリグリセリド増加	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
尿中ヘモグロビン陽性	3	(1.3)	3	1.1	0				0				3	(0.5)	3	0.5
白血球数減少	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
γ－グルタミルトランスフェラーゼ増加	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
血中クレアチニン増加	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
便潜血陽性	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
ＱＲＳ軸異常	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
アスパラギン酸アミノトランスフェラーゼ増加	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
リンパ球形態異常	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肝機能検査異常	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血圧上昇	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血小板数減少	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血中カルシトニン増加	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血中ブドウ糖減少	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
心電図Ｔ波	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
心電図Ｔ波振幅減少	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
低比重リポ蛋白増加	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
尿中アルブミン／クレアチニン比異常	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
尿中アルブミン陽性	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
尿中血	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
尿中蛋白陽性	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
便潜血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
膵酵素検査異常	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
筋骨格系および結合組織障害	32	(13.4)	40	14.8	44	(18.3)	52	20.3	19	(15.8)	23	16.9	95	(15.8)	115	17.3

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class / Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
背部痛	7	(2.9)	8	3.0	13	(5.4)	13	5.1	9	(7.5)	9	6.6	29	(4.8)	30	4.5
関節痛	7	(2.9)	7	2.6	10	(4.1)	10	3.9	1	(0.8)	1	0.7	18	(3.0)	18	2.7
関節周囲炎	4	(1.7)	4	1.5	4	(1.7)	4	1.6	1	(0.8)	1	0.7	9	(1.5)	9	1.4
四肢痛	4	(1.7)	5	1.8	3	(1.2)	3	1.2	1	(0.8)	1	0.7	8	(1.3)	9	1.4
筋骨格痛	1	(0.4)	1	0.4	4	(1.7)	4	1.6	0				5	(0.8)	5	0.8
筋肉痛	0				2	(0.8)	2	0.8	3	(2.5)	3	2.2	5	(0.8)	5	0.8
筋骨格硬直	2	(0.8)	3	1.1	1	(0.4)	2	0.8	1	(0.8)	1	0.7	4	(0.7)	6	0.9
筋痙縮	0				1	(0.4)	1	0.4	2	(1.7)	2	1.5	3	(0.5)	3	0.5
頚部痛	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
椎間板突出	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
滑液嚢腫	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
筋骨格系胸痛	0				0				2	(1.7)	2	1.5	2	(0.3)	2	0.3
肩回旋筋腱板症候群	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
変形性関節症	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
変形性脊椎症	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
顎関節症候群	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
関節炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
関節障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
筋骨格不快感	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
筋膜炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
腰部脊柱管狭窄症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
骨粗鬆症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
脊柱管狭窄症	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
側腹部痛	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
足底筋膜炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
弾発指	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
椎間板障害	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
腱炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
腱鞘炎	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
眼障害	35	(14.6)	48	17.7	35	(14.5)	37	14.4	8	(6.7)	8	5.9	78	(13.0)	93	14.0
糖尿病網膜症	11	(4.6)	11	4.1	15	(6.2)	15	5.8	5	(4.2)	5	3.7	31	(5.2)	31	4.7
白内障	7	(2.9)	8	3.0	3	(1.2)	3	1.2	1	(0.8)	1	0.7	11	(1.8)	12	1.8
眼乾燥	2	(0.8)	2	0.7	3	(1.2)	3	1.2	0				5	(0.8)	5	0.8
眼精疲労	2	(0.8)	2	0.7	3	(1.2)	3	1.2	0				5	(0.8)	5	0.8
網膜出血	3	(1.3)	4	1.5	1	(0.4)	1	0.4	1	(0.8)	1	0.7	5	(0.8)	6	0.9
アレルギー性結膜炎	3	(1.3)	4	1.5	1	(0.4)	1	0.4	0				4	(0.7)	5	0.8
眼瞼炎	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
緑内障	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
黄斑症	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
結膜出血	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
網膜滲出物	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
開放隅角緑内障	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
角膜びらん	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
眼そう痒症	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
眼脂	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
眼充血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
眼瞼浮腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
結膜充血	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
光視症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
高眼圧症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
視神経乳頭陥凹	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
硝子体浮遊物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
糖尿病性網膜浮腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
複視	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
網膜血管瘤	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
網膜障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
網膜色素脱失	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
網膜変性	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
神経系障害	27	(11.3)	42	15.5	28	(11.6)	42	16.4	4	(3.3)	5	3.7	59	(9.8)	89	13.4
頭痛	7	(2.9)	15	5.5	11	(4.6)	20	7.8	1	(0.8)	2	1.5	19	(3.2)	37	5.6
浮動性めまい	5	(2.1)	5	1.8	5	(2.1)	6	2.3	0				10	(1.7)	11	1.7
感覚鈍麻	1	(0.4)	1	0.4	4	(1.7)	5	1.9	0				5	(0.8)	6	0.9
頚動脈硬化症	2	(0.8)	2	0.7	2	(0.8)	2	0.8	0				4	(0.7)	4	0.6
体位性めまい	2	(0.8)	2	0.7	2	(0.8)	2	0.8	0				4	(0.7)	4	0.6
味覚異常	1	(0.4)	1	0.4	3	(1.2)	3	1.2	0				4	(0.7)	4	0.6
糖尿病性ニューロパチー	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
傾眠	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
手根管症候群	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
末梢性ニューロパチー	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
意識消失	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
起立不耐性	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
緊張性頭痛	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
頚腕症候群	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
坐骨神経痛	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
錯感覚	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
三叉神経痛	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
神経痛	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
第７脳神経麻痺	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
注意力障害	1	(0.4)	3	1.1	0				0				1	(0.2)	3	0.5
片頭痛	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
肋間神経痛	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
代謝および栄養障害	23	(9.6)	26	9.6	32	(13.3)	38	14.8	4	(3.3)	4	2.9	59	(9.8)	68	10.2
食欲減退	17	(7.1)	20	7.4	31	(12.9)	35	13.6	0				48	(8.0)	55	8.3
高尿酸血症	3	(1.3)	3	1.1	1	(0.4)	1	0.4	1	(0.8)	1	0.7	5	(0.8)	5	0.8
高脂血症	1	(0.4)	1	0.4	0				2	(1.7)	2	1.5	3	(0.5)	3	0.5
痛風	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
高コレステロール血症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脂質異常症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
脱水	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
傷害、中毒および処置合併症	23	(9.6)	24	8.9	24	(10.0)	25	9.7	10	(8.3)	12	8.8	57	(9.5)	61	9.2
挫傷	5	(2.1)	5	1.8	4	(1.7)	4	1.6	2	(1.7)	2	1.5	11	(1.8)	11	1.7
靭帯捻挫	4	(1.7)	5	1.8	2	(0.8)	2	0.8	1	(0.8)	1	0.7	7	(1.2)	8	1.2
歯牙破折	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
節足動物咬傷	0				2	(0.8)	2	0.8	1	(0.8)	1	0.7	3	(0.5)	3	0.5
熱中症	2	(0.8)	2	0.7	0				1	(0.8)	1	0.7	3	(0.5)	3	0.5
フューム吸引性呼吸障害	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
創傷	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
足骨折	0				0				2	(1.7)	2	1.5	2	(0.3)	2	0.3
凍瘡	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
動物咬傷	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
肉離れ	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
熱射病	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
肋骨骨折	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
サンバーン	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
外傷後頚部症候群	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
関節損傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
筋断裂	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
腰椎骨折	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
擦過傷	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
上顎炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
節足動物刺傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
爪損傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
熱傷	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
半月板損傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
皮膚擦過傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
尾骨骨折	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
裂傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
腱損傷	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
腱断裂	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
靭帯損傷	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
皮膚および皮下組織障害	25	(10.5)	36	13.3	22	(9.1)	30	11.7	7	(5.8)	8	5.9	54	(9.0)	74	11.2
湿疹	4	(1.7)	4	1.5	6	(2.5)	7	2.7	2	(1.7)	2	1.5	12	(2.0)	13	2.0
そう痒症	4	(1.7)	5	1.8	2	(0.8)	2	0.8	0				6	(1.0)	7	1.1
脂漏性皮膚炎	2	(0.8)	3	1.1	4	(1.7)	4	1.6	0				6	(1.0)	7	1.1
皮下出血	1	(0.4)	1	0.4	2	(0.8)	4	1.6	1	(0.8)	1	0.7	4	(0.7)	6	0.9
アレルギー性皮膚炎	2	(0.8)	3	1.1	1	(0.4)	1	0.4	0				3	(0.5)	4	0.6
過角化	3	(1.3)	3	1.1	0				0				3	(0.5)	3	0.5
接触性皮膚炎	0				2	(0.8)	2	0.8	1	(0.8)	1	0.7	3	(0.5)	3	0.5
発疹	0				2	(0.8)	2	0.8	1	(0.8)	1	0.7	3	(0.5)	3	0.5
冷汗	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
蕁麻疹	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
掌蹠角皮症	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
線状出血	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
皮膚炎	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
うっ滞性皮膚炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
アトピー性皮膚炎	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
円形脱毛症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
貨幣状湿疹	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
乾皮症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
汗疹	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
紅斑	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
神経皮膚炎	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
多汗症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
点状出血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
皮脂欠乏性湿疹	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
皮膚潰瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
皮膚嚢腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
薬疹	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
呼吸器、胸郭および縦隔障害	18	(7.5)	18	6.6	26	(10.8)	34	13.2	9	(7.5)	12	8.8	53	(8.8)	64	9.6
上気道の炎症	2	(0.8)	2	0.7	11	(4.6)	18	7.0	0				13	(2.2)	20	3.0
咳嗽	3	(1.3)	3	1.1	1	(0.4)	1	0.4	3	(2.5)	3	2.2	7	(1.2)	7	1.1
喘息	2	(0.8)	2	0.7	2	(0.8)	2	0.8	3	(2.5)	4	2.9	7	(1.2)	8	1.2
アレルギー性鼻炎	4	(1.7)	4	1.5	2	(0.8)	2	0.8	0				6	(1.0)	6	0.9
口腔咽頭痛	1	(0.4)	1	0.4	3	(1.2)	3	1.2	1	(0.8)	1	0.7	5	(0.8)	5	0.8
鼻漏	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
慢性気管支炎	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
しゃっくり	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
咽喉絞扼感	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
咽喉刺激感	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
喉頭不快感	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
睡眠時無呼吸症候群	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
声帯の炎症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
声帯肥厚	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
肺気腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肺腫瘤	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
肺嚢胞	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
発声障害	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
鼻出血	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
鼻閉塞	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
慢性閉塞性肺疾患	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
腎および尿路障害	13	(5.4)	13	4.8	17	(7.1)	20	7.8	4	(3.3)	7	5.1	34	(5.7)	40	6.0
腎嚢胞	3	(1.3)	3	1.1	7	(2.9)	7	2.7	1	(0.8)	1	0.7	11	(1.8)	11	1.7
腎結石症	4	(1.7)	4	1.5	4	(1.7)	4	1.6	2	(1.7)	2	1.5	10	(1.7)	10	1.5

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
尿管結石	1	(0.4)	1	0.4	4	(1.7)	4	1.6	1	(0.8)	1	0.7	6	(1.0)	6	0.9
頻尿	1	(0.4)	1	0.4	3	(1.2)	3	1.2	0				4	(0.7)	4	0.6
水腎症	0				1	(0.4)	1	0.4	1	(0.8)	1	0.7	2	(0.3)	2	0.3
夜間頻尿	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
アルブミン尿	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血尿	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
腎腫大	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
尿路結石	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
膀胱炎様症状	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
一般・全身障害および投与部位の状態	13	(5.4)	17	6.3	15	(6.2)	15	5.8	5	(4.2)	5	3.7	33	(5.5)	37	5.6
倦怠感	4	(1.7)	4	1.5	4	(1.7)	4	1.6	0				8	(1.3)	8	1.2
疲労	2	(0.8)	2	0.7	3	(1.2)	3	1.2	0				5	(0.8)	5	0.8
発熱	1	(0.4)	1	0.4	2	(0.8)	2	0.8	1	(0.8)	1	0.7	4	(0.7)	4	0.6
末梢性浮腫	1	(0.4)	1	0.4	0				3	(2.5)	3	2.2	4	(0.7)	4	0.6
口渇	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
早期満腹	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
悪寒	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
異常感	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
炎症	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
乾燥症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
胸部不快感	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
注射部位硬結	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
注射部位熱感	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
注射部位疼痛	1	(0.4)	2	0.7	0				0				1	(0.2)	2	0.3
無力症	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肝胆道系障害	9	(3.8)	10	3.7	8	(3.3)	12	4.7	3	(2.5)	4	2.9	20	(3.3)	26	3.9
肝嚢胞	2	(0.8)	2	0.7	4	(1.7)	4	1.6	0				6	(1.0)	6	0.9

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class / Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Additional OAD N	(%)	E	R	Total N	(%)	E	R
脂肪肝	2	(0.8)	3	1.1	2	(0.8)	2	0.8	2	(1.7)	3	2.2	6	(1.0)	8	1.2
胆石症	3	(1.3)	3	1.1	2	(0.8)	2	0.8	0				5	(0.8)	5	0.8
胆嚢ポリープ	1	(0.4)	1	0.4	4	(1.7)	4	1.6	0				5	(0.8)	5	0.8
肝機能異常	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
心臓障害	8	(3.3)	9	3.3	10	(4.1)	11	4.3	2	(1.7)	2	1.5	20	(3.3)	22	3.3
動悸	4	(1.7)	4	1.5	2	(0.8)	2	0.8	0				6	(1.0)	6	0.9
上室性期外収縮	1	(0.4)	1	0.4	2	(0.8)	2	0.8	0				3	(0.5)	3	0.5
右脚ブロック	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
心室性期外収縮	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
心房細動	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
完全房室ブロック	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
脚ブロック	0				1	(0.4)	2	0.8	0				1	(0.2)	2	0.3
左室肥大	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
第一度房室ブロック	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
第二度房室ブロック	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
不整脈	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
精神障害	6	(2.5)	6	2.2	10	(4.1)	11	4.3	3	(2.5)	3	2.2	19	(3.2)	20	3.0
不眠症	4	(1.7)	4	1.5	8	(3.3)	8	3.1	3	(2.5)	3	2.2	15	(2.5)	15	2.3
うつ病	0				2	(0.8)	2	0.8	0				2	(0.3)	2	0.3
ストレス	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
不安	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
不安障害	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
血管障害	6	(2.5)	6	2.2	10	(4.1)	10	3.9	2	(1.7)	2	1.5	18	(3.0)	18	2.7
高血圧	4	(1.7)	4	1.5	7	(2.9)	7	2.7	2	(1.7)	2	1.5	13	(2.2)	13	2.0
大動脈石灰化	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
大動脈瘤	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
末梢血管障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
末梢冷感	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	6	(2.5)	6	2.2	8	(3.3)	11	4.3	2	(1.7)	3	2.2	16	(2.7)	20	3.0
大腸腺腫	2	(0.8)	2	0.7	2	(0.8)	2	0.8	0				4	(0.7)	4	0.6
皮膚乳頭腫	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
びまん性大細胞型Ｂ細胞性リンパ腫	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
メラノサイト性母斑	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
胃癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
化膿性肉芽腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
肝臓血管腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
血管脂肪腫	0				0				1	(0.8)	2	1.5	1	(0.2)	2	0.3
甲状腺新生物	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
脂肪腫	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
消化管粘膜下腫瘍	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
食道癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
前立腺の良性新生物	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
直腸癌	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
膀胱乳頭腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
耳および迷路障害	6	(2.5)	7	2.6	7	(2.9)	9	3.5	1	(0.8)	1	0.7	14	(2.3)	17	2.6
回転性めまい	4	(1.7)	4	1.5	2	(0.8)	2	0.8	0				6	(1.0)	6	0.9
耳鳴	1	(0.4)	1	0.4	4	(1.7)	4	1.6	0				5	(0.8)	5	0.8
耳そう痒症	1	(0.4)	1	0.4	0				1	(0.8)	1	0.7	2	(0.3)	2	0.3
難聴	1	(0.4)	1	0.4	1	(0.4)	1	0.4	0				2	(0.3)	2	0.3
頭位性回転性めまい	0				1	(0.4)	2	0.8	0				1	(0.2)	2	0.3
生殖系および乳房障害	3	(1.3)	4	1.5	5	(2.1)	5	1.9	2	(1.7)	2	1.5	10	(1.7)	11	1.7

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Additional OAD				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
良性前立腺肥大症	0				3	(1.2)	3	1.2	0				3	(0.5)	3	0.5
月経困難症	1	(0.4)	2	0.7	0				1	(0.8)	1	0.7	2	(0.3)	3	0.5
前立腺炎	0				0				1	(0.8)	1	0.7	1	(0.2)	1	0.2
前立腺石灰化	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
不正子宮出血	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
閉経期障害	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
勃起不全	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
免疫系障害	2	(0.8)	2	0.7	2	(0.8)	2	0.8	1	(0.8)	1	0.7	5	(0.8)	5	0.8
季節性アレルギー	1	(0.4)	1	0.4	2	(0.8)	2	0.8	1	(0.8)	1	0.7	4	(0.7)	4	0.6
薬物過敏症	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
内分泌障害	2	(0.8)	2	0.7	1	(0.4)	1	0.4	0				3	(0.5)	3	0.5
甲状腺嚢腫	2	(0.8)	2	0.7	0				0				2	(0.3)	2	0.3
甲状腺腫	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
外科および内科処置	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
静脈瘤手術	1	(0.4)	1	0.4	0				0				1	(0.2)	1	0.2
妊娠、産褥および周産期の状態	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2
妊娠嘔吐	0				1	(0.4)	1	0.4	0				1	(0.2)	1	0.2

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The exposure time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, OAD: Oral anti-diabetic drug, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

2.7.6.24 NN9535-4092

2.7.6.24.1 臨床試験概要

治験依頼者名： Novo Nordisk Pharma Ltd., 2-1-1, Marunouchi, Chiyoda-ku Tokyo, Japan	
有効成分名： セマグルチド	
Trial Registration ID-number： NCT02254291	UTN：U1111-1140-5334 IND number：該当なし EudraCT number：該当なし Japanese registration number：JapicCTI-142663
治験の標題： 日本人 2 型糖尿病患者を対象とした、セマグルチドの週 1 回投与及びシタグリプチンの 1 日 1 回投与の単独療法における安全性及び有効性の比較検討	
治験責任医師名： 治験実施施設（全 25 施設）ごとに 1 名の治験責任医師が任命された。以下の治験責任医師が治験総括報告書の内容を確認し、署名する「治験総括報告書への署名責任を有する医師（signatory investigator）」に指名された。 [redacted]	
治験実施施設： 本試験は日本国内で 25 施設において実施された。	
公表文献（引用文献）： 本臨床試験概要作成時点での公表文献はなし	
治験期間： 開始日：2014 年 10 月 2 日 終了日：2015 年 11 月 11 日	**開発のフェーズ**： 第 3a 相
Cut-off date： ここに提示する結果は、2016 年 2 月 12 日の時点での臨床データベースに基づいている。	
報告書作成日： 2016 年 9 月 2 日	
目的： <u>主要目的</u>： 日本人 2 型糖尿病患者を対象として、セマグルチド（0.5 及び 1.0 mg）の週 1 回投与（単独療法）及びシタグリプチン（100 mg）の 1 日 1 回投与（単独療法）の 30 週間の安全性を比較検討する。 <u>副次的目的</u>： 投与後 30 週の以下の項目に対する、セマグルチド（0.5 及び 1.0 mg）の週 1 回投与（単独療法）及びシタグリプチン（100 mg）の 1 日 1 回投与（単独療法）の有効性を比較検討する。 – 血糖コントロール – 体重減少の誘導及び維持 – 有効性に関するその他のパラメータ	
治験方法： 本試験は、日本人 2 型糖尿病患者を対象として、セマグルチド（0.5 及び 1.0 mg）の週 1 回投与（単独療法）及びシタグリプチン（100 mg）の 1 日 1 回投与（単独療法）の安全性及び有効性を比較検討する、無作為割り付け、非盲検、並行群、実薬対照、1 ヵ国、多施設共同試験であった。被験者は、スクリーニング時	

に食事・運動療法に加えて経口糖尿病薬単剤による治療（以下、経口糖尿病薬による単独療法）又は食事・運動療法のみを受けている日本人 2 型糖尿病患者（年齢 20 歳以上、性別不問）であった。

本試験は、スクリーニング来院（来院 1）、8 週間の wash-out 期間（スクリーニング時に経口糖尿病薬による単独療法を受けている被験者に適用）又は 2 週間のスクリーニング期間（スクリーニング時に食事・運動療法のみを受けている被験者に適用）、30 週間の投与期間及び 5 週間の事後調査期間から構成された。

スクリーニング来院後、適格例は無作為割り付けのために来院し、セマグルチド（0.5 又は 1.0 mg）週 1 回もしくはシタグリプチン（100 mg）1 日 1 回の 30 週間投与のいずれかに、1:1:1 の割合で無作為に割り付けられた。セマグルチドの投与を受ける被験者では、投与期間は用量漸増期間及び用量維持期間に分けられた。

無作為割り付け後、被験者は事前に規定された用量漸増法に従った。セマグルチド 0.5 mg 群では、0.25 mg を 4 回（4 週間）投与した後に 0.5 mg の維持用量へ増量し、セマグルチド 1.0 mg 群では、0.25 mg の 4 回（4 週間）投与とそれに続く 0.5 mg の 4 回（4 週間）投与の後に 1.0 mg の維持用量へ増量した。維持用量に達した後、残りの試験期間中において用量変更を行わないこととした。シタグリプチンは錠剤で提供され、食事時間に関係なく 1 日のいずれかの時点で 1 日 1 回経口投与した。治験薬に起因すると疑われる安全性の理由により必要に応じて投与を中止できることとし、その場合は、急性膵炎の疑いが否定された場合を除き、投与を再開しないこととした。治験薬の投与は投与後 30 週の来院 12 まで継続した。各被験者の最終予定来院は、実際の最終投与来院日から 5 週間後の事後調査来院であった。各被験者の試験参加期間は、前治療として経口糖尿病薬による単独療法を受けている被験者で 43 週間、前治療として食事・運動療法のみを受けている被験者で 37 週間であった。

ノボ ノルディスク社は、盲検化された安全性データの継続的な安全性審査を行う、社内のセマグルチド安全性委員会を設置した。このセマグルチド安全性委員会は、本試験の全体的な安全性審査の責任を負った。進行中のセマグルチドの心血管系アウトカム試験（NN9535-3744）から得られる非盲検化された安全性データを独立して確認し、評価するために設立された外部データモニタリング委員会（DMC）が、本試験で認められたすべての主要な心血管イベント（MACE）を評価した。また、特定の事象の継続的な判定、標準化及び評価を行うため、独立した外部のイベント判定委員会が設立された。当該判定は、独立した外部の医学専門家が統一基準に基づいて一貫性を持って事象を確認することを目的とした。

計画及び解析された被験者数：

無作為割り付けする予定症例数を 306 例として、計 360 例のスクリーニングが計画された。実際には 340 例がスクリーニングを受け、うち 308 例が無作為割り付けされた。

	Sema 0.5 mg N (%)	Sema 1.0 mg N (%)	Sitagliptin N (%)	Total N (%)
Screened				340
Screening failures				32 (9.4)
Randomised	103	102	103	308
Exposed/FAS/SAS	103 (100)	102 (100)	103 (100)	308 (100)
Treatment completers[1]	100 (97.1)	87 (85.3)	100 (97.1)	287 (93.2)
Trial completers[2]	103 (100)	99 (97.1)	101 (98.1)	303 (98.4)
Premature treatment discontinuers	3 (2.9)	15 (14.7)	3 (2.9)	21 (6.8)
Other		3 (2.9)	1 (1.0)	4 (1.3)
Pregnancy	0	0	0	0
Protocol violation		1 (1.0)		1 (0.3)
Due to adverse event	3 (2.9)	11 (10.8)	2 (1.9)	16 (5.2)

Sema: semaglutide, N: Number of subjects, %: Percentages of randomised subjects, FAS: Full Analysis Set, SAS: Safety Analysis Set.
[1] Subjects who completed treatment according to end-of-trial eCRF form.
[2] Subjects with a follow-up visit.

診断及び主要な組入れ基準：

主な選択基準：

性別不問、年齢 20 歳以上（同意取得時点）、スクリーニング時に経口糖尿病薬による単独療法を受けている被験者では HbA1c 6.5%以上、9.5%以下（48 mmol/mol 以上、80 mmol/mol 以下）、食事・運動療法のみを

受けている被験者では HbA1c 7.0%以上、10.5%以下（53 mmol/mol 以上、91 mmol/mol 以下）であり、以下のいずれかに該当する日本人 2 型糖尿病患者。 a）スクリーニングの 30 日以上前から、食事・運動療法に加えて経口糖尿病薬単剤（国内で承認されている最高用量の半分以下）による安定した治療を受けている b）スクリーニングの 30 日以上前から、安定した食事・運動療法を受けている **主な除外基準**： 妊婦、授乳婦、妊娠を希望している女性被験者、又は妊娠可能で 5 週間の事後調査期間を含めた試験期間中に適切な避妊法を受け入れられない女性被験者。スクリーニング前 90 日以内に、週 1 回投与のグルカゴン様ペプチド-1（GLP-1）受容体作動薬の投与を受けた被験者。スクリーニング前 60 日以内に、何らかの血糖降下薬（ただし、経口糖尿病薬による単独療法を受けている被験者における前治療の経口糖尿病薬を除く）の投与を受けた被験者〔ただし、併発疾患のための短期間のインスリン投与（合計で 7 日以内）については可とする〕。被験者の安全を脅かしたり、治験実施計画書の遵守を困難にしたりする可能性があると判断された疾患を有する被験者（治験責任医師の判断による）。慢性又は特発性急性膵炎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濃度が 50 ng/L（pg/mL）以上である被験者。本人又は家族が甲状腺髄様癌又は多発性内分泌腫瘍症候群 2 型の既往歴を有する被験者。腎機能障害〔4 変数 Modification of Diet in Renal Disease 式による推算糸球体濾過量（eGFR）が 60 ml/min/1.73 m^2 未満〕を有する被験者。無作為割り付け前 90 日以内に急性冠動脈疾患又は脳血管疾患を発現した被験者。心不全〔ニューヨーク心臓協会（NYHA）分類クラス IV〕を有する被験者。 **主な投与中止基準**： 治験薬との関連が疑われる安全性の懸念がある場合、又は治験薬投与に受け入れがたい非忍容性が認められる場合。 **中止・脱落基準**： 被験者は、同意を撤回することにより、いつでも自由意思により試験を中止することができた。
被験薬、用量及び投与方法、ロット番号： セマグルチド注射液（1.34 mg/mL）〔PDS290 ペン型注入器（1.5 mL）と一体化したプレフィルド製剤〕を、食事時間に関係なく 1 日のいずれかの時点において 0.5 mg 又は 1.0 mg を大腿部、腹部又は上腕部のいずれかに週 1 回皮下投与した。セマグルチドのロット番号（有効期限）：DV40009（2016 年 4 月 10 日）
投与期間： 30 週間
対照薬、用量及び投与方法、ロット番号： シタグリプチン（100 mg、錠剤で提供）を 1 日 1 回経口投与した。シタグリプチンのロット番号（有効期限）：A002009（2016 年 4 月 30 日） セマグルチドプラセボ注射液（テストペンのみに使用）は、PDS290 ペン型注入器（1.5 mL）に充填された状態で提供され、セマグルチド 0.5 mg 又は 1.0 mg に相当する液量を皮下投与した。プラセボの組成は、有効成分が含まれていないことを除き、セマグルチド治験薬の組成と同じであった。プラセボのロット番号（有効期限）：DV40008（2016 年 2 月 13 日）
評価基準：**有効性** HbA1c、体重、空腹時血糖値、収縮期及び拡張期血圧
評価基準：**安全性** 治験薬投与下で発現した有害事象〔（Treatment Emergent Adverse Event、以下、有害事象とする）：これには、独立した外部のイベント判定委員会により判定される事前に規定した特に注目すべき医学的事象が含まれる〕、低血糖、脈拍数及び安全性に関する臨床検査項目
統計手法： **被験者数の設定** 本試験の被験者数は、「経口血糖降下薬の臨床評価方法に関するガイドライン」の要求事項に基づいて設定

した。本ガイドラインでは、300 例以上の日本人被験者が被験薬による治療を 6 ヵ月以上受けることを求めている。本試験では、合計 306 例の被験者を、セマグルチド 0.5 mg、セマグルチド 1.0 mg 又はシタグリプチン 100 mg 投与のいずれかに 1:1:1 の割合で無作為割り付けすることとした。この被験者数により、無作為割り付けされた治療の中止率を 20%と仮定し、それぞれの投与群で 81 例の被験者が 6 ヵ月の治療を完了すると予想された。別途実施する試験（NN9535-3623 及び NN9535-4091）を加え、合計 300 例の日本人被験者がセマグルチドの単独療法で 6 ヵ月の投与を完了すると予想された。15%のスクリーニング不適格例を仮定し、合計 360 例の被験者を本試験に組み入れることとした。

解析対象集団の定義

最大の解析対象集団〔full analysis set（FAS）〕及び安全性解析対象集団〔safety analysis set（SAS）〕の両集団には、無作為割り付けされてセマグルチド又はシタグリプチンの投与を少なくとも 1 回受けたすべての被験者が含まれた。FAS の被験者は「無作為割り付けされたとおり（as randomised）」の評価、また SAS の被験者は「治療されたとおりの（as treated）」の評価に寄与した。

観察期間

In-trial 期間：無作為割り付け後に被験者が試験参加者とみなされ、データが系統的に収集される観察期間。この期間は有効性及び安全性の補足的解析に用いられた。

On-treatment 期間：被験者が投与を受け、治験薬に曝露されていると考えられる観察期間。この期間は、判定されたイベント、心電図及び低血糖を含む有害事象等、安全性エンドポイントの評価における主要観察期間であった。

レスキュー治療を伴わない on-treatment 期間：糖尿病治療薬によるレスキュー後に収集された情報をこの観察期間から除外した。具体的には、治験薬の初回投与日以降に記録され、on-treatment 期間の終了日とレスキュー治療の開始日のうち早い日付までに記録された観測値を含めた。この期間は、有効性エンドポイントの評価における主要観察期間であった。

統計解析

プライマリーエンドポイント：30 週間の治験薬投与下で発現した有害事象の発現件数

治験薬投与下で発現した有害事象（TEAE）は、他のすべての安全性エンドポイントと同様、SAS を用いて解析した。TEAE は、発現日（又は重症度の悪化）が on treatment 観察期間内である有害事象と定義した。TEAE については記述的に要約し、少なくとも 1 件発現した被験者数（N）、少なくとも 1 件発現した被験者の割合（%）、発現件数（E）及び 100 人・年あたりの発現件数（R）を示した。

有効性に関する主な補足的セカンダリーエンドポイント：ベースラインから投与後 30 週までの以下の項目の変化量

- HbA1c
- 体重
- 空腹時血糖値
- 収縮期及び拡張期血圧

解析は FAS に基づいて行った。有効性に関するエンドポイントは標準的な繰り返し測定に対する混合モデル（MMRM）を用いて解析した。無作為割り付けされた治療の中止又はレスキュー治療の開始前までの予定された来院時に得られたすべてのベースライン後の測定値を目的変数として含めた。モデルには、治療及びスクリーニング時の前治療（食事・運動療法又は経口糖尿病薬による単独療法）を固定効果、ベースライン値を共変量として含め、すべてについて来院内で入れ子にした。欠測データに関しては missing at random（MAR）に従うと仮定した。投与後 30 週におけるセマグルチドの各用量群及びシタグリプチンの群間差の推定値及び対応する両側 p 値及び 95%信頼区間を提示した。

感度分析

主要解析の安定性を検討するため、投与後 30 週までの HbA1c 及び体重の変化量について、4 つの異なる補足的な感度分析を、FAS を用いて実施した。これらの 4 つの事前規定した感度分析では、欠測データの影響による結果への感度を検討した。完了例に対して MMRM 法で解析した。糖尿病患者を対象とした過去の臨床試験と比較評価するために last observation carried forward（LOCF）法に基づいて解析を行った。Pattern

mixture モデル（PMM）に基づく解析では、セマグルチド両用量群の欠測データの推移がシタグリプチン群の推移に従うと仮定して欠測データを補完することにより、セマグルチドの効果が徐々に取り除かれた。この解析では、セマグルチドに好ましくない方向への MAR の仮定からの乖離を検討した。最後に、被験者が治療を受けていたか否か、又はレスキュー治療を受けていたか否かに関わらず、無作為割り付け後に収集されたすべてのデータを用いた in-trial 期間の MMRM 解析を行った。

投与後 30 週までに以下の目標を達成した被験者の割合（はい／いいえ）：

- HbA1c 7.0%（53 mmol/mol）未満：米国糖尿病学会（ADA）目標値
- HbA1c 6.5%（48 mmol/mol）以下：米国臨床内分泌学会（AACE）目標値

これらのエンドポイントのそれぞれについて、同様のロジスティック回帰モデルで解析し、オッズ比及び95%信頼区間を用いて提示した。モデルには、治療及びスクリーニング時の前治療を固定効果、ベースラインの HbA1c を共変量として含めた。投与後 30 週における欠測データは HbA1c の解析に用いた MMRM に基づいて補完した。

安全性に関する主な補足的セカンダリーエンドポイント

- 低血糖は、ノボ ノルディスク社及びADAで定める低血糖分類に基づいて分類した。治験薬投与下で発現した低血糖（Treatment Emergent hypoglycaemic episode、以下、低血糖とする）は記述的に要約し、100人・年あたりの発現件数として示した。
- 事前に規定した特に注目すべき有害事象については、MedDRA検索（MedDRA Ver.18.0）に基づき評価した。これはノボ ノルディスク社 Global Safetyにより定義され、事前に規定した基本語で構成された。
- 脈拍は標準的なMMRMを用いて解析した。
- すべての臨床検査項目を、SASを用いて記述統計量により要約して評価した。

重要なこととして、すべてのエンドポイントに関するデータの提示にあたり、「有意」という表現は統計解析により裏付けられる場合にのみ用いる。

被験者背景：

	Sema 0.5 mg N (%)	Sema 1.0 mg N (%)	Sitagliptin N (%)	Total N (%)
Number of subjects	103	102	103	308
Sex				
Female	24 (23.3)	27 (26.5)	22 (21.4)	73 (23.7)
Male	79 (76.7)	75 (73.5)	81 (78.6)	235 (76.3)
Age (years)				
Mean (SD)	58.8 (10.4)	58.1 (11.6)	57.9 (10.1)	58.3 (10.7)
Body weight (kg)				
Mean (SD)	67.81 (11.74)	70.80 (16.38)	69.41 (12.85)	69.34 (13.80)
Body mass index (kg/m2)				
Mean (SD)	25.11 (3.80)	26.05 (5.23)	25.14 (3.56)	25.43 (4.27)
Race				
Japanese	103 (100.0)	102 (100.0)	103 (100.0)	308 (100.0)
Smoker status				
Current smoker	28 (27.2)	21 (20.6)	29 (28.2)	78 (25.3)
Never smoked	38 (36.9)	43 (42.2)	37 (35.9)	118 (38.3
Previous smoker	37 (35.9)	38 (37.3)	37 (35.9)	112 (36.4)
Renal function				
Normal	65 (63.1)	71 (69.6)	66 (64.1)	202 (65.6)
Mild Renal Impairment	38 (36.9)	31 (30.4)	37 (35.9)	106 (34.4)
Moderate Renal Impairment	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe Renal Impairment	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
End stage Renal Impairment	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
HbA1c (%)				
Mean (SD)	8.23 (1.02)	8.01 (0.85)	8.20 (0.89)	8.15 (0.93)
Fasting plasma glucose (mmol/L)				
N	102	102	102	306
Mean (SD)	9.22 (2.08)	9.15 (1.81)	9.52 (1.98)	9.30 (1.96)
Duration of Diabetes (years)				
Mean (SD)	7.99 (5.22)	7.83 (6.87)	8.10 (6.67)	7.97 (6.28)
MDRD eGFR (mL/min/1.73 m2)				
N	103	102	103	308

Mean (SD)	96.73 (19.67)	103.2 (21.97)	97.96 (18.62)	99.28 (20.2

N: Number of subjects, %: Percentage of subjects, BMI: Body mass index, MDRD: Modification of diet in renal disease, eGFR: estimated glomerular filtration rate, SD: standard deviation

有効性の結果：

有効性に関する主な補足的セカンダリーエンドポイント：HbA1c の変化量

- ベースラインから投与後30週までのHbA1cについて、シタグリプチン群（-0.74%）と比較して、セマグルチド0.5 mg群（-1.87%）及びセマグルチド1.0 mg群（-2.18%）で有意に大きな低下がみられた。シタグリプチン群との群差の推定値は、セマグルチド0.5 mg群で-1.13%（95%信頼区間：-1.32; -0.94）、セマグルチド1.0 mg群で-1.44%（95%信頼区間：-1.63; -1.24）であった。
- 4つの感度分析すべてで有意差が認められ、MMRM法を用いた主要解析の安定性が裏付けられた。

有効性に関する主な補足的セカンダリーエンドポイント：体重の変化量

- ベースラインから投与後30週までの体重について、シタグリプチン群（0.02 kg、-0.01%）と比較して、セマグルチド0.5 mg群（-2.21 kg、-3.30%）及びセマグルチド1.0 mg群（-3.87 kg、-5.67%）で有意に大きな減少がみられた。シタグリプチン群との群差の推定値は、セマグルチド0.5 mg群で-2.22 kg（95%信頼区間：-3.02; -1.42）、セマグルチド1.0 mg群で-3.88 kg（95%信頼区間：-4.70; -3.07）であった。体重減少率（%）では、シタグリプチン群との群差の推定値は、セマグルチド0.5 mg群で-3.29%（95%信頼区間：-4.39 ; -2.18）及びセマグルチド1.0 mg群で-5.66%（95%信頼区間：-6.79; -4.53）であった。
- 4つの感度分析すべてで有意差が認められ、MMRM法を用いた主要解析の安定性が裏付けられた。

有効性に関する他の補足的セカンダリーエンドポイント

HbA1c の目標値

- HbA1cの目標値を達成した被験者の割合は、シタグリプチン群と比較してセマグルチド0.5 mg群及びセマグルチド1.0 mg群で高く、以下の2つの目標値を達成した被験者についてのオッズは、シタグリプチン群と比較してセマグルチド両用量群で有意に高かった。
  - HbA1c 6.5%以下（AACEの目標値）を達成した被験者の割合は、セマグルチド0.5 mg群で71%、セマグルチド1.0 mg群で87%及びシタグリプチン群で16%であり、オッズ比の推定値はセマグルチド0.5 mg群：18.70（95%信頼区間：8.73; 40.04）、セマグルチド1.0 mg群：45.19（95%信頼区間：19.36; 105.47）であった。
  - HbA1c 7.0%未満（ADAの目標値）を達成した被験者の割合は、セマグルチド0.5 mg群で84%、セマグルチド1.0 mg群で95%及びシタグリプチン群で35%であり、オッズ比の推定値はセマグルチド0.5 mg群：16.53（95%信頼区間：7.39; 36.99）、セマグルチド1.0 mg群：43.66（95%信頼区間：15.67; 121.62）であった。

糖代謝

- 空腹時血糖値は、シタグリプチン群と比較してセマグルチド両用量群で有意な低下を示した。シタグリプチン群との群差の推定値は、セマグルチド0.5 mg群：-1.47 mmol/L（95%信頼区間：-1.78; -1.16）、セマグルチド1.0 mg群：-1.99 mmol/L（95%信頼区間：-2.30; -1.67）であった。mg/dLで示した場合の群差の推定値は、セマグルチド0.5 mg群： -26.54 mg/dL（95%信頼区間：-32.13; -20.96）、セマグルチド1.0 mg群：-35.83 mg/dL（95%信頼区間：-41.53; -30.13）であった。

血圧

- 投与後30週までの拡張期血圧は、すべての投与群で低下を示したが、シタグリプチン群と比較してセマグルチド群で有意な変化はみられなかった。投与後30週までの収縮期血圧は、シタグリプチン群と比較してセマグルチド1.0 mg群において有意に低下した。群差の推定値は-6.01（95%信頼区間：-9.16; -2.85）であった。一方、セマグルチド0.5 mg群とシタグリプチン群の間に有意差はみられなかった。

安全性の結果：

30 週間の投与期間において、セマグルチド及びシタグリプチンは全般的に安全で忍容性も良好であり、セマグルチドの安全性及び忍容性は概ね他の GLP-1 受容体作動薬と一致していた。

プライマリーエンドポイント：有害事象の発現件数

- 死亡は報告されなかった。

- On-treatment期間において、何らかの有害事象を発現した被験者の割合及び有害事象の単位時間あたりの発現件数は、シタグリプチン群と比較してセマグルチド両用量群で高かった（セマグルチド0.5 mg群：74.8%、331.8件／100人･年、セマグルチド1.0 mg群：71.6%、312.6件／100人･年、シタグリプチン群：66.0%、267.4件／100人･年）。この差は主に、シタグリプチン群と比較してセマグルチド両用量群で胃腸障害の有害事象が多く報告されたことに起因していた。 他の器官別大分類では、臨床検査、代謝および栄養障害に属する有害事象も、シタグリプチン群と比較してセマグルチド両用量群で多く報告された。
  - いずれの投与群においても、有害事象の大部分は軽度又は中等度であった（セマグルチド0.5 mg群：228件中226件、セマグルチド1.0 mg群：197件中196件、シタグリプチン群：186件中181件）。加えて、被験者が発現した有害事象の大部分は、試験終了時点の転帰が「回復」又は「軽快」であった（セマグルチド0.5 mg群：228件中198件、セマグルチド1.0 mg群：197件中173件、シタグリプチン群：186件中135件）。
  - 最も高頻度で報告された有害事象は、セマグルチド両用量群では器官別大分類の胃腸障害に分類される有害事象であったのに対し、シタグリプチン群では器官別大分類の感染症および寄生虫症に分類される有害事象であった。
- 重篤な有害事象の発現件数はいずれの投与群においても少なく、セマグルチド0.5 mg群、セマグルチド1.0 mg群及びシタグリプチン群でそれぞれ7件、2件及び3件であり、3群間で同程度であった。報告された重篤な有害事象について、投与群及び基本語を通じて一定の傾向は認められなかった。
- 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0.5 mg群（2.9%）及びシタグリプチン群（1.9%）で低かったが、セマグルチド1.0 mg群（10.8%）では高かった。セマグルチド1.0 mg群で投与の中止に至った重篤な有害事象が多く発現したことは、主に、胃腸障害の有害事象により投与を中止した被験者が多かったことに起因していた（15件中9件）。

<u>低血糖</u>

- 重大な低血糖は報告されなかった。重大な又は血糖値確定症候性低血糖は、セマグルチド1.0 mg群で1例1件が報告された。

<u>注目すべき安全性領域</u>

- 胃腸障害の有害事象
  - 胃腸障害の有害事象は、本試験において最も高頻度で報告された有害事象であった。最も高頻度（いずれかの投与群において被験者の5%以上）で報告された有害事象は、多い順に便秘、悪心、下痢及び腹部不快感であり、これらすべての事象において単位時間あたりの発現件数及び発現した被験者の割合は、シタグリプチン群と比較してセマグルチド両用量群で多かった。上位3つの基本語を発現した被験者の割合は、便秘ではセマグルチド0.5 mg群、セマグルチド1.0 mg群及びシタグリプチン群でそれぞれ14.6%、11.8%及び3.9%、悪心ではセマグルチド0.5 mg群、セマグルチド1.0 mg群及びシタグリプチン群でそれぞれ10.7%、12.7%及び0%、下痢ではセマグルチド0.5 mg群、セマグルチド1.0 mg群及びシタグリプチン群でそれぞれ6.8%、8.8%及び1.9%であった。セマグルチドの用量増加に伴って、胃腸障害の有害事象の単位時間あたりの発現件数は増加した（セマグルチド0.5 mg群：91.7件/100人・年、セマグルチド1.0 mg群：130.1件/100人・年）。
  - 大部分の胃腸障害の有害事象は投与開始後16週間以内に発現し、発現期間の中央値は投与群によって異なった。
  - 大部分の有害事象が軽度又は中等度であり、重篤な胃腸障害の有害事象は報告されなかった。
- 心血管系事象
  - イベント判定委員会により、2件の心血管系事象が確認された。無症候性心筋梗塞及び経皮的血行再建が、いずれもセマグルチド0.5 mg群で認められた。無症候性心筋梗塞は、MACEと判定された。MedDRA検索により、計17例で19件の心血管系事象（セマグルチド0.5 mg群、セマグルチド1.0 mg群及びシタグリプチン群で、それぞれ4例6件、7例7件及び6例6件）が特定された。心血管系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、3つの投与群間で同様であった。セマグルチド0.5 mg群で3件の重篤な有害事象が認められ、このうち1件（冠動脈ステント挿入）

は、イベント判定委員会で確認された事象であった。これらの重篤な有害事象で治験薬の投与の中止に至ったものはなく、事象の種類及び発現頻度に明らかな差はみられなかった。
  - ベースラインから投与終了時にかけて、脈拍数はいずれの投与群においても増加した（セマグルチド0.5 mg群、セマグルチド1.0 mg群及びシタグリプチン群でそれぞれ4.54拍／分、6.08拍／分及び1.14拍／分）。ベースラインから投与終了時にかけて脈拍数は、シタグリプチン群と比較してセマグルチド両用量群で有意に増加した。
  - 全般的に、心電図異常がみられた被験者の割合は、心電図異常のカテゴリーの大部分において投与群間で同様であった。測定結果の大部分（92.8～97.6%）は、ベースライン時及び投与後30週において「正常」であり、投与群間で明らかな差はみられなかった。シタグリプチン群の1例で、最終投与来院時（投与後30週）に「正常」から「異常、臨床的に問題あり」への変化が認められた。
- 膵炎
  - イベント判定委員会により膵炎は確認されず、MedDRA検索によって特定された事象もなかった。
  - ベースラインから投与終了時（投与後30週）までに、リパーゼ及びアミラーゼの平均値は、すべての投与群で増加し（セマグルチド0.5 mg群、セマグルチド1.0 mg群及びシタグリプチン群でそれぞれリパーゼ：27%、34%及び5%、アミラーゼ：16%、17%及び5%の増加）、シタグリプチン群と比較してセマグルチド両用量群で有意な増加を示した。被験者の大部分において、リパーゼ及びアミラーゼは試験期間を通じて基準範囲上限の2倍未満であり、リパーゼ又はアミラーゼの基準範囲上限のそれぞれ5倍超及び2倍超を示した被験者のほとんどで、外れ値を示したのは1回のみであった。リパーゼが基準範囲上限の5倍超を示した被験者8例中4例、及びアミラーゼが基準範囲上限の2倍超を示した被験者7例中3例で、胃腸障害の有害事象、肝胆道系事象及び膵炎に関連した有害事象の併発が報告された。
- 肝胆道系障害
  - MedDRA検索により、4例4件の胆嚢に関連する有害事象が特定された。このうち3件はセマグルチド1.0 mg群で報告され、器官別大分類の肝胆道系障害に属する胆嚢炎、胆石症及び高ビリルビン血症であった。1件はセマグルチド0.5 mg群で報告され、器官別大分類の臨床検査に属する血中ビリルビン増加であった。4件中1件（胆嚢炎）が重篤な有害事象で、当該事象を発現した被験者については、胆嚢切除後に回復が確認された。非重篤な3件及び重篤な1件のいずれの事象も投与の中止には至らなかった。いずれの事象も、おおよそ投与後12～27週の間に発現した。
  - 全般的に、肝機能検査値に変動する傾向がみられたが、平均値の増加は認められなかった。総ビリルビン、アラニンアミノトランスフェラーゼ（ALT）、アスパラギン酸アミノトランスフェラーゼ（AST）及びアルカリホスファターゼ（ALP）の外れ値は認められなかった。これら4つのパラメータについて、ベースラインからの平均変化量はセマグルチド両用量群とシタグリプチン群で同程度であり、臨床的に問題となる変化は認められなかった。Hy's lawの定義に合致する被験者は認められなかった。
- 新生物
  - 全般的に、イベント判定委員会に新生物と判定された事象の件数は少なく、3つの投与群間で同程度であった（セマグルチド0.5 mg群、セマグルチド1.0 mg群及びシタグリプチン群でそれぞれ2例2件、2例3件及び4例5件）。イベント判定委員会に新生物と判定された事象10件のうち、2件が悪性新生物（第4期の膵癌1件及び膀胱癌1件）であった。イベント判定委員会により確認された新生物は主に被験者1例に1件ずつの発現であり、その種類（原発組織又は臓器）及び分類（良性及び悪性）の分布は3つの投与群間で概して同様であった。MedDRA検索では、新生物に関連した有害事象の発現件数は、セマグルチド1.0 mg群及びシタグリプチン群と比較して、セマグルチド0.5 mg群でわずかに多かった（セマグルチド0.5 mg群、セマグルチド1.0 mg群及びシタグリプチン群でそれぞれ7例11件、4例4件及び5例8件）。
  - 本試験では、MedDRA検索によりシタグリプチン群の1件が甲状腺新生物と特定されたが、イベント判定委員会で甲状腺新生物と確認されたものはなかった。
- 甲状腺障害

- イベント判定委員会により甲状腺切除を必要とする甲状腺疾患又は甲状腺新生物は確認されなかった。
- カルシトニンの平均及び個々のカルシトニン値について、投与期間を通じて投与群内又は投与群間で臨床的に問題となる変化は認められなかった。

- 腎障害
  - 広域のMedDRA標準検索式（acute renal failure；急性腎不全）で特定された事象は少なかった（セマグルチド0.5 mg群：1件、シタグリプチン群：1件）。これらの事象はいずれも非重篤であり、投与の中止に至らなかった。
  - すべての腎機能に関連する臨床検査項目及び尿検査項目について、投与群内及び投与群間で臨床的に問題となる経時的変化は認められなかった。
- 免疫原性に関連する有害事象及び注射部位反応
  - 計12例13件のアレルギー反応が報告された。そのうち11例12件が皮膚障害に関連したものであった（セマグルチド0.5 mg群：2例2件、セマグルチド1.0 mg群：3例3件、シタグリプチン群：6例7件）。セマグルチド0.5 mg群で、1例1件の眼障害に関連する事象が報告された。いずれの事象も非重篤で、軽度又は中等度であり、治験薬との因果関係は「なし」と判定された。
  - セマグルチド1.0 mg群で1例が抗セマグルチド抗体陽性（3.47% B/T）となったが、内因性GLP-1に対する交叉反応は示さなかった。当該被験者は、事後調査来院時に抗セマグルチド抗体陰性となったため、*in vitro*での中和作用の検査は行わなかった。
  - 2例2件の免疫複合体疾患が報告された（セマグルチド0.5 mg群：1件、シタグリプチン群：1件）。シタグリプチン群で報告された尿中蛋白陽性は、治験薬との因果関係が「あり」と判定された。いずれの事象も治験薬の投与の中止に至らなかった。
  - セマグルチド0.5 mg群で1例1件の注射部位反応が報告された。報告された事象は注射部位内出血であり、非重篤かつ軽度、ま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。
- 投薬過誤、過量投与及び治験薬による病原体感染の疑いに該当する事象は報告されなかった。稀な事象において、臨床的に問題となる所見は報告されなかった。

<u>その他の臨床検査項目、身体所見及び妊娠</u>

- 注目すべき安全性領域に記載されていない血液生化学的検査又は血液学的検査に関するパラメータについて、臨床的に問題となる変化は認められなかった。
- 身体所見について、臨床的に問題となる投与群間の違いは認められなかった。
- 妊娠はいずれの投与群でも報告されなかった。

全体の結論：

- 日本人2型糖尿病患者において、セマグルチド及びシタグリプチンは安全で忍容性が良好であった。
  - シタグリプチン群と比較して、セマグルチド両用量群で有害事象の発現頻度が高く、これは主に胃腸障害の有害事象に起因するものであった。
  - 重篤な有害事象を発現した被験者の割合は低く、投与群間で明らかな差はみられなかった。発現した事象は複数の器官別大分類にまたがっており、特定の事象への偏りもみられなかった。
  - 有害事象により投与を中止した被験者は、セマグルチド0.5 mg群及びシタグリプチン群と比較してセマグルチド1.0 mg群で多く、これは主に胃腸障害の有害事象に起因するものであった。
- シタグリプチン群と比較してセマグルチド両用量群の血糖降下作用が有意に大きかった。
- シタグリプチン群と比較してセマグルチド両用量群の体重減少効果が有意に大きかった。

本試験は、ヘルシンキ宣言の精神及びICH-GCPを遵守して実施された。

2.7.6.24.2. 有害事象

表 2.7.6.24.2-1 有害事象（器官別大分類、高位グループ語及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	103				102				103				308			
Exposure time (year)	68.7				63.0				69.6				201.3			
Events	77	(74.8)	228	331.8	73	(71.6)	197	312.6	68	(66.0)	186	267.4	218	(70.8)	611	303.6
感染症および寄生虫症	30	(29.1)	41	59.7	32	(31.4)	45	71.4	41	(39.8)	67	96.3	103	(33.4)	153	76.0
詳細不明な感染体による感染症	24	(23.3)	33	48.0	27	(26.5)	38	60.3	39	(37.9)	60	86.3	90	(29.2)	131	65.1
鼻咽頭炎	17	(16.5)	21	30.6	18	(17.6)	22	34.9	30	(29.1)	42	60.4	65	(21.1)	85	42.2
咽頭炎	2	(1.9)	2	2.9	3	(2.9)	3	4.8	3	(2.9)	3	4.3	8	(2.6)	8	4.0
胃腸炎	1	(1.0)	1	1.5	2	(2.0)	2	3.2	2	(1.9)	2	2.9	5	(1.6)	5	2.5
歯周炎	1	(1.0)	1	1.5	3	(2.9)	3	4.8	0				4	(1.3)	4	2.0
上気道感染	0				2	(2.0)	2	3.2	2	(1.9)	2	2.9	4	(1.3)	4	2.0
外耳炎	0				1	(1.0)	1	1.6	2	(1.9)	2	2.9	3	(1.0)	3	1.5
歯肉炎	2	(1.9)	2	2.9	0				1	(1.0)	1	1.4	3	(1.0)	3	1.5
気管支炎	0				0				2	(1.9)	2	2.9	2	(0.6)	2	1.0
結膜炎	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
鼻炎	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
扁桃炎	1	(1.0)	1	1.5	0				1	(1.0)	3	4.3	2	(0.6)	4	2.0
膀胱炎	0				0				2	(1.9)	2	2.9	2	(0.6)	2	1.0
急性中耳炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
胸壁膿瘍	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
耳下腺炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
爪感染	0				1	(1.0)	2	3.2	0				1	(0.3)	2	1.0
尿道炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
肺炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
ウイルス感染症	5	(4.9)	6	8.7	6	(5.9)	6	9.5	3	(2.9)	3	4.3	14	(4.5)	15	7.5
インフルエンザ	2	(1.9)	2	2.9	1	(1.0)	1	1.6	2	(1.9)	2	2.9	5	(1.6)	5	2.5
口腔ヘルペス	1	(1.0)	1	1.5	2	(2.0)	2	3.2	0				3	(1.0)	3	1.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
帯状疱疹	1	(1.0)	1	1.5	2	(2.0)	2	3.2	0				3	(1.0)	3	1.5
ウイルス性胃腸炎	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
陰部ヘルペス	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
眼部単純ヘルペス	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
真菌感染症	1	(1.0)	1	1.5	0				3	(2.9)	4	5.8	4	(1.3)	5	2.5
足部白癬	1	(1.0)	1	1.5	0				3	(2.9)	3	4.3	4	(1.3)	4	2.0
爪真菌症	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
細菌感染症	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
ヘリコバクター感染	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
細菌性腸炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
胃腸障害	39	(37.9)	63	91.7	42	(41.2)	82	130.1	17	(16.5)	28	40.3	98	(31.8)	173	85.9
消化管徴候および症状	24	(23.3)	31	45.1	28	(27.5)	46	73.0	3	(2.9)	3	4.3	55	(17.9)	80	39.7
悪心	11	(10.7)	12	17.5	13	(12.7)	22	34.9	0				24	(7.8)	34	16.9
腹部不快感	4	(3.9)	4	5.8	7	(6.9)	8	12.7	0				11	(3.6)	12	6.0
上腹部痛	4	(3.9)	4	5.8	3	(2.9)	4	6.3	2	(1.9)	2	2.9	9	(2.9)	10	5.0
嘔吐	4	(3.9)	5	7.3	2	(2.0)	3	4.8	1	(1.0)	1	1.4	7	(2.3)	9	4.5
消化不良	2	(1.9)	3	4.4	3	(2.9)	4	6.3	0				5	(1.6)	7	3.5
おくび	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
腹痛	0				2	(2.0)	2	3.2	0				2	(0.6)	2	1.0
腹部膨満	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
心窩部不快感	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
軟便	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
消化管運動および排泄障害	21	(20.4)	26	37.8	22	(21.6)	28	44.4	8	(7.8)	9	12.9	51	(16.6)	63	31.3
便秘	15	(14.6)	16	23.3	12	(11.8)	12	19.0	4	(3.9)	4	5.8	31	(10.1)	32	15.9
下痢	7	(6.8)	9	13.1	9	(8.8)	14	22.2	2	(1.9)	3	4.3	18	(5.8)	26	12.9
胃食道逆流性疾患	1	(1.0)	1	1.5	2	(2.0)	2	3.2	2	(1.9)	2	2.9	5	(1.6)	5	2.5
消化管炎症性疾患	1	(1.0)	1	1.5	3	(2.9)	3	4.8	5	(4.9)	5	7.2	9	(2.9)	9	4.5
慢性胃炎	1	(1.0)	1	1.5	1	(1.0)	1	1.6	4	(3.9)	4	5.8	6	(1.9)	6	3.0

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Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胃炎	0				2	(2.0)	2	3.2	1	(1.0)	1	1.4	3	(1.0)	3	1.5
歯牙および歯肉の状態	1	(1.0)	1	1.5	1	(1.0)	1	1.6	4	(3.9)	4	5.8	6	(1.9)	6	3.0
齲歯	1	(1.0)	1	1.5	0				4	(3.9)	4	5.8	5	(1.6)	5	2.5
歯周病	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
口腔内軟部組織疾患	2	(1.9)	3	4.4	0				2	(1.9)	2	2.9	4	(1.3)	5	2.5
口内炎	2	(1.9)	3	4.4	0				1	(1.0)	1	1.4	3	(1.0)	4	2.0
口唇炎	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
消化管血行障害	1	(1.0)	1	1.5	1	(1.0)	1	1.6	1	(1.0)	1	1.4	3	(1.0)	3	1.5
痔核	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
痔出血	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
良性消化管新生物	0				1	(1.0)	1	1.6	2	(1.9)	2	2.9	3	(1.0)	3	1.5
胃ポリープ	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
大腸ポリープ	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
直腸ポリープ	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
消化管潰瘍および穿孔	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
びらん性胃炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
十二指腸潰瘍	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
腹部ヘルニアおよびその他の腹壁状態	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
裂孔ヘルニア	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
臨床検査	19	(18.4)	31	45.1	14	(13.7)	18	28.6	8	(7.8)	13	18.7	41	(13.3)	62	30.8
消化管検査	12	(11.7)	20	29.1	8	(7.8)	11	17.5	5	(4.9)	7	10.1	25	(8.1)	38	18.9
リパーゼ増加	10	(9.7)	12	17.5	7	(6.9)	8	12.7	4	(3.9)	5	7.2	21	(6.8)	25	12.4
アミラーゼ増加	6	(5.8)	7	10.2	2	(2.0)	2	3.2	2	(1.9)	2	2.9	10	(3.2)	11	5.5
血中トリプシン増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
膵酵素検査異常	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
酵素検査ＮＥＣ	2	(1.9)	2	2.9	3	(2.9)	3	4.8	1	(1.0)	1	1.4	6	(1.9)	6	3.0

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Sitagliptin N	(%)	E	R	Total N	(%)	E	R
血中クレアチンホスホキナーゼ増加	2	(1.9)	2	2.9	3	(2.9)	3	4.8	1	(1.0)	1	1.4	6	(1.9)	6	3.0
肝胆道系検査	3	(2.9)	4	5.8	0				1	(1.0)	2	2.9	4	(1.3)	6	3.0
アラニンアミノトランスフェラーゼ増加	2	(1.9)	2	2.9	0				1	(1.0)	2	2.9	3	(1.0)	4	2.0
γ－グルタミルトランスフェラーゼ増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血中ビリルビン増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
身体的診察および器官系の状態に関する事項	0				3	(2.9)	3	4.8	0				3	(1.0)	3	1.5
体重減少	0				3	(2.9)	3	4.8	0				3	(1.0)	3	1.5
血液学的検査（血液型検査を含む）	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
白血球数減少	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
白血球数増加	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
腎尿路系検査および尿検査	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
血中クレアチニン増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
尿中蛋白陽性	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
蛋白および化学的検査ＮＥＣ	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
Ｃ－反応性蛋白増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血中アルブミン増加	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
細胞遺伝学的検査	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
糖鎖抗原１９－９増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
心血管系検査（酵素検査を除く）	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血圧低下	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
水分、電解質および無機質検査	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
血中ナトリウム増加	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
筋骨格系および結合組織障害	10	(9.7)	11	16.0	5	(4.9)	5	7.9	12	(11.7)	14	20.1	27	(8.8)	30	14.9
筋骨格系および結合組織障害ＮＥＣ	6	(5.8)	6	8.7	2	(2.0)	2	3.2	5	(4.9)	5	7.2	13	(4.2)	13	6.5

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System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
背部痛	3	(2.9)	3	4.4	1	(1.0)	1	1.6	1	(1.0)	1	1.4	5	(1.6)	5	2.5
筋骨格痛	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
側腹部痛	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
筋骨格系胸痛	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
筋骨格不快感	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
頚部痛	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
四肢痛	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
関節障害	3	(2.9)	4	5.8	1	(1.0)	1	1.6	3	(2.9)	3	4.3	7	(2.3)	8	4.0
関節周囲炎	2	(1.9)	2	2.9	0				1	(1.0)	1	1.4	3	(1.0)	3	1.5
変形性関節症	2	(1.9)	2	2.9	0				1	(1.0)	1	1.4	3	(1.0)	3	1.5
関節痛	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
筋骨格系および結合組織変形（椎間板障害を含む）	1	(1.0)	1	1.5	1	(1.0)	1	1.6	2	(1.9)	2	2.9	4	(1.3)	4	2.0
腰部脊柱管狭窄症	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
脊柱管狭窄症	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
椎間板突出	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
筋障害	0				1	(1.0)	1	1.6	2	(1.9)	2	2.9	3	(1.0)	3	1.5
筋肉痛	0				1	(1.0)	1	1.6	2	(1.9)	2	2.9	3	(1.0)	3	1.5
腱、靱帯および軟骨障害	0				0				2	(1.9)	2	2.9	2	(0.6)	2	1.0
弾発指	0				0				2	(1.9)	2	2.9	2	(0.6)	2	1.0
眼障害	12	(11.7)	14	20.4	5	(4.9)	6	9.5	5	(4.9)	6	8.6	22	(7.1)	26	12.9
網膜、脈絡膜および硝子体の出血および血管障害	4	(3.9)	4	5.8	4	(3.9)	4	6.3	4	(3.9)	4	5.8	12	(3.9)	12	6.0
糖尿病網膜症	4	(3.9)	4	5.8	2	(2.0)	2	3.2	4	(3.9)	4	5.8	10	(3.2)	10	5.0
網膜出血	0				2	(2.0)	2	3.2	0				2	(0.6)	2	1.0
眼部構造変化、沈着および変性ＮＥＣ	1	(1.0)	1	1.5	1	(1.0)	1	1.6	1	(1.0)	1	1.4	3	(1.0)	3	1.5
視神経乳頭障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5

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System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Sitagliptin N	(%)	E	R	Total N	(%)	E	R
網膜色素脱失	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
網膜裂孔	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
眼前方部構造変化、沈着および変性	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
白内障	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
眼部感染、刺激症状および炎症	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
ぶどう膜炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
アレルギー性結膜炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
眼部障害ＮＥＣ	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
眼乾燥	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
眼球感覚神経障害ＮＥＣ	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
眼精疲労	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
眼球新生物	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
結膜嚢胞	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
眼神経筋障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
眼瞼痙攣	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
眼部出血および血管障害ＮＥＣ	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
結膜出血	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
緑内障および高眼圧症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
緑内障	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
代謝および栄養障害	10	(9.7)	12	17.5	10	(9.8)	10	15.9	2	(1.9)	2	2.9	22	(7.1)	24	11.9
食欲および総合的栄養摂取障害	9	(8.7)	10	14.6	8	(7.8)	8	12.7	0				17	(5.5)	18	8.9
食欲減退	9	(8.7)	10	14.6	8	(7.8)	8	12.7	0				17	(5.5)	18	8.9
プリンおよびピリミジン代謝障害	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
高尿酸血症	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
脂質代謝障害	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
脂質異常症	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
電解質および水分バランス異常	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
脱水	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0

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System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
皮膚および皮下組織障害	8	(7.8)	8	11.6	4	(3.9)	4	6.3	8	(7.8)	10	14.4	20	(6.5)	22	10.9
表皮および皮膚異常	5	(4.9)	5	7.3	2	(2.0)	2	3.2	7	(6.8)	8	11.5	14	(4.5)	15	7.5
そう痒症	1	(1.0)	1	1.5	0				2	(1.9)	2	2.9	3	(1.0)	3	1.5
湿疹	1	(1.0)	1	1.5	1	(1.0)	1	1.6	1	(1.0)	2	2.9	3	(1.0)	4	2.0
薬疹	1	(1.0)	1	1.5	0				2	(1.9)	2	2.9	3	(1.0)	3	1.5
発疹	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
脂漏性皮膚炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
接触性皮膚炎	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
皮脂欠乏性湿疹	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
皮膚付属器状態	3	(2.9)	3	4.4	1	(1.0)	1	1.6	0				4	(1.3)	4	2.0
ざ瘡	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
円形脱毛症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
汗疹	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
嵌入爪	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
血管浮腫および蕁麻疹	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
蕁麻疹	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
角化および皮膚異栄養性障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
過角化	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
呼吸器、胸郭および縦隔障害	5	(4.9)	7	10.2	6	(5.9)	6	9.5	7	(6.8)	9	12.9	18	(5.8)	22	10.9
呼吸器系障害ＮＥＣ	2	(1.9)	3	4.4	5	(4.9)	5	7.9	6	(5.8)	7	10.1	13	(4.2)	15	7.5
咳嗽	2	(1.9)	2	2.9	0				3	(2.9)	3	4.3	5	(1.6)	5	2.5
上気道の炎症	0				2	(2.0)	2	3.2	2	(1.9)	2	2.9	4	(1.3)	4	2.0
口腔咽頭痛	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
呼吸困難	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
湿性咳嗽	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
鼻閉塞	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
鼻漏	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5

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System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Sitagliptin N	(%)	E	R	Total N	(%)	E	R
上気道障害（感染を除く）	2	(1.9)	3	4.4	1	(1.0)	1	1.6	1	(1.0)	1	1.4	4	(1.3)	5	2.5
逆流性喉頭炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
声帯障害	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
鼻閉	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
副鼻腔嚢胞	1	(1.0)	2	2.9	0				0				1	(0.3)	2	1.0
気管支障害（新生物を除く）	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
喘息	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
神経系障害	12	(11.7)	14	20.4	0				5	(4.9)	6	8.6	17	(5.5)	20	9.9
神経学的障害ＮＥＣ	7	(6.8)	8	11.6	0				1	(1.0)	1	1.4	8	(2.6)	9	4.5
浮動性めまい	2	(1.9)	2	2.9	0				1	(1.0)	1	1.4	3	(1.0)	3	1.5
味覚異常	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
意識消失	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
傾眠	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
体位性めまい	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
知覚過敏	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
頭痛	2	(1.9)	2	2.9	0				3	(2.9)	3	4.3	5	(1.6)	5	2.5
頭痛	2	(1.9)	2	2.9	0				3	(2.9)	3	4.3	5	(1.6)	5	2.5
運動障害（パーキンソニズムを含む）	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
パーキンソン病	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
振戦	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
中枢神経系血管障害	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
一過性脳虚血発作	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
頚動脈硬化症	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
精神的機能障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
認知症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
末梢性ニューロパチー	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
糖尿病性ニューロパチー	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肝胆道系障害	4	(3.9)	4	5.8	5	(4.9)	5	7.9	3	(2.9)	4	5.8	12	(3.9)	13	6.5
肝および肝胆道系障害	3	(2.9)	3	4.4	3	(2.9)	3	4.8	3	(2.9)	3	4.3	9	(2.9)	9	4.5
脂肪肝	0				2	(2.0)	2	3.2	1	(1.0)	1	1.4	3	(1.0)	3	1.5
肝機能異常	0				0				2	(1.9)	2	2.9	2	(0.6)	2	1.0
肝嚢胞	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
高ビリルビン血症	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
薬物性肝障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
胆嚢障害	1	(1.0)	1	1.5	2	(2.0)	2	3.2	1	(1.0)	1	1.4	4	(1.3)	4	2.0
胆嚢ポリープ	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
胆石症	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
胆嚢炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
傷害、中毒および処置合併症	4	(3.9)	5	7.3	2	(2.0)	2	3.2	3	(2.9)	5	7.2	9	(2.9)	12	6.0
損傷ＮＥＣ	3	(2.9)	4	5.8	0				3	(2.9)	3	4.3	6	(1.9)	7	3.5
節足動物刺傷	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
靱帯捻挫	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
挫傷	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
頭部損傷	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
腱断裂	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
骨および関節損傷	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
手骨折	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
半月板損傷	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
物理的要因による損傷	0				1	(1.0)	1	1.6	1	(1.0)	2	2.9	2	(0.6)	3	1.5
熱傷	0				1	(1.0)	1	1.6	1	(1.0)	2	2.9	2	(0.6)	3	1.5
腎および尿路障害	2	(1.9)	2	2.9	3	(2.9)	3	4.8	3	(2.9)	4	5.8	8	(2.6)	9	4.5
腎障害（腎症を除く）	1	(1.0)	1	1.5	1	(1.0)	1	1.6	2	(1.9)	2	2.9	4	(1.3)	4	2.0
腎嚢胞	1	(1.0)	1	1.5	1	(1.0)	1	1.6	1	(1.0)	1	1.4	3	(1.0)	3	1.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Sitagliptin N	(%)	E	R	Total N	(%)	E	R
腎後性腎不全	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
尿石症	1	(1.0)	1	1.5	1	(1.0)	1	1.6	1	(1.0)	1	1.4	3	(1.0)	3	1.5
腎結石症	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
尿管結石	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
尿路系徴候および症状	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
血尿	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
心臓障害	1	(1.0)	1	1.5	2	(2.0)	2	3.2	4	(3.9)	4	5.8	7	(2.3)	7	3.5
不整脈	0				2	(2.0)	2	3.2	1	(1.0)	1	1.4	3	(1.0)	3	1.5
第一度房室ブロック	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
心室性期外収縮	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
心障害徴候および症状	0				0				2	(1.9)	2	2.9	2	(0.6)	2	1.0
動悸	0				0				2	(1.9)	2	2.9	2	(0.6)	2	1.0
冠動脈障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
狭心症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
心筋障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
左室肥大	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
精神障害	2	(1.9)	2	2.9	1	(1.0)	1	1.6	4	(3.9)	4	5.8	7	(2.3)	7	3.5
睡眠障害	1	(1.0)	1	1.5	1	(1.0)	1	1.6	4	(3.9)	4	5.8	6	(1.9)	6	3.0
不眠症	1	(1.0)	1	1.5	1	(1.0)	1	1.6	3	(2.9)	3	4.3	5	(1.6)	5	2.5
中期不眠症	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
躁病と双極性気分障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
双極性障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3	(2.9)	3	4.4	1	(1.0)	1	1.6	2	(1.9)	3	4.3	6	(1.9)	7	3.5
悪性および詳細不明の消化管新生物	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
消化管粘膜下腫瘍	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Sitagliptin N	(%)	E	R	Total N	(%)	E	R
膵癌第４期	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
悪性および詳細不明の腎尿路系新生物	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
膀胱癌	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
悪性および詳細不明の内分泌新生物	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
甲状腺新生物	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
悪性および詳細不明の軟部組織新生物	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
軟部組織新生物	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
消化器の良性新生物	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
肛門直腸の良性新生物	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
良性肝胆道系新生物	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
肝臓血管腫	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
一般・全身障害および投与部位の状態	2	(1.9)	6	8.7	0				2	(1.9)	2	2.9	4	(1.3)	8	4.0
全身障害ＮＥＣ	1	(1.0)	4	5.8	0				1	(1.0)	1	1.4	2	(0.6)	5	2.5
倦怠感	1	(1.0)	4	5.8	0				0				1	(0.3)	4	2.0
末梢性浮腫	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
体温異常	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
発熱	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
投与部位反応	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
注射部位内出血	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血管障害	0				4	(3.9)	4	6.3	0				4	(1.3)	4	2.0
高血圧性血管障害	0				3	(2.9)	3	4.8	0				3	(1.0)	3	1.5
高血圧	0				3	(2.9)	3	4.8	0				3	(1.0)	3	1.5
血圧低下、非特異的血圧障害およびショック	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
起立性低血圧	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
耳および迷路障害	1	(1.0)	1	1.5	1	(1.0)	1	1.6	1	(1.0)	1	1.4	3	(1.0)	3	1.5
内耳および第８脳神経障害	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
回転性めまい	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
外耳障害（先天性障害を除く）	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
耳垢栓塞	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
生殖系および乳房障害	1	(1.0)	1	1.5	1	(1.0)	1	1.6	1	(1.0)	1	1.4	3	(1.0)	3	1.5
子宮、骨盤および広間膜障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
子宮ポリープ	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
前立腺障害（感染および炎症を除く）	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
前立腺石灰化	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
男性生殖器系感染および炎症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
前立腺炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
外科および内科処置	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
血管治療手技	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
冠動脈ステント挿入	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
頭頸部治療手技	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
抜歯	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
血液およびリンパ系障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
非溶血性貧血と骨髄抑制	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
貧血	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
先天性、家族性および遺伝性障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
先天性皮膚および皮下組織異常	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
皮様嚢腫	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5

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Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
内分泌障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
副腎障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
副腎障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
免疫系障害	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
アレルギー性疾患	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
季節性アレルギー	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.24.2- 2　重篤な有害事象（器官別大分類、高位グループ語及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	103				102				103				308			
Exposure time (year)	68.7				63.0				69.6				201.3			
Events	6	(5.8)	7	10.2	2	(2.0)	2	3.2	2	(1.9)	3	4.3	10	(3.2)	12	6.0
感染症および寄生虫症	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
ウイルス感染症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
帯状疱疹	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
詳細不明な感染体による感染症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
肺炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
肝胆道系障害	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
肝および肝胆道系障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
肝機能異常	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
胆嚢障害	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
胆嚢炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
悪性および詳細不明の消化管新生物	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
膵癌第４期	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
悪性および詳細不明の腎尿路系新生物	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
膀胱癌	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
外科および内科処置	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血管治療手技	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
冠動脈ステント挿入	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Sitagliptin N	(%)	E	R	Total N	(%)	E	R
心臓障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
冠動脈障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
狭心症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
神経系障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
神経学的障害ＮＥＣ	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
意識消失	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
腎および尿路障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
腎障害（腎症を除く）	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
腎後性腎不全	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
生殖系および乳房障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
男性生殖器系感染および炎症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
前立腺炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
精神障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
躁病と双極性気分障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
双極性障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, high level group term and preferred term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.24.2- 3　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（器官別大分類及び基本語別） - on-treatment 期間 - 安全性解析対象集団

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	103				102				103				308			
Exposure time (year)	68.7				63.0				69.6				201.3			
Events	49	(47.6)	93	135.3	48	(47.1)	93	147.6	18	(17.5)	24	34.5	115	(37.3)	210	104.3
胃腸障害	32	(31.1)	51	74.2	34	(33.3)	61	96.8	7	(6.8)	8	11.5	73	(23.7)	120	59.6
便秘	14	(13.6)	15	21.8	10	(9.8)	10	15.9	3	(2.9)	3	4.3	27	(8.8)	28	13.9
悪心	10	(9.7)	11	16.0	13	(12.7)	22	34.9	0				23	(7.5)	33	16.4
腹部不快感	4	(3.9)	4	5.8	7	(6.9)	8	12.7	0				11	(3.6)	12	6.0
下痢	4	(3.9)	5	7.3	5	(4.9)	7	11.1	1	(1.0)	1	1.4	10	(3.2)	13	6.5
嘔吐	4	(3.9)	5	7.3	1	(1.0)	2	3.2	1	(1.0)	1	1.4	6	(1.9)	8	4.0
上腹部痛	3	(2.9)	3	4.4	1	(1.0)	1	1.6	1	(1.0)	1	1.4	5	(1.6)	5	2.5
消化不良	1	(1.0)	1	1.5	3	(2.9)	4	6.3	0				4	(1.3)	5	2.5
おくび	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
胃食道逆流性疾患	0				2	(2.0)	2	3.2	0				2	(0.6)	2	1.0
口内炎	2	(1.9)	3	4.4	0				0				2	(0.6)	3	1.5
腹痛	0				2	(2.0)	2	3.2	0				2	(0.6)	2	1.0
腹部膨満	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
慢性胃炎	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
十二指腸潰瘍	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
心窩部不快感	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
軟便	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
臨床検査	13	(12.6)	18	26.2	10	(9.8)	14	22.2	4	(3.9)	7	10.1	27	(8.8)	39	19.4
リパーゼ増加	7	(6.8)	7	10.2	6	(5.9)	7	11.1	2	(1.9)	2	2.9	15	(4.9)	16	7.9
アミラーゼ増加	5	(4.9)	5	7.3	2	(2.0)	2	3.2	0				7	(2.3)	7	3.5
体重減少	0				3	(2.9)	3	4.8	0				3	(1.0)	3	1.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
アラニンアミノトランスフェラーゼ増加	1	(1.0)	1	1.5	0				1	(1.0)	2	2.9	2	(0.6)	3	1.5
血中アルブミン増加	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
血中クレアチニン増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血中クレアチンホスホキナーゼ増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血中トリプシン増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血中ナトリウム増加	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
血中ビリルビン増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
尿中蛋白陽性	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
白血球数減少	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
白血球数増加	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
膵酵素検査異常	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
代謝および栄養障害	8	(7.8)	9	13.1	8	(7.8)	8	12.7	1	(1.0)	1	1.4	17	(5.5)	18	8.9
食欲減退	8	(7.8)	9	13.1	7	(6.9)	7	11.1	0				15	(4.9)	16	7.9
脂質異常症	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
感染症および寄生虫症	2	(1.9)	2	2.9	4	(3.9)	4	6.3	1	(1.0)	1	1.4	7	(2.3)	7	3.5
胃腸炎	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
結膜炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
口腔ヘルペス	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
歯周炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
耳下腺炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
尿道炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
神経系障害	4	(3.9)	4	5.8	0				1	(1.0)	1	1.4	5	(1.6)	5	2.5
頭痛	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
傾眠	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
頚動脈硬化症	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
味覚異常	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
眼障害	2	(1.9)	2	2.9	2	(2.0)	2	3.2	0				4	(1.3)	4	2.0
糖尿病網膜症	2	(1.9)	2	2.9	1	(1.0)	1	1.6	0				3	(1.0)	3	1.5
網膜出血	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
呼吸器、胸郭および縦隔障害	1	(1.0)	1	1.5	1	(1.0)	1	1.6	1	(1.0)	1	1.4	3	(1.0)	3	1.5
咳嗽	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
逆流性喉頭炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
声帯障害	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
肝胆道系障害	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
肝機能異常	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
高ビリルビン血症	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
皮膚および皮下組織障害	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
そう痒症	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
一般・全身障害および投与部位の状態	1	(1.0)	4	5.8	0				0				1	(0.3)	4	2.0
倦怠感	1	(1.0)	4	5.8	0				0				1	(0.3)	4	2.0
筋骨格系および結合組織障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
関節痛	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
血管障害	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
起立性低血圧	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
耳および迷路障害	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
回転性めまい	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心臓障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
動悸	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
腎および尿路障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
腎後性腎不全	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
生殖系および乳房障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
前立腺炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.24.2- 4　重度の有害事象（器官別大分類及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	103				102				103				308			
Exposure time (year)	68.7				63.0				69.6				201.3			
Events	2	(1.9)	2	2.9	1	(1.0)	1	1.6	2	(1.9)	5	7.2	5	(1.6)	8	4.0
胃腸障害	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
胃炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
一般・全身障害および投与部位の状態	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
発熱	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
感染症および寄生虫症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
帯状疱疹	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
肝胆道系障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
肝機能異常	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
血液およびリンパ系障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
貧血	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
神経系障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
意識消失	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
腎および尿路障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
腎後性腎不全	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
膵癌第４期	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.24.2- 5　中等度の有害事象（器官別大分類及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	103				102				103				308			
Exposure time (year)	68.7				63.0				69.6				201.3			
Events	13	(12.6)	23	33.5	9	(8.8)	12	19.0	10	(9.7)	10	14.4	32	(10.4)	45	22.4
感染症および寄生虫症	3	(2.9)	3	4.4	2	(2.0)	2	3.2	3	(2.9)	3	4.3	8	(2.6)	8	4.0
インフルエンザ	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
胃腸炎	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
咽頭炎	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
眼部単純ヘルペス	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
細菌性腸炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
帯状疱疹	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
肺炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
鼻咽頭炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
胃腸障害	2	(1.9)	2	2.9	3	(2.9)	5	7.9	0				5	(1.6)	7	3.5
悪心	1	(1.0)	1	1.5	2	(2.0)	3	4.8	0				3	(1.0)	4	2.0
下痢	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
腹痛	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
筋骨格系および結合組織障害	1	(1.0)	1	1.5	0				2	(1.9)	2	2.9	3	(1.0)	3	1.5
筋骨格痛	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
筋肉痛	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
腰部脊柱管狭窄症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
呼吸器、胸郭および縦隔障害	1	(1.0)	1	1.5	1	(1.0)	1	1.6	1	(1.0)	1	1.4	3	(1.0)	3	1.5
逆流性喉頭炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
声帯障害	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
喘息	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
神経系障害	3	(2.9)	3	4.4	0				0				3	(1.0)	3	1.5
一過性脳虚血発作	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
頭痛	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
認知症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
代謝および栄養障害	3	(2.9)	3	4.4	0				0				3	(1.0)	3	1.5
高尿酸血症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
食欲減退	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
脱水	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
臨床検査	3	(2.9)	3	4.4	0				0				3	(1.0)	3	1.5
リパーゼ増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血圧低下	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
白血球数減少	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
肝胆道系障害	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
胆嚢炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
薬物性肝障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
眼障害	2	(1.9)	3	4.4	0				0				2	(0.6)	3	1.5
ぶどう膜炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
網膜裂孔	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
緑内障	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
傷害、中毒および処置合併症	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
手骨折	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
腱断裂	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
皮膚および皮下組織障害	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
蕁麻疹	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
外科および内科処置	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
冠動脈ステント挿入	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血管障害	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
高血圧	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
耳および迷路障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
耳垢栓塞	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
心臓障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
狭心症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
精神障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
双極性障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
肝臓血管腫	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5

MedDRA version 18.0. Note: The 'on-treatment' summary includes treatment-emergent adverse events with onset at or after the date of the first trial product dose and before or at the date of the last trial product dose plus 5 weeks plus the 7 days visit window for the end-of-treatment follow-up visit (=42 days). The observation time is the duration of this period. Table is sorted in descending order by system organ class, preferred term based on the total percentage of subjects experiencing at least one event.
Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.24.2- 6　軽度の有害事象（器官別大分類及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	103				102				103				308			
Exposure time (year)	68.7				63.0				69.6				201.3			
Events	73	(70.9)	203	295.4	68	(66.7)	184	292.0	67	(65.0)	171	245.8	208	(67.5)	558	277.2
感染症および寄生虫症	28	(27.2)	37	53.8	32	(31.4)	43	68.2	40	(38.8)	64	92.0	100	(32.5)	144	71.5
鼻咽頭炎	17	(16.5)	21	30.6	18	(17.6)	21	33.3	30	(29.1)	42	60.4	65	(21.1)	84	41.7
咽頭炎	2	(1.9)	2	2.9	3	(2.9)	3	4.8	2	(1.9)	2	2.9	7	(2.3)	7	3.5
インフルエンザ	2	(1.9)	2	2.9	1	(1.0)	1	1.6	1	(1.0)	1	1.4	4	(1.3)	4	2.0
胃腸炎	1	(1.0)	1	1.5	2	(2.0)	2	3.2	1	(1.0)	1	1.4	4	(1.3)	4	2.0
歯周炎	1	(1.0)	1	1.5	3	(2.9)	3	4.8	0				4	(1.3)	4	2.0
上気道感染	0				2	(2.0)	2	3.2	2	(1.9)	2	2.9	4	(1.3)	4	2.0
足部白癬	1	(1.0)	1	1.5	0				3	(2.9)	3	4.3	4	(1.3)	4	2.0
外耳炎	0				1	(1.0)	1	1.6	2	(1.9)	2	2.9	3	(1.0)	3	1.5
口腔ヘルペス	1	(1.0)	1	1.5	2	(2.0)	2	3.2	0				3	(1.0)	3	1.5
歯肉炎	2	(1.9)	2	2.9	0				1	(1.0)	1	1.4	3	(1.0)	3	1.5
ウイルス性胃腸炎	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
気管支炎	0				0				2	(1.9)	2	2.9	2	(0.6)	2	1.0
結膜炎	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
鼻炎	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
扁桃炎	1	(1.0)	1	1.5	0				1	(1.0)	3	4.3	2	(0.6)	4	2.0
膀胱炎	0				0				2	(1.9)	2	2.9	2	(0.6)	2	1.0
ヘリコバクター感染	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
陰部ヘルペス	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
急性中耳炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
胸壁膿瘍	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
耳下腺炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
帯状疱疹	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
爪感染	0				1	(1.0)	2	3.2	0				1	(0.3)	2	1.0

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Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
爪真菌症	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
尿道炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
胃腸障害	38	(36.9)	61	88.8	40	(39.2)	76	120.6	17	(16.5)	28	40.3	95	(30.8)	165	82.0
便秘	15	(14.6)	16	23.3	12	(11.8)	12	19.0	4	(3.9)	4	5.8	31	(10.1)	32	15.9
悪心	10	(9.7)	11	16.0	11	(10.8)	19	30.2	0				21	(6.8)	30	14.9
下痢	6	(5.8)	8	11.6	8	(7.8)	13	20.6	2	(1.9)	3	4.3	16	(5.2)	24	11.9
腹部不快感	4	(3.9)	4	5.8	7	(6.9)	8	12.7	0				11	(3.6)	12	6.0
上腹部痛	4	(3.9)	4	5.8	3	(2.9)	4	6.3	2	(1.9)	2	2.9	9	(2.9)	10	5.0
嘔吐	4	(3.9)	5	7.3	2	(2.0)	3	4.8	1	(1.0)	1	1.4	7	(2.3)	9	4.5
慢性胃炎	1	(1.0)	1	1.5	1	(1.0)	1	1.6	4	(3.9)	4	5.8	6	(1.9)	6	3.0
胃食道逆流性疾患	1	(1.0)	1	1.5	2	(2.0)	2	3.2	2	(1.9)	2	2.9	5	(1.6)	5	2.5
消化不良	2	(1.9)	3	4.4	3	(2.9)	4	6.3	0				5	(1.6)	7	3.5
齲歯	1	(1.0)	1	1.5	0				4	(3.9)	4	5.8	5	(1.6)	5	2.5
口内炎	2	(1.9)	3	4.4	0				1	(1.0)	1	1.4	3	(1.0)	4	2.0
おくび	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
胃炎	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
痔核	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
腹部膨満	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
裂孔ヘルニア	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
びらん性胃炎	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
胃ポリープ	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
口唇炎	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
歯周病	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
痔出血	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
十二指腸潰瘍	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
心窩部不快感	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
大腸ポリープ	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
直腸ポリープ	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
軟便	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5

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Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腹痛	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
臨床検査	17	(16.5)	28	40.7	14	(13.7)	18	28.6	8	(7.8)	13	18.7	39	(12.7)	59	29.3
リパーゼ増加	9	(8.7)	11	16.0	7	(6.9)	8	12.7	4	(3.9)	5	7.2	20	(6.5)	24	11.9
アミラーゼ増加	6	(5.8)	7	10.2	2	(2.0)	2	3.2	2	(1.9)	2	2.9	10	(3.2)	11	5.5
血中クレアチンホスホキナーゼ増加	2	(1.9)	2	2.9	3	(2.9)	3	4.8	1	(1.0)	1	1.4	6	(1.9)	6	3.0
アラニンアミノトランスフェラーゼ増加	2	(1.9)	2	2.9	0				1	(1.0)	2	2.9	3	(1.0)	4	2.0
体重減少	0				3	(2.9)	3	4.8	0				3	(1.0)	3	1.5
Ｃ－反応性蛋白増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
γ－グルタミルトランスフェラーゼ増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血中アルブミン増加	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
血中クレアチニン増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血中トリプシン増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
血中ナトリウム増加	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
血中ビリルビン増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
糖鎖抗原１９－９増加	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
尿中蛋白陽性	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
白血球数増加	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
膵酵素検査異常	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
筋骨格系および結合組織障害	9	(8.7)	10	14.6	5	(4.9)	5	7.9	12	(11.7)	12	17.3	26	(8.4)	27	13.4
背部痛	3	(2.9)	3	4.4	1	(1.0)	1	1.6	1	(1.0)	1	1.4	5	(1.6)	5	2.5
関節周囲炎	2	(1.9)	2	2.9	0				1	(1.0)	1	1.4	3	(1.0)	3	1.5
変形性関節症	2	(1.9)	2	2.9	0				1	(1.0)	1	1.4	3	(1.0)	3	1.5
関節痛	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
筋肉痛	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
側腹部痛	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
弾発指	0				0				2	(1.9)	2	2.9	2	(0.6)	2	1.0

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Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
筋骨格系胸痛	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
筋骨格痛	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
筋骨格不快感	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
頚部痛	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
腰部脊柱管狭窄症	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
四肢痛	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
脊柱管狭窄症	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
椎間板突出	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
眼障害	10	(9.7)	11	16.0	5	(4.9)	6	9.5	5	(4.9)	6	8.6	20	(6.5)	23	11.4
糖尿病網膜症	4	(3.9)	4	5.8	2	(2.0)	2	3.2	4	(3.9)	4	5.8	10	(3.2)	10	5.0
眼乾燥	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
白内障	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
網膜出血	0				2	(2.0)	2	3.2	0				2	(0.6)	2	1.0
アレルギー性結膜炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
眼精疲労	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
眼瞼痙攣	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
結膜出血	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
結膜嚢胞	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
視神経乳頭障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
網膜色素脱失	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
代謝および栄養障害	8	(7.8)	9	13.1	10	(9.8)	10	15.9	2	(1.9)	2	2.9	20	(6.5)	21	10.4
食欲減退	8	(7.8)	9	13.1	8	(7.8)	8	12.7	0				16	(5.2)	17	8.4
脂質異常症	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
高尿酸血症	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
脱水	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
皮膚および皮下組織障害	8	(7.8)	8	11.6	3	(2.9)	3	4.8	8	(7.8)	9	12.9	19	(6.2)	20	9.9
そう痒症	1	(1.0)	1	1.5	0				2	(1.9)	2	2.9	3	(1.0)	3	1.5

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Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
湿疹	1	(1.0)	1	1.5	1	(1.0)	1	1.6	1	(1.0)	2	2.9	3	(1.0)	4	2.0
薬疹	1	(1.0)	1	1.5	0				2	(1.9)	2	2.9	3	(1.0)	3	1.5
発疹	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
ざ瘡	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
円形脱毛症	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
過角化	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
汗疹	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
脂漏性皮膚炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
接触性皮膚炎	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
皮脂欠乏性湿疹	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
嵌入爪	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
呼吸器、胸郭および縦隔障害	4	(3.9)	6	8.7	5	(4.9)	5	7.9	6	(5.8)	8	11.5	15	(4.9)	19	9.4
咳嗽	2	(1.9)	2	2.9	0				3	(2.9)	3	4.3	5	(1.6)	5	2.5
上気道の炎症	0				2	(2.0)	2	3.2	2	(1.9)	2	2.9	4	(1.3)	4	2.0
口腔咽頭痛	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
呼吸困難	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
湿性咳嗽	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
鼻閉	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
鼻閉塞	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
鼻漏	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
副鼻腔嚢胞	1	(1.0)	2	2.9	0				0				1	(0.3)	2	1.0
喘息	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
神経系障害	10	(9.7)	10	14.6	0				5	(4.9)	6	8.6	15	(4.9)	16	7.9
頭痛	1	(1.0)	1	1.5	0				3	(2.9)	3	4.3	4	(1.3)	4	2.0
浮動性めまい	2	(1.9)	2	2.9	0				1	(1.0)	1	1.4	3	(1.0)	3	1.5
味覚異常	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
パーキンソン病	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
傾眠	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5

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Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
頚動脈硬化症	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
振戦	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
体位性めまい	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
知覚過敏	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
糖尿病性ニューロパチー	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
肝胆道系障害	3	(2.9)	3	4.4	4	(3.9)	4	6.3	2	(1.9)	3	4.3	9	(2.9)	10	5.0
脂肪肝	0				2	(2.0)	2	3.2	1	(1.0)	1	1.4	3	(1.0)	3	1.5
肝嚢胞	2	(1.9)	2	2.9	0				0				2	(0.6)	2	1.0
胆嚢ポリープ	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
肝機能異常	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
高ビリルビン血症	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
胆石症	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
腎および尿路障害	2	(1.9)	2	2.9	3	(2.9)	3	4.8	3	(2.9)	3	4.3	8	(2.6)	8	4.0
腎嚢胞	1	(1.0)	1	1.5	1	(1.0)	1	1.6	1	(1.0)	1	1.4	3	(1.0)	3	1.5
血尿	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
腎結石症	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0
尿管結石	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
傷害、中毒および処置合併症	4	(3.9)	5	7.3	1	(1.0)	1	1.6	2	(1.9)	4	5.8	7	(2.3)	10	5.0
節足動物刺傷	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
熱傷	0				1	(1.0)	1	1.6	1	(1.0)	2	2.9	2	(0.6)	3	1.5
靱帯捻挫	1	(1.0)	1	1.5	0				1	(1.0)	1	1.4	2	(0.6)	2	1.0
挫傷	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
頭部損傷	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
半月板損傷	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
心臓障害	0				2	(2.0)	2	3.2	4	(3.9)	4	5.8	6	(1.9)	6	3.0
第一度房室ブロック	0				1	(1.0)	1	1.6	1	(1.0)	1	1.4	2	(0.6)	2	1.0

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
動悸	0				0				2	(1.9)	2	2.9	2	(0.6)	2	1.0
左室肥大	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
心室性期外収縮	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
精神障害	1	(1.0)	1	1.5	1	(1.0)	1	1.6	4	(3.9)	4	5.8	6	(1.9)	6	3.0
不眠症	1	(1.0)	1	1.5	1	(1.0)	1	1.6	3	(2.9)	3	4.3	5	(1.6)	5	2.5
中期不眠症	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3	(2.9)	3	4.4	1	(1.0)	1	1.6	1	(1.0)	1	1.4	5	(1.6)	5	2.5
甲状腺新生物	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
消化管粘膜下腫瘍	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
軟部組織新生物	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
肛門直腸の良性新生物	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
膀胱癌	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
一般・全身障害および投与部位の状態	2	(1.9)	6	8.7	0				1	(1.0)	1	1.4	3	(1.0)	7	3.5
倦怠感	1	(1.0)	4	5.8	0				0				1	(0.3)	4	2.0
注射部位内出血	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
発熱	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
末梢性浮腫	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
血管障害	0				3	(2.9)	3	4.8	0				3	(1.0)	3	1.5
高血圧	0				2	(2.0)	2	3.2	0				2	(0.6)	2	1.0
起立性低血圧	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
生殖系および乳房障害	1	(1.0)	1	1.5	1	(1.0)	1	1.6	1	(1.0)	1	1.4	3	(1.0)	3	1.5
子宮ポリープ	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
前立腺炎	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
前立腺石灰化	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Sitagliptin				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
耳および迷路障害	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
回転性めまい	1	(1.0)	1	1.5	1	(1.0)	1	1.6	0				2	(0.6)	2	1.0
外科および内科処置	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
抜歯	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
先天性、家族性および遺伝性障害	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
皮様嚢腫	1	(1.0)	1	1.5	0				0				1	(0.3)	1	0.5
内分泌障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
副腎障害	0				0				1	(1.0)	1	1.4	1	(0.3)	1	0.5
免疫系障害	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5
季節性アレルギー	0				1	(1.0)	1	1.6	0				1	(0.3)	1	0.5

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Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure. seq.: sequelae, %: percentage of subjects experiencing at least one event.

2.7.6.25 NN9535-3744

2.7.6.25.1 臨床試験概要

治験依頼者名： Novo Nordisk A/S, Novo Allé, DK-2880 Bagsvaerd, Denmark	
有効成分名： セマグルチド	
Trial ID： NN9535-3744	
Trial Registration ID-number： NCT01720446	UTN：U1111-1131-7227 IND number：79,754 EudraCT number：2012-002839-28
治験の標題： SUSTAIN 6 – 長期アウトカム試験 2 型糖尿病患者を対象として、セマグルチドの心血管系及びその他の長期アウトカムについて比較検討する、長期、無作為割り付け、二重盲検、プラセボ対照、多国籍、多施設試験	
治験責任医師名： 治験実施施設（全 229 施設）ごとに 1 名の治験責任医師が任命された。以下の治験責任医師が治験総括報告書の内容を確認し、署名する「治験総括報告書への署名責任を有する医師（signatory investigator）」に指名された。 • [redacted] • [redacted]	
治験実施施設： 本試験は以下の 20 ヵ国 229 施設において実施された：アルジェリア（4 施設）、アルゼンチン（7 施設）、オーストラリア（8 施設）、ブラジル（8 施設）、ブルガリア（5 施設）、カナダ（13 施設）、デンマーク（5 施設）、ドイツ（7 施設）、イスラエル（6 施設）、イタリア（6 施設）、マレーシア（6 施設）、メキシコ（9 施設）、ポーランド（5 施設）、ロシア（11 施設）、スペイン（6 施設）、台湾（4 施設）、タイ（5 施設）、トルコ（10 施設）、英国（8 施設）及び米国（96 施設）	
公表文献（引用文献）： Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, et al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med. 2016.	
治験期間： 開始日（最初の被験者の初回来院日）：2013 年 2 月 21 日 終了日（最後の被験者の最終来院日）：2016 年 3 月 15 日	**開発のフェーズ**： 第 3a 相
Cut-off date： ここに提示する結果は、2016 年 6 月 22 日の時点での臨床データベース及び 2016 年 3 月 22 日の時点での安全性データベースに基づいている。	
報告書作成日： 2016 年 10 月 24 日	
目的： <u>主要目的：</u> • 成人2型糖尿病患者を対象として、セマグルチドの投与により許容できない心血管系リスクの増加がみ	

られないことをプラセボと比較し確認する。そのために、最初の主要な心血管イベント（MACE）を発現するまでの時間を比較し、セマグルチドとプラセボのハザード比の両側95%信頼区間の上限が1.8未満であることを示す。

副次的目的：

- 心血管系イベントリスクが高い成人2型糖尿病患者を対象として、標準治療にセマグルチド0.5 mg及び1.0 mg（週1回投与）を追加したときの長期的な安全性及び有効性をプラセボと比較して評価する。

治験方法：

本試験は、心血管イベントのリスクが高い 2 型糖尿病患者（男女）を対象として、糖尿病の標準治療にセマグルチドを追加したときの心血管に対する安全性及び長期アウトカムをプラセボと比較して評価する、長期、多施設、多国籍、無作為割り付け、二重盲検、並行群間比較試験であった。

MACE の可能性がある事象、死亡及び事前に定義された特に注目すべき医学的事象（MESI）等の特定の事象について盲検下で継続的な判定及び評価を行うため、外部の独立したイベント判定委員会が本試験に対して設立された。

本試験の継続的な安全性審査を行うために外部の独立したデータモデリング委員会（DMC）が設立され、非盲検データに基づいて評価が行われた。

本試験は、最大 2 週間のスクリーニング期間、無作為割り付けのための来院（来院 2）、104 週間の投与期間及び 5 週間の投与後事後調査期間で構成された。無作為割り付け来院では、被験者はセマグルチド 0.5 mg、セマグルチド 1.0 mg 又は同じ用量のプラセボの週 1 回投与に、それぞれ 1:1:1:1 の割合で割り付けられた。試験期間は一部事象の発現状況に依存的であった。イベント判定委員会により MACE と確認された 3 種類の事象を発現した被験者が 122 例に達した時点ならびに早くても最後の被験者が無作為割り付けされてから 104 週間後に試験を終了することとした。イベント判定委員会により確認された MACE の集積率が予想より高かったため、計画された MACE の件数は予定より早く達した。そのため、各被験者の試験期間は、104 週間の治験薬投与及び投与後 5 週間の事後調査を合わせた、計 109 週間となった。

被験者は規定の用量漸増法に従い、セマグルチド又はプラセボの維持用量 0.5 mg 又は 1.0 mg に到達させた。割り付けられたすべての被験者は用量 0.25 mg から開始し、4 週間の投与を受けた後、各用量を増量（倍増）した。これにより、0.5 mg 群は投与後 4 週間、1.0 mg 群は投与後 8 週間で維持用量に達した。

被験者は、最初の 6 ヵ月間は毎月 1 回、残りの試験期間中は 3 ヵ月毎に 1 回の頻度で治験実施施設に来院し、来院と来院の間に毎月 1 回治験責任医師との電話コンタクトを行うこととした。

無作為割り付けされたすべての被験者のアウトカムデータを収集するため真摯な努力がなされた。各被験者に対して、割り付けられた治療及び治験実施計画書の全般的な遵守状況に関わらず、同意を撤回しない限り試験期間中調査が行われた。被験者が試験を終了せず同意も撤回しなかった場合は、追跡不能例とみなすこととした。データベースロックまでこれらの被験者の生命状態（vital status）の把握を試みることとした。生命状態も把握できない被験者については、生命状態追跡不能例とみなすこととした。

治験責任医師は、良好な血糖コントロールを維持するための「目標（現在のガイドラインにおける目標値）達成に向けた治療」が推奨された。そのため、良好な血糖コントロールを維持することを目的として、治験責任医師の判断により、本試験で割り付けられた治療法に血糖降下薬〔GLP-1 受容体作動薬、DPP-4 阻害薬及びプラムリンタイドのようなインクレチン経路に影響を及ぼす薬剤を除く〕を追加することが認められた。

無作為割り付けでは、各層の分布が均等化されるように、以下の 3 つの層別因子によって層別した；ベースライン時の心血管系疾患の所見（臨床的／潜在的）、ベースライン時のインスリン治療（なし／Basal インスリン／混合型インスリン）、GFR 値が 30 mL/min/1.73m^2 未満を示す腎機能疾患（なし／あり）。

試験デザインにより、重度の腎機能障害を有する被験者は常に「心血管系疾患の臨床的所見がある」層に層別された。以上の層別の結果、9 つの層に分けられた。

計画及び解析された被験者数：

無作為割り付け予定症例数として 3260 例が計画され、実際には 4346 例がスクリーニングされ、うち 3297 例が無作為割り付けされた。98.0%の被験者が試験を完了し、無作為割り付けされた被験者の 99.6%の生命

状態を把握した。
被験者内訳 - 要約 - 無作為割り付けされたすべての被験者：

	Sema N	(%)	Placebo N	(%)	Total N	(%)
Screened					4346	
Screening failures					1049	
Full analysis set (all randomised subjects)	1648	(100.0%)	1649	(100.0%)	3297	(100.0%)
Safety analysis set (all exposed subjects)	1642	(99.6%)	1644	(99.7%)	3286	(99.7%)
Treatment completers [1]	1297	(78.7%)	1339	(81.2%)	2636	(80.0%)
Trial completers	1623	(98.5%)	1609	(97.6%)	3232	(98.0%)
Subjects who died during the trial	62	(3.8%)	60	(3.6%)	122	(3.7%)
Subjects who attended visit 26	1561	(94.7%)	1549	(93.9%)	3110	(94.3%)
Premature treatment discontinuers [2]	350	(21.2%)	310	(18.8%)	660	(20.0%)
Gastrointestinal tolerability	124	(7.5%)	18	(1.1%)	142	(4.3%)
Withdrawal of informed consent	2	(0.1%)	2	(0.1%)	4	(0.1%)
Adverse event other than related to gastrointestinal tolerability	92	(5.6%)	93	(5.6%)	185	(5.6%)
Introduction of disallowed medication	6	(0.4%)	16	(1.0%)	22	(0.7%)
Suspicion of placebo (without introduction of disallowed medication)	6	(0.4%)	25	(1.5%)	31	(0.9%)
Randomised in error	25	(1.5%)	22	(1.3%)	47	(1.4%)
Resistance to injections	2	(0.1%)	2	(0.1%)	4	(0.1%)
Trial fatigue	10	(0.6%)	26	(1.6%)	36	(1.1%)
Other	83	(5.0%)	106	(6.4%)	189	(5.7%)
Withdrawals in relation to or after treatment discontinuation [3]	7	(0.4%)	8	(0.5%)	15	(0.5%)
Last known vital status for subjects not completing the trial	25	(1.5%)	40	(2.4%)	65	(2.0%)
Subjects lost to follow-up [4]	18	(1.1%)	32	(1.9%)	50	(1.5%)
Alive	14	(0.8%)	26	(1.6%)	40	(1.2%)
Dead	1	(0.1%)	2	(0.1%)	3	(0.1%)
Unknown	3	(0.2%)	4	(0.2%)	7	(0.2%)
Withdrawals	7	(0.4%)	8	(0.5%)	15	(0.5%)
Alive	3	(0.2%)	4	(0.2%)	7	(0.2%)
Dead	1	(0.1%)	1	(0.1%)	2	(0.1%)
Unknown	3	(0.2%)	3	(0.2%)	6	(0.2%)

Sema: semaglutide, N: Number of subjects, %: Percentages are based on randomised subjects, Visit 26: Follow-up visit.
[1]: Subjects, who were exposed, did not discontinue treatment prematurely, who did not withdraw from trial and who were not lost to follow-up before the last treatment visit. [2]: Subjects who are not exposed, but have given a reason for premature treatment discontinuation are also included. [3]: All cases were withdrawal of informed consent. [4]: Subjects who did not complete the trial and did not withdraw from trial.

診断及び主要な組入れ基準：

主な選択基準：

性別不問、2 型糖尿病患者、年齢 50 歳以上でスクリーニング時に心血管系疾患の臨床的所見もしくは年齢 60 歳以上でスクリーニング時に心血管系疾患の潜在的所見があり、スクリーニング時の HbA1c が 7.0%以上、下記のいずれかの治療歴がある被験者；糖尿治療薬による治療歴なし、経口糖尿病薬 1～2 剤での治療歴、Neutral Protamin Hagedorn（NPH）ヒトインスリン、持効型インスリンアナログ又は混合型インスリンの単独療法又はこれらのインスリンと経口糖尿病薬 1～2 剤との併用療法による治療歴。

主な除外基準：

1 型糖尿病患者。スクリーニング前 90 日以内にグルカゴン様ペプチド-1（GLP-1）受容体作動薬（エキセナチド、リラグルチド等）又はプラムリンタイドの投与を受けた被験者。スクリーニング前 30 日以内にいずれかのジペプチジルペプチダーゼ 4（DPP-4）阻害薬の投与を受けた被験者。スクリーニング前 90 日以内に Basal インスリン又は混合型インスリン以外のインスリンを投与した被験者（ただし、併発疾患のための短期間の投与を除く）。急性の糖尿病合併症（ケトアシドーシス等）を予防する目的で緊急な治療強化を要した急性血糖コントロール不全をスクリーニング前 90 日以内に発症した被験者。慢性膵炎又は急性

膵炎（特発性膵炎）の既往歴を有する被験者。無作為割り付け前 90 日以内に急性冠動脈疾患又は脳血管疾患を発現した被験者。冠動脈、頸動脈又は末梢動脈再建術を受ける予定のある被験者。慢性心不全〔New York Heart Association（NYHA）分類クラス IV〕を有する被験者。本人又は家族が多発性内分泌腫瘍症候群 2 型（MEN 2）もしくは家族性甲状腺髄様癌の既往歴を有する被験者。非家族性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濃度が 50 ng/L 以上の被験者。

主な中止・脱落基準：

被験者が妊娠した場合に同意書の撤回をもって被験者は試験への参加を中止することとした。

被験薬、用量及び投与方法、ロット番号：

セマグルチド注射液（1.34 mg/mL）〔PDS290 ペン型注入器（1.5 mL）と一体化したプレフィルド製剤〕を、食事時間に関係なく 1 日のいずれかの時点において 0.5 mg 又は 1.0 mg を大腿部、腹部又は上腕部のいずれかに週 1 回皮下投与した。ロット番号（有効期限）：BV40330（2014 年 3 月 26 日）、BV40398（2014 年 3 月 26 日）、BV40439（2014 年 7 月 4 日）、CV40054（2014 年 10 月 4 日）、CV40076（2014 年 10 月 4 日）、BV40434（2015 年 4 月 1 日）、BV40329（2015 年 6 月 26 日）、CV40317（2015 年 10 月 10 日）、CV40344（2015 年 10 月 10 日）、DV40225（2017 年 5 月 7 日）。

投与期間：

104 週間

対照薬、用量及び投与方法、ロット番号：

セマグルチドプラセボは、PDS290 ペン型注入器（1.5 mL）と一体化したプレフィルド製剤として供給され、セマグルチド 0.5 mg 及び 1.0 mg と同量を皮下投与した。プラセボの組成は、有効成分が含まれていないことを除き、セマグルチド治験薬の組成と同じであった。プラセボのロット番号（有効期限）：BV40314（2014 年 3 月 23 日）、BV40320（2014 年 3 月 23 日）、BV40377（2014 年 3 月 23 日）、CV40023（2015 年 4 月 1 日）、CV40075（2014 年 10 月 1 日）、CV40023（2015 年 4 月 1 日）、BV40438（2015 年 4 月 1 日）、CV40139（2015 年 7 月 29 日）、DV40039（2016 年 2 月 13 日）、DV40231（2017 年 5 月 5 日）。

評価基準：事象発現までの時間に関する分析

以下の項目が評価対象となった：心血管死、非致死性心筋梗塞、非致死性脳卒中、冠動脈及び末梢血行再建、入院を要する不安定狭心症、心不全による入院、すべての死亡、細小血管イベント（腎症及び糖尿病網膜症）。

評価基準：有効性

以下の有効性の項目が評価対象となった：HbA1c、体重、空腹時血糖値、収縮期及び拡張期血圧、脂質プロファイル〔総コレステロール、高比重リポタンパク質（HDL）コレステロール、低比重リポタンパク質（LDL）コレステロール、トリグリセリド及び遊離脂肪酸〕、追加の血糖降下薬を要する被験者の割合、患者報告アウトカム（PRO）：質問票（SF-36v2^{TM}）スコア。

評価基準：安全性

以下の安全性の項目が評価対象となった：治験薬投与下で発現した有害事象〔Treatment Emergent Adverse Event（以下、有害事象とする）、外部の独立した判定委員会により判定される、事前に規定された MESI を含む〕、低血糖、脈拍数及び安全性に関する臨床検査項目。

統計手法：

被験者数は、各投与群の主要イベント発現率を年間 1.98%、脱落率を 10.0%以下、平均観察期間を 2.1 年、真のハザード比を 1.0 と仮定して算出した。これらの仮定に基づくと、122 例の主要アウトカムを発現した被験者を得るために計 3260 例の無作為割り付け例数が必要とされた。この場合、ハザード比が 1.8 超であることを棄却するための検出力は 90%であった。

解析対象集団

ICH-E9 ガイドラインに基づき、以下の解析対象集団が治験実施計画書で定義され、盲検解除前に統計解析計画書に明記された：

- 最大の解析対象集団〔full analysis set（FAS）〕：すべての無作為割り付けされた被験者が含まれた。

FASの統計的な評価はintention-to-treat（ITT）の原則に従い、FASに含まれた被験者は「as randomised（無作為割り付けされたとおりの）」評価に寄与した。

- 安全性解析対象集団〔safety analysis set（SAS）〕：治験薬の投与を少なくとも1回受けたすべての被験者が含まれた。SASに含まれた被験者は、治療期間の大部分において使用した治療薬に基づいた評価に寄与する。このことは、「as treated（治療されたとおりの）」の評価に寄与したことを意味する。

観察期間

本試験では以下の 2 つの観察期間を定義した：

In-trial 観察期間：被験者が試験参加者とみなされ、データが系統的に収集される観察期間であり、無作為割り付けの日から試験終了日までの期間とする。試験終了日とは、試験完了例においては計画された試験終了来院日又は死亡日のいずれか早い日であり、脱落例及び追跡不能例においては治験実施施設と最後のコンタクトを直接とった日として定義した。

On-treatment 観察期間：In-trial 期間の一部であり、被験者が治験薬に曝露されていると考えられる観察期間であり、治験薬の初回投与から各被験者の治療終了までの期間。治療終了とは、最終投与日の 5 週間後に予定される治療終了時事後調査来院日、最終投与日の 42 日後*、もしくは被験者の in-trial 期間の最終日のいずれか早い日として定義した〔*有効性エンドポイント及び安全性エンドポイント（心電図、判定された事象、有害事象、低血糖を除く）については、対象とする期間として、投与終了後 42 日間ではなく 7 日間が設定された〕。

主要解析

- プライマリーエンドポイントは、無作為割り付けから、最初のMACE（心血管死、非致死性心筋梗塞又は非致死性脳卒中と定義された）を発現するまでの時間であった。

主要解析は in-trial 観察期間を用いた FAS に基づいて行った。プライマリーエンドポイントは、治療（セマグルチド、プラセボ）を固定効果として、層別 Cox 比例ハザードモデルで解析した。このモデルでは、無作為割り付け時に用いられた 3 種類の層別因子によるすべての組み合わせ（計 9 層）で層別した。事象の発現がなかった被験者は in-trial 観察期間の終了時点で打ち切りとした。この解析は検証的解析と位置付けられた。

事前に規定したプライマリーエンドポイントの感度分析は、被験者集団の選択と曝露に対する打ち切りの規定を変更して行った。プライマリーエンドポイントの探索的解析は、in-trial 観察期間を用いた FAS に基づき、被験者背景及びベースライン時の疾患パラメータによるサブグループに基づいて行われた。各サブグループ解析では、プライマリーエンドポイントは、治療（セマグルチド、プラセボ）とサブグループの間の交互作用を固定効果として含めた非層別 Cox 比例ハザードモデルで解析した。

セカンダリーエンドポイントの解析

主要目的を検討する補足的セカンダリーエンドポイント：事象発現までの時間

以下の事象発現までの時間に関するセカンダリーエンドポイントを、主要目的を検討する補足的エンドポイントとした。

- 無作為割り付けから、最初の広義の複合的心血管アウトカムの発現までの時間。広義の心血管アウトカムはMACE、冠動脈及び末梢血行再建、入院を要する不安定狭心症、もしくは心不全による入院と定義した。
- 無作為割り付けから、広義の複合的心血管アウトカムのうち各疾患の発現までの時間。
- 無作為割り付けから、すべての死亡、非致死性心筋梗塞又は非致死性脳卒中の最初の発現までの時間。

末梢血行再建を除く以上のすべてのアウトカムはイベント判定委員会により確認された事象であった。末梢血行再建に関する基本語一覧は事後的に特定されたものであった。以上の事象における発現までの時間のエンドポイントは、プライマリーエンドポイントと同じ手法で解析した。

副次的目的を検討する有効性に関する検証的エンドポイント

以下の有効性に関するセカンダリーエンドポイントは検証的エンドポイントと位置付けられた。

- ベースラインから投与後104週までの体重の変化量（kg）

- ベースライン時に混合型インスリンを使用していた被験者のベースラインから投与後30週までのHbA1cの変化量
- ベースライン時にSU単独療法を受けていた被験者のベースラインから投与後30週までのHbA1cの変化量

これらの 3 つのエンドポイントにおいて、2 種類の仮説を検定した。

- セマグルチド1.0 mgのプラセボに対する優越性
- セマグルチド0.5 mgのプラセボに対する優越性

HbA1c 及び体重の変化量について、治療間差の推定値の両側 95%信頼区間の上限が、HbA1c 及び体重でそれぞれ 0%及び 0 kg を下回る場合に優越性が検証されることとした。これらの解析は in-trial 観察期間を用いた FAS に基づいて行った。エンドポイントは繰り返し測定に対する混合モデル（MMRM）を用いて解析した。解析では、予定来院時に得られたすべてのベースライン後の測定値を目的変数、治療（セマグルチド 0.5 mg、セマグルチド 1.0 mg 及びプラセボの 3 種類）及び層別因子（9 層）を固定効果、ならびにベースライン値を共変量として含み、すべての変数について来院内で入れ子にした。HbA1c の解析モデルでは、治療とサブグループ（SU 単独療法に関するサブグループ解析では 2 種類、インスリンに関するサブグループ解析では 3 種類）の間の交互作用を含めた。同一被験者内の測定値において無構造共分散行列を仮定した。有効性に関する検証的解析の安定性を評価するために様々な感度分析を行った。

副次的目的を検討する補足的セカンダリーエンドポイント：

有効性エンドポイント（連続変数）は以下のとおり。

- 以下の項目における、ベースラインから投与期間中の最終測定までの変化量
  - 体重
  - HbA1c及び空腹時血糖値
  - 脂質プロファイル（総コレステロール、HDLコレステロール、LDLコレステロール、トリグリセリド及び遊離脂肪酸）
  - 収縮期及び拡張期血圧
- SF-36v2^{TM}の患者報告アウトカム（PRO）スコアのベースラインから投与期間中の最終測定までの変化量

有効性に関する一連のエンドポイントは、in-trial 観察期間を用いた FAS に基づき、MMRM 法で解析された。解析モデルは、治療（セマグルチド 0.5 mg、セマグルチド 1.0 mg、プラセボ 0.5 mg 及びプラセボ 1.0 mg の 4 群）及び層別因子（9 層）を固定効果、該当するベースライン値を共変量として含め、すべての変数について来院内で入れ子にした。同一被験者内の測定値において無構造共分散行列を仮定した。感度分析として、in-trial 及び on-treatment の両期間における最終測定値の共分散分析モデルを用いた。

有効性エンドポイント（分類変数）：

- 追加の血糖降下薬の必要性（はい／いいえ）

このエンドポイントは、治療（セマグルチド 0.5 mg、セマグルチド 1.0 mg、プラセボ 0.5 mg 及びプラセボ 1.0 mg の 4 種類）及び層別因子（9 層）を固定効果、ベースラインの HbA1c を共変量として含め、ロジスティック回帰モデルを用いて解析した。この解析は in-trial 観察期間を用いた FAS に基づいて行った。

安全性に関するエンドポイント：事象発現までの時間（細小血管イベント）

- 無作為割り付けから、最初の糖尿病網膜症の発現までの時間。糖尿病網膜症の定義は、網膜光凝固又は硝子体内注射を要する状態、硝子体出血、糖尿病を原因とする失明〔視力が良い方の眼を最も矯正した状態にてスネレン視力表20/200（6/60）以下又は視野20度以下と定義〕と定めた。
- 無作為割り付けから、最初の腎症の新規発現又は悪化までの時間。腎症の定義は、持続的な微量アルブミン尿（300 mg/g超）の新規発現、血清クレアチニン値が継続して倍増し、かつMDRDで計算したクレアチニンクリアランスが45 mL/min/1.73m^{2}以下、継続的な腎代替療法を要する場合（急性の改善可能な原因を有する場合を除く）、又は腎疾患による死亡と定めた。

これらの事象の発現までの時間に関するエンドポイントは、プライマリーエンドポイントと同じ手法で解析した。

最初の糖尿病網膜症の発現までの時間に関して、被験者背景及びベースライン時の疾患のパラメータによ

るサブグループで、in-trial 観察期間を用いた FAS に基づき、事後的な探索的解析を行った。プライマリーエンドポイントのサブグループ解析に適用したものと同様の統計モデルを適用した。

さらに、糖尿病網膜症の最初の発現までの時間に対する血糖値の急激な変化の影響に関する事後的な媒介分析（mediator analysis）を行った。この分析では非層別 Cox 比例ハザードモデルを用いて解析した。モデルには、治療（セマグルチド、プラセボ）を固定効果、投与後 16 週の HbA1c の変化量（%）を共変量として含め、さらに HbA1c の低下の予測因子であり、糖尿病網膜症のリスクの予測因子と考えられる因子を含めた。その因子とは、ベースラインの HbA1c、ベースライン時の網膜症既往歴（はい／いいえ／不明）、及びベースライン時の糖尿病罹患期間であった。投与後 16 週の HbA1c の変化量が、血糖値の急激な変化を代表する媒介（mediator）として選択された。

その他の安全性に関するセカンダリーエンドポイント：

安全性に関するエンドポイントは、全般的に、in-trial 期間のデータを用いた FAS 及び on-treatment 期間のデータを用いた SAS に基づいて要約した。

ノボ ノルディスク社の Global Safety が事前に定義した基本語から構成される MedDRA 分類について、MedDRA Ver.18.0 に基づき評価した。低血糖は、ノボ ノルディスク社及び ADA の低血糖分類に従って分類した。脈拍、アミラーゼ、リパーゼ及び尿中アルブミン／クレアチニン比（UACR）は、ベースライン値を共変量として、有効性に関する一連のエンドポイントの解析と同様の MMRM 法で個別に解析した。すべての臨床検査値は記述統計量で要約して評価した。抗セマグルチド抗体は in-trial 観察期間を用いた FAS に基づき、治療ごとに記述的に要約した。

イベント判定委員会が確認した新生物の発現までの時間：

新生物の最初の発現までの時間の評価のために、プライマリーエンドポイントの解析で用いたモデルと同様の Cox 比例ハザードモデル（事後的）を用いた。すべての新生物、悪性度ごとの新生物及び発現臓器ごとの悪性新生物に対して個別に解析した。

被験者背景：

4 つの投与群（セマグルチド 0.5 mg、セマグルチド 1.0 mg、プラセボ 0.5 mg、プラセボ 1.0 mg）に割り付けられた被験者は、被験者背景及びベースライン時の特性に関してよく一致しており、セマグルチド及びプラセボについて以下のとおりであった。

被験者背景及びベースライン時特性（カテゴリー変数）– 要約 – FAS

	Sema		Placebo		Total	
	N	(%)	N	(%)	N	(%)
Number of subjects	1648		1649		3297	
Sex						
Female	635	(38.5)	660	(40.0)	1295	(39.3)
Male	1013	(61.5)	989	(60.0)	2002	(60.7)
Race						
White	1384	(84.0)	1352	(82.0)	2736	(83.0)
Black or African American	108	(6.6)	113	(6.9)	221	(6.7)
Asian	121	(7.3)	152	(9.2)	273	(8.3)
American Indian or Alaska Native	3	(0.2)	7	(0.4)	10	(0.3)
Native Hawaiian or Other Pacific Islander	3	(0.2)	0	(0.0)	3	(0.1)
Other	29	(1.8)	25	(1.5)	54	(1.6)
Ethnicity						
Hispanic or Latino	256	(15.5)	254	(15.4)	510	(15.5)
Not Hispanic or Latino	1392	(84.5)	1395	(84.6)	2787	(84.5)
Smoker status						
Current smoker	204	(12.4)	202	(12.2)	406	(12.3)
Never smoked	754	(45.8)	739	(44.8)	1493	(45.3)
Previous smoker	690	(41.9)	707	(42.9)	1397	(42.4)
Unknown			1	(0.1)	1	(0.0)
Renal impairment						
Normal	493	(29.9)	497	(30.1)	990	(30.0)
Mild	686	(41.6)	682	(41.4)	1368	(41.5)
Moderate	423	(25.7)	409	(24.8)	832	(25.2)
Severe	41	(2.5)	54	(3.3)	95	(2.9)

End stage	5 (0.3)	7 (0.4)	12 (0.4)
Insulin treatment			
None	692 (42.0)	692 (42.0)	1384 (42.0)
Basal insulin	515 (31.3)	531 (32.2)	1046 (31.7)
Premix insulin	441 (26.8)	426 (25.8)	867 (26.3)
SU monotherapy			
No	1589 (96.4)	1585 (96.1)	3174 (96.3)
Yes	59 (3.6)	64 (3.9)	123 (3.7)
Clinical evidence of CV disease			
No	295 (17.9)	267 (16.2)	562 (17.0)
Yes	1353 (82.1)	1382 (83.8)	2735 (83.0)

Sema: semaglutide, N: Number of subjects, %: Percentage of subjects, BMI: Body mass index, MDRD: Modification of diet in renal disease, eGFR: estimated glomerular filtration rate. Baseline information is defined as the measurement at the latest assessment before dosing. The renal function categories are based on the MDRD eGFR.

被験者背景及びベースライン時特性（連続型変数）– 要約 – FAS

	Sema Mean	(SD)	Placebo Mean	(SD)	Total Mean	(SD)
Age (years)	64.7	(7.2)	64.6	(7.5)	64.6	(7.4)
Body weight (kg)	92.33	(20.66)	91.86	(20.55)	92.09	(20.60)
Height (m)	1.675	(0.100)	1.671	(0.101)	1.673	(0.101)
Body mass index (kg/m2)	32.80	(6.23)	32.80	(6.16)	32.80	(6.20)
Waist circumference (cm)	110.1	(14.67)	110.3	(14.86)	110.2	(14.76)
HbA1c (%)	8.70	(1.45)	8.70	(1.47)	8.70	(1.46)
HbA1c (mmol/mol)	71.59	(15.90)	71.55	(16.11)	71.57	(16.01)
Fasting plasma glucose (mmol/L)	10.22	(3.72)	10.28	(3.65)	10.25	(3.68)
Fasting plasma glucose (mg/dL)	184.1	(67.06)	185.2	(65.68)	184.7	(66.37)
Duration of diabetes (years)	14.17	(8.20)	13.60	(8.02)	13.89	(8.11)
Diastolic BP (mmHg)	76.99	(10.00)	77.10	(10.04)	77.05	(10.02)
Systolic BP (mmHg)	136.0	(17.47)	135.3	(16.82)	135.6	(17.15)
Pulse rate (beats/min)	72.11	(11.05)	71.98	(10.77)	72.05	(10.91)
LDL-cholesterol, calculated (mmol/L)	2.32	(0.95)	2.33	(0.99)	2.33	(0.97)
LDL-cholesterol, calculated (mg/dL)	89.67	(36.84)	90.08	(38.13)	89.87	(37.49)
HDL-cholesterol (mmol/L)	1.18	(0.33)	1.17	(0.33)	1.17	(0.33)
HDL-cholesterol (mg/dL)	45.45	(12.72)	45.21	(12.61)	45.33	(12.66)
MDRD GFR 'estimated' (mL/min/1.73 m2)	75.88	(25.88)	76.39	(27.19)	76.13	(26.54)

Sema: semaglutide, SD: Standard deviation, MDRD: Modification of diet in renal disease, GFR: glomerular filtration rate. The baseline value is defined as the latest pre-dosing value. Body mass index is calculated based on baseline measurement of body weight and height.

事象発現までの時間に関する解析の結果：

MACE：

- イベント判定委員会により、セマグルチド投与後で1648例108件（6.6%）、プラセボ投与後で1649例146件（8.9%）のMACEが確認された。最初に発現したMACEの総件数（計254件）は、当初の計画数の2倍以上であった。
- プライマリーエンドポイントである、イベント判定委員会により確認されたMACEを最初に発現するまでの時間について、セマグルチドのプラセボに対する非劣性（主要仮説）は検証された（95%信頼区間の上限は1.8未満、P<0.0001）。セマグルチドの投与を受けた被験者は、プラセボの投与を受けた被験者と比較して、MACEアウトカム（プライマリーエンドポイント）のリスクが有意に低かった。ハザード比は0.74（95%信頼区間：0.58; 0.95）（p=0.0167）であり、これはリスクが26%低下したことを示している。セマグルチドの各用量群（0.5 mg及び1.0 mg）においても同様のリスク低下が認められた。
- MACEの各疾患については、非致死性心筋梗塞及び非致死性脳卒中のハザード比の結果はそれぞれ0.74（95%信頼区間：0.51; 1.08）及び0.61（95%信頼区間：0.38; 0.99）、p=0.1194及びp=0.0438であった。この結果はMACEに対するセマグルチドの全般的に有益な治療効果を示した。心血管死の発現については、セマグルチド及びプラセボで同様であった〔ハザード比0.98（95%信頼区間0.65; 1.48）、（p=0.9181）〕。

- すべての感度分析から主要解析の結果は裏付けられた。
- MACEに対する効果について、いずれの部分集団においても違いは認められなかった。

その他の複合的な心血管エンドポイント：

- すべての死亡、非致死性心筋梗塞、非致死性脳卒中で構成される、複合的な心血管エンドポイントについて、セマグルチドはプラセボと比較して発現リスクを23%低下させ、その違いは有意であった〔ハザード比0.77（95%信頼区間：0.61; 0.97）〕。
- MACE、血行再建、入院を要する不安定狭心症及び心不全による入院で構成される、広義の複合的心血管エンドポイントについて、セマグルチドはプラセボと比較して発現リスクを26%低下させ、その違いは有意であった〔ハザード比0.74（95%信頼区間：0.62; 0.89）〕。

心血管エンドポイントの各疾患：

- 複合的心血管エンドポイントの各疾患におけるハザード比（推定値）とその95%信頼区間は以下のとおり；心血管死：0.98（95%信頼区間：0.65; 1.48）、非致死性心筋梗塞：0.74（95%信頼区間：0.51; 1.08）、非致死性脳卒中：0.61（95%信頼区間：0.38; 0.99）、すべての死亡：1.05（95%信頼区間：0.74; 1.50）、血行再建：0.65（95%信頼区間：0.50; 0.86）、入院を要する不安定狭心症：0.82（95%信頼区間：0.47; 1.44）、心不全による入院：1.11（95%信頼区間：0.77; 1.61）

細小血管エンドポイント：

- イベント判定委員会で確認された糖尿病網膜症について、プラセボ（1.8 %）と比較してセマグルチド（3.0%）でリスクが有意に増加した〔ハザード比：1.76（95%信頼区間：1.11; 2.78）〕。治療間差は試験の初期から認められ、試験期間中継続してみられた。糖尿病網膜症の既往歴を有さない被験者ではリスクの増加はみられなかった。イベント判定委員会で確認された糖尿病網膜症を試験期間中に発現した被験者の大部分は、糖尿病網膜症の既往歴があり、ベースライン時での糖尿病罹患期間が長く、ベースラインのHbA1cが高く、インスリンを使用していた。糖尿病網膜症のリスク増加は、プラセボよりセマグルチドで初期にHbA1cがより急激に低下したことが影響していると考えられた。
- 腎症の新規発現又は悪化のリスクは、プラセボと比較してセマグルチドで有意に低かった〔ハザード比0.64（95%信頼区間：0.46; 0.88）〕。腎症の発現リスク低下は、主に「持続的顕性アルブミン尿の新規発現」によるものであった。
- 糖尿病網膜症あるいは腎症の新規発現又は悪化のいずれかの発現までの時間はセカンダリーエンドポイントであった。ハザード比（推定値）は0.86（95%信頼区間：0.66; 1.12）であった。

有効性の結果：

検証的セカンダリーエンドポイント - 投与後 104 週の体重の変化量

- ベースラインから投与後104週までの体重の減少量について、セマグルチド0.5 mg群及び1.0 mg群の、プラセボ併合群に対する優越性が示された。群差の推定値はセマグルチド0.5 mgで-2.95 kg（95%信頼区間：-3.47; -2.44）、セマグルチド1.0 mgで-4.27 kg（95%信頼区間：-4.78; -3.75）であった。ベースライン平均値が92.09 kgであった体重は、投与後104週には、プラセボ併合群（0.62 kg）と比較してセマグルチド0.5 mg群（3.57 kg）及び1.0 mg群（4.88 kg）で大きく減少した。
- 本解析結果の安定性は3つの感度分析により裏付けられた。感度分析から得られた群差の推定値は有意であり、主要解析結果と同程度であった。

検証的セカンダリーエンドポイント – 投与後 30 週の HbA1c の変化量

- サブグループ（ベースライン時の治療：SU単独療法又は混合型インスリン）におけるベースラインから投与後30週のHbA1cの低下量について、セマグルチド0.5 mg群及び1.0 mg群のプラセボ併合群に対する優越性が示された。
  - ベースライン時にSUによる単独療法を受けていた被験者：セマグルチド0.5 mg及び1.0 mgのプラセボ群と比較した群差の推定値は、それぞれ-1.74%（95%信頼区間：-2.28; -1.19）及び-1.64%（95%信頼区間：-2.16; -1.12）であった。
  - ベースライン時に混合型インスリンを使用していた被験者：セマグルチド0.5 mg及び1.0 mgのプラセボとの群差の推定値は、それぞれ-0.86%（95%信頼区間：-1.06; -0.66）及び-1.37%（95%信頼区間：-1.57; -1.17）であった。

- それぞれのサブグループに対する結果（検証的セカンダリーエンドポイントの結果）の安定性は、5つの異なる感度分析により裏付けられた。感度分析から得られた群差の推定値は有意であり、主要解析結果と同程度であった。

有効性に関する補足的セカンダリーエンドポイント：

投与後 104 週の HbA1c：

- 投与後104週におけるHbA1cは、プラセボ（0.5 mgで-0.44%、1.0 mgで-0.36%）と比較してセマグルチド（0.5 mgで-1.09%、1.0 mgで-1.41%）で大きく低下した。セマグルチド0.5 mg及び1.0 mgでは同用量のプラセボと比較して、HbA1cの有意な低下を示した。セマグルチド0.5 mg群及び1.0 mg群の、同用量のプラセボ各用量群との群差の推定値は、それぞれ-0.66%（95%信頼区間：-0.80; -0.52）及び-1.05%（95%信頼区間：-1.19; -0.91）であった。

追加の血糖降下薬の必要性：

- 投与後104週において、目標血糖値を達成するために試験期間中に追加の血糖降下薬を必要とした被験者の割合は、プラセボ（0.5 mgで42%、1.0 mgで39%）と比較してセマグルチド（0.5 mgで21%、1.0 mgで19%）で低かった。セマグルチド0.5 mg群及び1.0 mg群のプラセボ各用量群とのオッズ比の推定値は、それぞれ0.33（95%信頼区間：0.27; 0.42）及び0.35（95%信頼区間：0.27; 0.44）であった。
- サブグループ（混合型インスリン又はSU単独療法）における投与後30週時点の血糖降下薬の追加について、セマグルチド投与の効果は認められなかった。
  - ベースライン時に混合型インスリンを使用していた被験者で血糖降下薬を追加した割合は、3群いずれにおいても低く、プラセボ併合群（4.7%）と比較してセマグルチド0.5 mg群（6.3%）又は1.0 mg群（3.7%）の間に有意な差はみられなかった。
  - ベースライン時にSUによる単独療法を受けていた被験者で血糖降下薬を追加した割合は、プラセボ併合群（31.3%）と比較してセマグルチド0.5 mg群（3.6%）で有意に低く、セマグルチド1.0 mg群（12.9%）で低い傾向がみられた。

糖代謝：

- 空腹時血糖値は、ベースラインから投与後104週にかけてプラセボの各用量群と比較してセマグルチド0.5 mg群及び1.0 mg群で有意に低下した。プラセボとの群差の推定値はセマグルチド0.5 mg及び1.0 mgでそれぞれ-0.72 mmol/L（95%信頼区間：-1.06; -0.38）及び-1.22 mmol/L（95%信頼区間：-1.56; -0.88）〔-13.05 mg/dL（95%信頼区間：-19.17; -6.94）及び-22.03 mg/dL（95%信頼区間：-28.15; -15.91）〕であった。

脂質：

- 全般的に、変化量はわずかであったが、プラセボ1.0 mgと比較してセマグルチド1.0 mgで血中脂質が改善された。
  - 投与後104週における遊離脂肪酸、HDLコレステロール及びトリグリセリドの値は、プラセボ1.0 mgと比較してセマグルチド1.0 mgで有意な改善がみられた。比の推定値はそれぞれ0.92（95%信頼区間：0.88; 0.96）、1.04（95%信頼区間：1.02; 1.06）及び0.93（95%信頼区間：0.89; 0.97）であった。一方、総コレステロール及びLDLコレステロールについて有意差は認められなかった。
  - 投与後104週における総コレステロール及びLDLコレステロールの値は、プラセボ0.5 mgと比較してセマグルチド0.5 mgで有意な改善がみられた。比の推定値はそれぞれ0.97（95%信頼区間：0.95; 1.00）及び0.96（95%信頼区間：0.93; 0.99）であった。一方、遊離脂肪酸、HDLコレステロール及びトリグリセリドについて有意差は認められなかった。

血圧：

- 投与後104週における収縮期血圧は、プラセボ1.0 mgと比較してセマグルチド1.0 mgで有意な低下を示した。群差の推定値は-2.59 mmHg（95%信頼区間：-4.09; -1.08）であった。一方、セマグルチド0.5 mgとプラセボ0.5 mgの間に有意な差は認められなかった。
- 拡張期血圧の変化量についてプラセボとセマグルチドの間で有意差は認められなかった。

PRO：

- SF-36v2^{TM}の精神的側面及び身体的側面のQOLサマリースコアについて、プラセボ1.0 mgと比較してセ

マグルチド1.0 mgで有意な改善がみられた。一方、セマグルチド0.5 mgとプラセボ0.5 mgの間に有意な差は認められなかった。

安全性の結果：

104 週間の投与期間中、セマグルチドは概ね安全で忍容性も良好であり、概してその安全性と忍容性は他の GLP-1 受容体作動薬と一致していた。

全体的な有害事象プロファイル

- 試験期間中（無作為割り付けからデータベースロックまで）に計132例が死亡した。このうち122例（3.7%）はイベント判定委員会により定められた2年間のin-trial期間中に死亡し、残りの10例（セマグルチドで5例、プラセボで5例）はin-trial期間終了後からデータベースロックまでの間に死亡した。in-trial期間中に死亡した122例のうち90例は心血管死（心血管死と確認された死亡及び原因が特定できない死亡を含む）と分類された。単位時間あたりの死亡件数はセマグルチド0.5 mg群、1.0 mg群及びプラセボ群でそれぞれ1.2、1.4及び1.4件／100人･年であった。in-trial期間の死亡のうち残りの32例は非心血管死と判定され、単位時間あたりの死亡件数はセマグルチド0.5 mg群、1.0 mg群及びプラセボ群でそれぞれ0.5、0.5及び0.4件／100人･年であった。転帰「死亡」の有害事象の種類は、セマグルチドとプラセボで同様であった。
- 有害事象を発現した被験者の割合は、セマグルチドとプラセボで同様であった（セマグルチド0.5 mgで88.9%、セマグルチド1.0 mgで88.2%及びプラセボで88.4%）。一方、単位時間あたりの発現件数は、プラセボ（313.2件／100人・年）と比較してセマグルチド（0.5 mgで334.7件／100人・年、1.0 mgで350.2件／100人・年）で多かった。この差は主にプラセボと比較してセマグルチドで胃腸障害の有害事象の報告件数が多かったことに起因していた。
- 有害事象の大部分は軽度又は中等度であり、有害事象を発現した被験者の大部分は試験終了時には回復又は軽快した。
- 最も高頻度で報告された有害事象は、セマグルチド投与後では器官別大分類の胃腸障害（悪心、嘔吐、下痢）であった一方、プラセボ投与後では器官別大分類の感染症及び寄生虫症に分類される有害事象であった。
- 重篤な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で低かった（セマグルチド0.5 mg、1.0 mg及びプラセボでそれぞれ32.1%、29.3%及び34.9%）。重篤な胃腸障害を発現した被験者の割合のみが、プラセボと比較してセマグルチドで高かった。報告された重篤な有害事象について、投与群及び基本語を通じてこのほかに一定の傾向はみられなかった。心血管アウトカムを評価する本試験に登録した被験者集団から予想されたとおり、いずれの投与群でも器官別大分類のうち心臓障害に分類される重篤な有害事象が最も高頻度に報告された。
- 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（6.7%）と比較してセマグルチド（0.5 mgで11.5%、1.0 mgで14.5%）で高かった。この差は主に最初の20週間に発現した胃腸障害の有害事象によるものであった。投与後30～35週における、投与の中止に至った有害事象の発現頻度は、すべての投与群で同様であった。
- セマグルチド1.0 mgで胃腸障害の有害事象の発現件数は増加したものの、全体的な有害事象プロファイルに違いはみられなかった。

低血糖

- いずれの投与群でも、約20%の被験者が1件以上の重大な又は血糖値確定症候性低血糖を発現した。
- 重大な又は血糖値確定症候性低血糖（夜間低血糖を含む）の発現件数及び発現した被験者数について、セマグルチドとプラセボの間に統計的な有意差はみられなかった。
- 重大な低血糖の報告はわずか（計68件）であり、その分布は各投与群で均等にみられた。発現したすべての被験者は重大な低血糖から回復した。
- 概して、いずれの投与群でも、重大な又は血糖値確定症候性低血糖の大部分において、発現時の背景治療はSU及び／又はインスリンであった。

注目すべき安全性領域

胃腸障害の有害事象

- 胃腸障害の有害事象の単位時間あたりの発現件数は、プラセボと比較してセマグルチド0.5 mg及び1.0 mgで多かった（セマグルチド0.5 mg、1.0 mg及びプラセボでそれぞれ81.2、94.9及び40.5件／100人・年）。最も高頻度（被験者の5%以上）で報告された有害事象は、悪心、下痢、嘔吐、便秘、消化不良、上腹部痛及び腹痛であった。これらの大部分は非重篤であり、軽度又は中等度であった。
- 有害事象の大部分が投与後の最初の3～4ヵ月の間に発現し、胃腸障害の有害事象（悪心、下痢及び嘔吐）の平均発現期間は3群（セマグルチド0.5 mg群、セマグルチド1.0 mg群及びプラセボ群）いずれにおいても2～7日間であった。

心血管系事象

- イベント判定委員会により確認されたすべての心血管イベント及びMedDRA検索で特定されたすべての心血管系事象に関する結果は、（イベント判定委員会により確認された）心血管イベントの初回発現までの時間に関する解析に基づく結論を裏付けた。
- ベースラインから投与終了時までの脈拍数は、プラセボと比較してセマグルチド0.5 mg及び1.0 mgで有意に増加した。プラセボとの群差の推定値はセマグルチド0.5 mg及び1.0 mgでそれぞれ2.75拍／分（95%信頼区間：1.75; 3.75）及び3.20拍／分（95%信頼区間：2.20; 4.21）であった。

膵炎

- イベント判定委員会により確認された膵炎の件数は、セマグルチドとプラセボの間で同様であった（セマグルチド0.5 mg、1.0 mg及びプラセボでそれぞれ5件、3件及び10件であった）。
- 投与終了時（104週）におけるリパーゼ及びアミラーゼのベースラインに対する比の推定値は、プラセボと比較してセマグルチドの両用量で有意に高かった〔リパーゼ及びアミラーゼについてそれぞれセマグルチド0.5 mgで1.26（95%信頼区間：1.20; 1.32）及び1.11（95%信頼区間：1.08; 1.14）、セマグルチド1.0 mgで1.32（95%信頼区間：1.26; 1.39）及び1.17（95%信頼区間：1.13; 1.20）であった〕。これらの所見の臨床的な意味は現時点では不明である。
- リパーゼ及び／又はアミラーゼが基準範囲上限の3倍超であったごく少数の被験者がイベント判定委員会により確認された膵炎を発現した。膵炎の確定診断と裏付けとなるリパーゼ及び／又はアミラーゼの上昇との関連はよく知られているが、今回のこの結果からセマグルチド投与後にみられた膵酵素の増加が膵炎の発症につながることは裏付けられなかった。

肝胆道系障害

- 胆嚢に関連する有害事象（セマグルチド0.5 mg、1.0 mg及びプラセボでそれぞれ3.5%、3.2%及び3.4%）及び重篤な有害事象（セマグルチド0.5 mg、1.0 mg及びプラセボでそれぞれ1.3%、0.5%及び1.2%）を発現した被験者の割合は、投与群間で同様であった。セマグルチドで最も高頻度で報告された胆嚢に関連する有害事象は胆石症であった。そのうちの数件は重篤又は重度であり、そのような事象を発現した被験者の割合はセマグルチドとプラセボの間で同様であった。
- 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倍超又は5倍超であった被験者数は、セマグルチド（0.5 mg及び1.0 mg）及びプラセボで同様に低かった。また、6例の被験者でALTとASTの基準範囲上限の3倍超及び総ビリルビンの基準範囲上限2倍超の併発（セマグルチド0.5 mg、1.0 mg及びプラセボでそれぞれ1例、2例及び3例）がみられた。これらのいずれの被験者においても肝臓関連パラメータの変化について説明できる妥当な理由があり、FDAのガイダンスによるとこれらの変化は薬剤が誘発した肝臓損傷に当てはまらなかった。

新生物

- イベント判定委員会により確認された新生物（全般）を発現した被験者は、セマグルチドで9.4%及びプラセボで8.4%であった。イベント判定委員会により確認された良性新生物を発現した被験者の割合は、セマグルチドで5.7%及びプラセボで4.2%であり、悪性新生物を発現した被験者の割合は、セマグルチドで4.0%及びプラセボで4.2%であった。事後解析の結果、イベント判定委員会により確認された新生物について、投与群を通じてセマグルチドとプラセボの間に明らかな差が認められなかった。
- イベント判定委員会により確認された新生物を発現した被験者数は、セマグルチド0.5 mg及びプラセボと比較してセマグルチド1.0 mgでわずかに多かった。この所見は、MedDRA検索で特定された新生物でも一致している。

- セマグルチド1.0 mgで良性新生物を発現した被験者の割合が高く、単位時間あたりの発現件数が多かったことは、主に直腸及び皮膚における新生物の発現に起因していた。
- 最も高頻度で報告された悪性新生物は、皮膚、男性生殖器、肺／気管支及び直腸に関する事象であった。イベント判定委員会に確認された悪性新生物は全般的に複数の臓器／組織部位にわたってみられ、特定の臓器に多くみられるという傾向はなかった。
- 本試験でC細胞に関する新生物は報告されなかった。
- カルシトニン値について、投与期間を通じて投与群内又は投与群間で臨床的に問題となる変化は認められなかった。
- 甲状腺、膵臓及び直腸に関する悪性新生物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とプラセボの間で同様であった。
- 件数が少ないため解釈には注意が必要であるが、セマグルチド1.0 mgで悪性新生物を発現した被験者の割合は比較的高く、それは主に皮膚の新生物によるものであった。
- 事後解析の結果、イベント判定委員会により確認された悪性新生物について、いずれの種類の事象においても投与群間で明らかな差は認められなかった。

腎障害

- 急性腎不全（広域のMedDRA検索による）の有害事象及び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0.5 mg（8.0%及び2.1%）とプラセボ（7.7%及び2.1%）の間で同様であった。これらの2群と比較してセマグルチド1.0 mg（4.9%及び1.1%）では発現頻度が低かった。最も高頻度で報告された重篤な有害事象は急性腎不全であったが、重篤な急性腎不全もセマグルチド0.5 mg及びプラセボと比較してセマグルチド1.0 mgで少なかった。
- 特にベースライン時に腎機能が正常であった被験者又は腎機能障害が軽度であった被験者では、セマグルチド投与によって推算糸球体濾過量（eGFR）値が初期に低下した。プラセボ投与後のeGFR値は、セマグルチドと比較して試験期間中より一定で、より高い割合で低下した。投与後104週におけるeGFR値は投与群間で有意な違いはみられなかった。

抗セマグルチド抗体

- 抗セマグルチド抗体の産生は低かった。ベースライン後のいずれかの時点の採血で、30例（1.9%）が抗セマグルチド抗体陽性であった。その内訳は、セマグルチド0.5 mg群で11例（1.4%）及びセマグルチド1.0 mg群で19例（2.3%）であった。抗セマグルチド抗体を有していた被験者のうち、19例（63.3%）が内因性GLP-1に対する交叉反応を有していた。抗セマグルチド抗体陽性の被験者における抗セマグルチド抗体価は低かった。個々の抗価の範囲は最大で12.97%（全放射能に対する結合放射能の割合）であった。事後調査来院では、4例（0.3%）が抗セマグルチド抗体陽性であったが、セマグルチドに対する中和作用をもつ抗セマグルチド抗体又は内因性GLP-1に対する中和作用を有する抗セマグルチド抗体はみられなかった。抗セマグルチド抗体陽性であった被験者のHbA1cの経時的変化から、抗セマグルチド抗体はセマグルチドの効果に影響を及ぼさないと考えられた。

全体の結論：

本試験では、被験者の 99.6%の生存状態が確認され、MACE におけるセマグルチドのプラセボに対する非劣性を示す（リスクが 80%増加することを否定したことに基づく）という主要目的が達成された。

- セマグルチドはプラセボと比較してMACEの発現リスクを26%低下させ、その違いは有意であった。
  - MACE発現リスクの低下は非致死性脳卒中及び非致死性心筋梗塞のリスク低下に起因していた。
- 本試験では、投与後2年においてプラセボと比較してセマグルチドで血糖コントロールの有意な改善が認められ、体重の低下について優越性が認められた。
  - サブグループ（ベースライン時の治療：SU単独療法又は混合型インスリン）におけるベースラインから30週のHbA1cの低下量について、セマグルチド0.5 mg及び1.0 mgのプラセボに対する優越性が示された。
  - 目標血糖値を達成するために追加の血糖降下薬を必要とした被験者数は、プラセボと比較してセマグルチドで有意に少なかった。
- 細小血管合併症の観点では、試験期間中にイベント判定委員会により確認された糖尿病網膜症のリスクは、プラセボと比較してセマグルチドで増加した。治療間差は試験中の初期から認められ、その後試験期間中継続してみられた。糖尿病網膜症の既往歴を有さない被験者では、リスクの増加はみられなかった。試験期間中にイベント判定委員会により確認された糖尿病網膜症を発現した被験者の大部分は、糖尿病網膜症の既往歴を有しており、ベースライン時での糖尿病罹患期間が長く、ベースラインのHbA1cが高く、インスリンを使用していた。糖尿病網膜症のリスク増加は、プラセボよりセマグルチドで多くみられたように初期にHbA1cがより急激に低下したことが影響していると考えられる。対照的に、セマグルチド投与によって腎症の発現リスクは有意に低下した。
- セマグルチドの忍容性は全般的に良好であった。糖尿病網膜症のリスク増加がみられたことを除き、セマグルチドの全般的な安全性プロファイルは他のGLP-1受容体作動薬における既知のクラス効果と一致していた。また、心血管系疾患発症リスクが高い被験者集団に対して、標準治療にセマグルチド投与を追加することにより、プラセボと比較してMACE発現リスクを低下させるという注目すべき特徴を有していた。

本試験は、ヘルシンキ宣言の精神（2013）、GCP に関する ICH ガイドライン（1996）、EN ISO 1455 Part1 及び Part2 ならびに FDA 21 CFR 312.120 を遵守して実施された。

2.7.6.25.2. 有害事象

表 2.7.6.25.2- 1 有害事象（器官別大分類、高位グループ語及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	823				819				819				825			
Exposure time (year)	1488.3				1443.9				1508.0				1526.8			
Events	732	(88.9)	4981	334.7	722	(88.2)	5056	350.2	730	(89.1)	4822	319.8	723	(87.6)	4684	306.8
胃腸障害	415	(50.4)	1208	81.2	426	(52.0)	1370	94.9	282	(34.4)	634	42.0	282	(34.2)	596	39.0
消化管徴候および症状	282	(34.3)	660	44.3	320	(39.1)	818	56.7	177	(21.6)	282	18.7	152	(18.4)	272	17.8
悪心	142	(17.3)	227	15.3	178	(21.7)	277	19.2	61	(7.4)	77	5.1	66	(8.0)	94	6.2
嘔吐	84	(10.2)	122	8.2	119	(14.5)	169	11.7	44	(5.4)	53	3.5	33	(4.0)	42	2.8
消化不良	51	(6.2)	67	4.5	63	(7.7)	87	6.0	20	(2.4)	22	1.5	18	(2.2)	19	1.2
腹痛	45	(5.5)	53	3.6	34	(4.2)	40	2.8	32	(3.9)	36	2.4	32	(3.9)	37	2.4
上腹部痛	33	(4.0)	35	2.4	42	(5.1)	52	3.6	20	(2.4)	23	1.5	18	(2.2)	31	2.0
腹部不快感	35	(4.3)	77	5.2	38	(4.6)	91	6.3	22	(2.7)	32	2.1	13	(1.6)	20	1.3
腹部膨満	17	(2.1)	23	1.5	24	(2.9)	28	1.9	14	(1.7)	18	1.2	8	(1.0)	8	0.5
放屁	13	(1.6)	21	1.4	26	(3.2)	32	2.2	10	(1.2)	11	0.7	5	(0.6)	6	0.4
おくび	10	(1.2)	13	0.9	19	(2.3)	21	1.5	0				0			
嚥下障害	7	(0.9)	7	0.5	3	(0.4)	3	0.2	2	(0.2)	2	0.1	3	(0.4)	3	0.2
下腹部痛	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	5	(0.6)	5	0.3
心窩部不快感	3	(0.4)	4	0.3	3	(0.4)	4	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1
変色便	0				0				3	(0.4)	3	0.2	2	(0.2)	2	0.1
レッチング	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
呼気臭	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
軟便	3	(0.4)	3	0.2	0				0				0			
胃腸音異常	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
硬便	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
消化器痛	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
吐き戻し	1	(0.1)	1	0.1	1	(0.1)	2	0.1	0				0			
キライディティ症候群	1	(0.1)	1	0.1	0				0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	1642				1644				3286			
Exposure time (year)	2932.2				3034.8				5967.0			
Events	1454	(88.6)	10037	342.3	1453	(88.4)	9506	313.2	2907	(88.5)	19543	327.5
胃腸障害	841	(51.2)	2578	87.9	564	(34.3)	1230	40.5	1405	(42.8)	3808	63.8
消化管徴候および症状	602	(36.7)	1478	50.4	329	(20.0)	554	18.3	931	(28.3)	2032	34.1
悪心	320	(19.5)	504	17.2	127	(7.7)	171	5.6	447	(13.6)	675	11.3
嘔吐	203	(12.4)	291	9.9	77	(4.7)	95	3.1	280	(8.5)	386	6.5
消化不良	114	(6.9)	154	5.3	38	(2.3)	41	1.4	152	(4.6)	195	3.3
腹痛	79	(4.8)	93	3.2	64	(3.9)	73	2.4	143	(4.4)	166	2.8
上腹部痛	75	(4.6)	87	3.0	38	(2.3)	54	1.8	113	(3.4)	141	2.4
腹部不快感	73	(4.4)	168	5.7	35	(2.1)	52	1.7	108	(3.3)	220	3.7
腹部膨満	41	(2.5)	51	1.7	22	(1.3)	26	0.9	63	(1.9)	77	1.3
放屁	39	(2.4)	53	1.8	15	(0.9)	17	0.6	54	(1.6)	70	1.2
おくび	29	(1.8)	34	1.2	0				29	(0.9)	34	0.6
嚥下障害	10	(0.6)	10	0.3	5	(0.3)	5	0.2	15	(0.5)	15	0.3
下腹部痛	4	(0.2)	4	0.1	6	(0.4)	6	0.2	10	(0.3)	10	0.2
心窩部不快感	6	(0.4)	8	0.3	2	(0.1)	2	0.1	8	(0.2)	10	0.2
変色便	0				5	(0.3)	5	0.2	5	(0.2)	5	0.1
レッチング	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
呼気臭	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
軟便	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
胃腸音異常	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
硬便	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
消化器痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
吐き戻し	2	(0.1)	3	0.1	0				2	(0.1)	3	0.1
キライディティ症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
異常便	0				0				0				1	(0.1)	1	0.1
空気嚥下	0				1	(0.1)	1	0.1	0				0			
消化管壁肥厚	0				0				0				1	(0.1)	1	0.1
白色便	1	(0.1)	1	0.1	0				0				0			
腹部圧痛	0				0				1	(0.1)	1	0.1	0			
腹部硬直	0				0				0				1	(0.1)	1	0.1
腹部腫瘤	0				1	(0.1)	1	0.1	0				0			
噴出性嘔吐	0				1	(0.1)	1	0.1	0				0			
糞塊	0				1	(0.1)	1	0.1	0				0			
消化管運動および排泄障害	207	(25.2)	379	25.5	233	(28.4)	391	27.1	130	(15.9)	211	14.0	124	(15.0)	168	11.0
下痢	145	(17.6)	274	18.4	145	(17.7)	242	16.8	94	(11.5)	155	10.3	83	(10.1)	109	7.1
便秘	46	(5.6)	52	3.5	78	(9.5)	96	6.6	33	(4.0)	38	2.5	36	(4.4)	38	2.5
胃食道逆流性疾患	30	(3.6)	38	2.6	35	(4.3)	39	2.7	10	(1.2)	10	0.7	13	(1.6)	14	0.9
過敏性腸症候群	8	(1.0)	8	0.5	3	(0.4)	3	0.2	1	(0.1)	1	0.1	5	(0.6)	5	0.3
胃排出不全	3	(0.4)	3	0.2	4	(0.5)	4	0.3	0				2	(0.2)	2	0.1
糖尿病性胃不全麻痺	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
排便回数増加	0				0				3	(0.4)	3	0.2	0			
十二指腸胃逆流	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
消化管運動障害	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
排便回数減少	0				2	(0.2)	2	0.1	0				0			
便習慣変化	0				2	(0.2)	2	0.1	0				0			
胃食道括約筋機能不全	0				0				1	(0.1)	1	0.1	0			
消化管運動過剰	1	(0.1)	1	0.1	0				0				0			
食道運動障害	1	(0.1)	1	0.1	0				0				0			
麻痺性イレウス	1	(0.1)	1	0.1	0				0				0			
消化管炎症性疾患	33	(4.0)	37	2.5	32	(3.9)	41	2.8	27	(3.3)	31	2.1	24	(2.9)	27	1.8
胃炎	17	(2.1)	17	1.1	22	(2.7)	24	1.7	10	(1.2)	11	0.7	10	(1.2)	10	0.7
慢性胃炎	6	(0.7)	6	0.4	4	(0.5)	4	0.3	9	(1.1)	9	0.6	5	(0.6)	5	0.3
十二指腸炎	2	(0.2)	2	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1	4	(0.5)	4	0.3

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
異常便	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
空気嚥下	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管壁肥厚	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
白色便	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹部圧痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腹部硬直	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腹部腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
噴出性嘔吐	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糞塊	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管運動および排泄障害	440	(26.8)	770	26.3	254	(15.5)	379	12.5	694	(21.1)	1149	19.3
下痢	290	(17.7)	516	17.6	177	(10.8)	264	8.7	467	(14.2)	780	13.1
便秘	124	(7.6)	148	5.0	69	(4.2)	76	2.5	193	(5.9)	224	3.8
胃食道逆流性疾患	65	(4.0)	77	2.6	23	(1.4)	24	0.8	88	(2.7)	101	1.7
過敏性腸症候群	11	(0.7)	11	0.4	6	(0.4)	6	0.2	17	(0.5)	17	0.3
胃排出不全	7	(0.4)	7	0.2	2	(0.1)	2	0.1	9	(0.3)	9	0.2
糖尿病性胃不全麻痺	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
排便回数増加	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
十二指腸胃逆流	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
消化管運動障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
排便回数減少	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
便習慣変化	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
胃食道括約筋機能不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
消化管運動過剰	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
食道運動障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
麻痺性イレウス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管炎症性疾患	65	(4.0)	78	2.7	51	(3.1)	58	1.9	116	(3.5)	136	2.3
胃炎	39	(2.4)	41	1.4	20	(1.2)	21	0.7	59	(1.8)	62	1.0
慢性胃炎	10	(0.6)	10	0.3	14	(0.9)	14	0.5	24	(0.7)	24	0.4
十二指腸炎	6	(0.4)	6	0.2	6	(0.4)	6	0.2	12	(0.4)	12	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
大腸炎	6	(0.7)	6	0.4	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
胃十二指腸炎	0				2	(0.2)	2	0.1	0				3	(0.4)	3	0.2
小腸炎	2	(0.2)	2	0.1	1	(0.1)	2	0.1	1	(0.1)	1	0.1	0			
食道炎	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
逆流性胃炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
出血性胃炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
潰瘍性大腸炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
クローン病	0				0				0				1	(0.1)	1	0.1
胃腸の炎症	0				0				1	(0.1)	1	0.1	0			
虚血性大腸炎	0				0				0				1	(0.1)	1	0.1
出血性腸炎	0				0				0				1	(0.1)	1	0.1
出血性直腸炎	0				0				1	(0.1)	1	0.1	0			
腸炎	0				0				0				1	(0.1)	1	0.1
腸間膜脂肪織炎	1	(0.1)	1	0.1	0				0				0			
肥厚性胃炎	0				0				1	(0.1)	1	0.1	0			
歯牙および歯肉の状態	19	(2.3)	21	1.4	15	(1.8)	17	1.2	19	(2.3)	24	1.6	20	(2.4)	24	1.6
歯痛	12	(1.5)	14	0.9	8	(1.0)	10	0.7	14	(1.7)	19	1.3	11	(1.3)	14	0.9
齲歯	3	(0.4)	3	0.2	3	(0.4)	3	0.2	3	(0.4)	3	0.2	7	(0.8)	7	0.5
歯周病	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
歯の脱落	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
埋伏歯	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
歯の障害	1	(0.1)	1	0.1	0				0				0			
歯槽骨吸収	0				0				1	(0.1)	1	0.1	0			
歯肉出血	0				1	(0.1)	1	0.1	0				0			
歯肉痛	0				1	(0.1)	1	0.1	0				0			
非感染性歯肉炎	0				0				0				1	(0.1)	1	0.1
変色歯	0				1	(0.1)	1	0.1	0				0			
良性消化管新生物	11	(1.3)	11	0.7	16	(2.0)	20	1.4	12	(1.5)	13	0.9	13	(1.6)	15	1.0
大腸ポリープ	8	(1.0)	8	0.5	11	(1.3)	13	0.9	9	(1.1)	9	0.6	8	(1.0)	10	0.7

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
大腸炎	8	(0.5)	8	0.3	3	(0.2)	3	0.1	11	(0.3)	11	0.2
胃十二指腸炎	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
小腸炎	3	(0.2)	4	0.1	1	(0.1)	1	<0.1	4	(0.1)	5	0.1
食道炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
逆流性胃炎	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
出血性胃炎	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
潰瘍性大腸炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
クローン病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胃腸の炎症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
虚血性大腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性直腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸間膜脂肪織炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肥厚性胃炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯牙および歯肉の状態	34	(2.1)	38	1.3	39	(2.4)	48	1.6	73	(2.2)	86	1.4
歯痛	20	(1.2)	24	0.8	25	(1.5)	33	1.1	45	(1.4)	57	1.0
齲歯	6	(0.4)	6	0.2	10	(0.6)	10	0.3	16	(0.5)	16	0.3
歯周病	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
歯の脱落	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
埋伏歯	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
歯の障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
歯槽骨吸収	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯肉出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
歯肉痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
非感染性歯肉炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
変色歯	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性消化管新生物	27	(1.6)	31	1.1	25	(1.5)	28	0.9	52	(1.6)	59	1.0
大腸ポリープ	19	(1.2)	21	0.7	17	(1.0)	19	0.6	36	(1.1)	40	0.7

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
胃ポリープ	1	(0.1)	1	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2	1	(0.1)	1	0.1
直腸ポリープ	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
十二指腸ポリープ	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
腸管ポリープ	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
憩室疾患	16	(1.9)	16	1.1	7	(0.9)	7	0.5	14	(1.7)	14	0.9	9	(1.1)	10	0.7
憩室	9	(1.1)	9	0.6	5	(0.6)	5	0.3	9	(1.1)	9	0.6	6	(0.7)	6	0.4
腸憩室	7	(0.9)	7	0.5	2	(0.2)	2	0.1	4	(0.5)	4	0.3	3	(0.4)	4	0.3
食道憩室	0				0				1	(0.1)	1	0.1	0			
消化管潰瘍および穿孔	9	(1.1)	9	0.6	11	(1.3)	13	0.9	12	(1.5)	13	0.9	8	(1.0)	11	0.7
びらん性胃炎	1	(0.1)	1	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1
胃潰瘍	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	4	0.3
消化性潰瘍	2	(0.2)	2	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1	0			
十二指腸潰瘍	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
びらん性食道炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
びらん性十二指腸炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
出血性胃潰瘍	2	(0.2)	2	0.1	0				0				0			
出血性大腸潰瘍	0				0				2	(0.2)	2	0.1	0			
胃十二指腸潰瘍	1	(0.1)	1	0.1	0				0				0			
回腸潰瘍	1	(0.1)	1	0.1	0				0				0			
出血性びらん性胃炎	0				0				0				1	(0.1)	1	0.1
出血性十二指腸潰瘍	0				1	(0.1)	1	0.1	0				0			
食道潰瘍	0				0				0				1	(0.1)	1	0.1
腹部ヘルニアおよびその他の腹壁状態	13	(1.6)	14	0.9	7	(0.9)	7	0.5	10	(1.2)	10	0.7	11	(1.3)	13	0.9
裂孔ヘルニア	3	(0.4)	3	0.2	6	(0.7)	6	0.4	4	(0.5)	4	0.3	6	(0.7)	6	0.4
鼠径ヘルニア	5	(0.6)	5	0.3	1	(0.1)	1	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2
臍ヘルニア	4	(0.5)	5	0.3	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
腹部ヘルニア	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	3	0.2
消化管の状態ＮＥＣ	10	(1.2)	10	0.7	15	(1.8)	15	1.0	2	(0.2)	2	0.1	12	(1.5)	14	0.9

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胃ポリープ	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
直腸ポリープ	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
十二指腸ポリープ	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腸管ポリープ	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
憩室疾患	23	(1.4)	23	0.8	23	(1.4)	24	0.8	46	(1.4)	47	0.8
憩室	14	(0.9)	14	0.5	15	(0.9)	15	0.5	29	(0.9)	29	0.5
腸憩室	9	(0.5)	9	0.3	7	(0.4)	8	0.3	16	(0.5)	17	0.3
食道憩室	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
消化管潰瘍および穿孔	20	(1.2)	22	0.8	20	(1.2)	24	0.8	40	(1.2)	46	0.8
びらん性胃炎	5	(0.3)	5	0.2	6	(0.4)	6	0.2	11	(0.3)	11	0.2
胃潰瘍	2	(0.1)	2	0.1	5	(0.3)	7	0.2	7	(0.2)	9	0.2
消化性潰瘍	6	(0.4)	6	0.2	1	(0.1)	1	<0.1	7	(0.2)	7	0.1
十二指腸潰瘍	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
びらん性食道炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
びらん性十二指腸炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
出血性胃潰瘍	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
出血性大腸潰瘍	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
胃十二指腸潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
回腸潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
出血性びらん性胃炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性十二指腸潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
食道潰瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腹部ヘルニアおよびその他の腹壁状態	20	(1.2)	21	0.7	21	(1.3)	23	0.8	41	(1.2)	44	0.7
裂孔ヘルニア	9	(0.5)	9	0.3	10	(0.6)	10	0.3	19	(0.6)	19	0.3
鼠径ヘルニア	6	(0.4)	6	0.2	7	(0.4)	7	0.2	13	(0.4)	13	0.2
臍ヘルニア	4	(0.2)	5	0.2	2	(0.1)	2	0.1	6	(0.2)	7	0.1
腹部ヘルニア	1	(0.1)	1	<0.1	3	(0.2)	4	0.1	4	(0.1)	5	0.1
消化管の状態ＮＥＣ	25	(1.5)	25	0.9	14	(0.9)	16	0.5	39	(1.2)	41	0.7

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
胃腸障害	6	(0.7)	6	0.4	9	(1.1)	9	0.6	1	(0.1)	1	0.1	3	(0.4)	4	0.3
食中毒	2	(0.2)	2	0.1	3	(0.4)	3	0.2	0				5	(0.6)	5	0.3
バレット食道	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
胃障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
胃酸過多	0				0				0				1	(0.1)	1	0.1
痔瘻	0				0				0				1	(0.1)	1	0.1
消化管血行障害	10	(1.2)	10	0.7	11	(1.3)	12	0.8	9	(1.1)	9	0.6	8	(1.0)	9	0.6
痔核	9	(1.1)	9	0.6	10	(1.2)	10	0.7	8	(1.0)	8	0.5	6	(0.7)	7	0.5
食道静脈瘤	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
胃腸虚血	0				0				0				1	(0.1)	1	0.1
腸管虚血	0				1	(0.1)	1	0.1	0				0			
脾臓動脈瘤	0				0				0				1	(0.1)	1	0.1
消化管出血ＮＥＣ	9	(1.1)	9	0.6	9	(1.1)	10	0.7	4	(0.5)	4	0.3	10	(1.2)	10	0.7
胃腸出血	4	(0.5)	4	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
直腸出血	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
上部消化管出血	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
血便排泄	0				3	(0.4)	3	0.2	0				1	(0.1)	1	0.1
メレナ	0				2	(0.2)	2	0.1	0				0			
下部消化管出血	1	(0.1)	1	0.1	0				0				0			
大腸出血	0				1	(0.1)	1	0.1	0				0			
腸出血	0				0				0				1	(0.1)	1	0.1
吐血	0				1	(0.1)	1	0.1	0				0			
門脈圧亢進性胃障害	0				1	(0.1)	1	0.1	0				0			
膵外分泌障害	14	(1.7)	15	1.0	4	(0.5)	5	0.3	4	(0.5)	4	0.3	9	(1.1)	9	0.6
膵炎	7	(0.9)	7	0.5	0				1	(0.1)	1	0.1	5	(0.6)	5	0.3
急性膵炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
膵嚢胞	5	(0.6)	5	0.3	0				1	(0.1)	1	0.1	0			
慢性膵炎	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
膵臓障害	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胃腸障害	15	(0.9)	15	0.5	4	(0.2)	5	0.2	19	(0.6)	20	0.3
食中毒	5	(0.3)	5	0.2	5	(0.3)	5	0.2	10	(0.3)	10	0.2
バレット食道	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
胃障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
胃酸過多	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
痔瘻	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
消化管血行障害	21	(1.3)	22	0.8	17	(1.0)	18	0.6	38	(1.2)	40	0.7
痔核	19	(1.2)	19	0.6	14	(0.9)	15	0.5	33	(1.0)	34	0.6
食道静脈瘤	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
胃腸虚血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸管虚血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脾臓動脈瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
消化管出血ＮＥＣ	18	(1.1)	19	0.6	14	(0.9)	14	0.5	32	(1.0)	33	0.6
胃腸出血	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
直腸出血	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
上部消化管出血	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
血便排泄	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
メレナ	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
下部消化管出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大腸出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腸出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
吐血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
門脈圧亢進性胃障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵外分泌障害	18	(1.1)	20	0.7	13	(0.8)	13	0.4	31	(0.9)	33	0.6
膵炎	7	(0.4)	7	0.2	6	(0.4)	6	0.2	13	(0.4)	13	0.2
急性膵炎	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
膵嚢胞	5	(0.3)	5	0.2	1	(0.1)	1	<0.1	6	(0.2)	6	0.1
慢性膵炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
膵臓障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
膵萎縮	0				1	(0.1)	1	0.1	0				0			
膵石灰化	1	(0.1)	1	0.1	0				0				0			
膵石症	0				1	(0.1)	1	0.1	0				0			
口腔内軟部組織疾患	3	(0.4)	6	0.4	3	(0.4)	3	0.2	7	(0.9)	7	0.5	4	(0.5)	5	0.3
口腔内潰瘍形成	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	2	(0.2)	3	0.2
嚥下痛	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
アフタ性口内炎	0				0				2	(0.2)	2	0.1	0			
口蓋障害	1	(0.1)	1	0.1	0				0				0			
口腔そう痒症	1	(0.1)	1	0.1	0				0				0			
口腔障害	0				0				0				1	(0.1)	1	0.1
口腔内出血	0				1	(0.1)	1	0.1	0				0			
口腔内痛	0				0				1	(0.1)	1	0.1	0			
口唇腫脹	0				0				1	(0.1)	1	0.1	0			
口唇浮腫	1	(0.1)	3	0.2	0				0				0			
歯肉腫脹	0				0				0				1	(0.1)	1	0.1
唾液腺疾患	1	(0.1)	1	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3	4	(0.5)	4	0.3
口内乾燥	1	(0.1)	1	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3	4	(0.5)	4	0.3
消化管狭窄および閉塞	4	(0.5)	4	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
小腸閉塞	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
食道狭窄	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
腸閉塞	2	(0.2)	2	0.1	0				0				0			
イレウス	1	(0.1)	1	0.1	0				0				0			
胃イレウス	0				0				0				1	(0.1)	1	0.1
小腸捻転	0				1	(0.1)	1	0.1	0				0			
肛門および直腸の状態ＮＥＣ	3	(0.4)	3	0.2	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0			
裂肛	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
直腸脱	1	(0.1)	1	0.1	0				0				0			
肛門そう痒症	0				1	(0.1)	1	0.1	0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
膵萎縮	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵石灰化	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵石症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔内軟部組織疾患	6	(0.4)	9	0.3	11	(0.7)	12	0.4	17	(0.5)	21	0.4
口腔内潰瘍形成	1	(0.1)	1	<0.1	4	(0.2)	5	0.2	5	(0.2)	6	0.1
嚥下痛	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
アフタ性口内炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
口蓋障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔そう痒症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口腔内出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔内痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口唇腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口唇浮腫	1	(0.1)	3	0.1	0				1	(<0.1)	3	0.1
歯肉腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
唾液腺疾患	4	(0.2)	4	0.1	8	(0.5)	8	0.3	12	(0.4)	12	0.2
口内乾燥	4	(0.2)	4	0.1	8	(0.5)	8	0.3	12	(0.4)	12	0.2
消化管狭窄および閉塞	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
小腸閉塞	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
食道狭窄	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腸閉塞	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
イレウス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃イレウス	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
小腸捻転	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肛門および直腸の状態ＮＥＣ	6	(0.4)	6	0.2	1	(0.1)	1	<0.1	7	(0.2)	7	0.1
裂肛	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
直腸脱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肛門そう痒症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
肛門周囲痛	1	(0.1)	1	0.1	0				0				0			
肛門肥大乳頭	0				0				1	(0.1)	1	0.1	0			
舌疾患	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
舌腫脹	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
舌障害	0				0				1	(0.1)	1	0.1	0			
舌痛	0				0				1	(0.1)	1	0.1	0			
舌浮腫	0				0				0				1	(0.1)	1	0.1
舌変色	0				1	(0.1)	1	0.1	0				0			
腹膜および後腹膜疾患	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
腹水	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
限局性腹腔内液貯留	0				0				1	(0.1)	1	0.1	0			
腹膜出血	1	(0.1)	1	0.1	0				0				0			
吸収不良性疾患	0				1	(0.1)	1	0.1	0				0			
セリアック病	0				1	(0.1)	1	0.1	0				0			
感染症および寄生虫症	360	(43.7)	738	49.6	341	(41.6)	684	47.4	374	(45.7)	810	53.7	375	(45.5)	773	50.6
詳細不明な感染体による感染症	294	(35.7)	545	36.6	282	(34.4)	503	34.8	319	(38.9)	605	40.1	315	(38.2)	564	36.9
尿路感染	75	(9.1)	100	6.7	63	(7.7)	75	5.2	63	(7.7)	93	6.2	64	(7.8)	83	5.4
鼻咽頭炎	59	(7.2)	80	5.4	52	(6.3)	69	4.8	74	(9.0)	95	6.3	65	(7.9)	83	5.4
上気道感染	50	(6.1)	56	3.8	45	(5.5)	53	3.7	57	(7.0)	68	4.5	61	(7.4)	84	5.5
気管支炎	40	(4.9)	47	3.2	35	(4.3)	38	2.6	49	(6.0)	52	3.4	50	(6.1)	64	4.2
肺炎	30	(3.6)	32	2.2	26	(3.2)	33	2.3	32	(3.9)	39	2.6	33	(4.0)	34	2.2
副鼻腔炎	23	(2.8)	27	1.8	26	(3.2)	42	2.9	31	(3.8)	40	2.7	23	(2.8)	29	1.9
胃腸炎	19	(2.3)	22	1.5	29	(3.5)	31	2.1	23	(2.8)	24	1.6	20	(2.4)	21	1.4
咽頭炎	14	(1.7)	14	0.9	16	(2.0)	21	1.5	9	(1.1)	9	0.6	14	(1.7)	14	0.9
限局性感染	10	(1.2)	11	0.7	11	(1.3)	12	0.8	15	(1.8)	19	1.3	10	(1.2)	12	0.8
膀胱炎	9	(1.1)	11	0.7	11	(1.3)	13	0.9	13	(1.6)	18	1.2	10	(1.2)	13	0.9
歯感染	11	(1.3)	14	0.9	10	(1.2)	10	0.7	4	(0.5)	5	0.3	6	(0.7)	6	0.4

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肛門周囲痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肛門肥大乳頭	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
舌疾患	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
舌腫脹	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
舌障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
舌痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
舌浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
舌変色	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹膜および後腹膜疾患	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
腹水	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
限局性腹腔内液貯留	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腹膜出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
吸収不良性疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
セリアック病	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染症および寄生虫症	701	(42.7)	1422	48.5	749	(45.6)	1583	52.2	1450	(44.1)	3005	50.4
詳細不明な感染体による感染症	576	(35.1)	1048	35.7	634	(38.6)	1169	38.5	1210	(36.8)	2217	37.2
尿路感染	138	(8.4)	175	6.0	127	(7.7)	176	5.8	265	(8.1)	351	5.9
鼻咽頭炎	111	(6.8)	149	5.1	139	(8.5)	178	5.9	250	(7.6)	327	5.5
上気道感染	95	(5.8)	109	3.7	118	(7.2)	152	5.0	213	(6.5)	261	4.4
気管支炎	75	(4.6)	85	2.9	99	(6.0)	116	3.8	174	(5.3)	201	3.4
肺炎	56	(3.4)	65	2.2	65	(4.0)	73	2.4	121	(3.7)	138	2.3
副鼻腔炎	49	(3.0)	69	2.4	54	(3.3)	69	2.3	103	(3.1)	138	2.3
胃腸炎	48	(2.9)	53	1.8	43	(2.6)	45	1.5	91	(2.8)	98	1.6
咽頭炎	30	(1.8)	35	1.2	23	(1.4)	23	0.8	53	(1.6)	58	1.0
限局性感染	21	(1.3)	23	0.8	25	(1.5)	31	1.0	46	(1.4)	54	0.9
膀胱炎	20	(1.2)	24	0.8	23	(1.4)	31	1.0	43	(1.3)	55	0.9
歯感染	21	(1.3)	24	0.8	10	(0.6)	11	0.4	31	(0.9)	35	0.6

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
結膜炎	6	(0.7)	6	0.4	11	(1.3)	14	1.0	7	(0.9)	7	0.5	3	(0.4)	3	0.2
下気道感染	6	(0.7)	7	0.5	7	(0.9)	8	0.6	7	(0.9)	8	0.5	6	(0.7)	6	0.4
歯膿瘍	5	(0.6)	6	0.4	4	(0.5)	4	0.3	9	(1.1)	9	0.6	5	(0.6)	5	0.3
鼻炎	1	(0.1)	1	0.1	5	(0.6)	5	0.3	15	(1.8)	15	1.0	2	(0.2)	2	0.1
急性副鼻腔炎	8	(1.0)	10	0.7	2	(0.2)	2	0.1	5	(0.6)	5	0.3	5	(0.6)	5	0.3
敗血症	5	(0.6)	5	0.3	4	(0.5)	4	0.3	5	(0.6)	5	0.3	5	(0.6)	5	0.3
憩室炎	5	(0.6)	5	0.3	2	(0.2)	2	0.1	4	(0.5)	6	0.4	5	(0.6)	5	0.3
骨髄炎	5	(0.6)	7	0.5	1	(0.1)	1	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1
外耳炎	5	(0.6)	6	0.4	3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1
創傷感染	2	(0.2)	3	0.2	2	(0.2)	2	0.1	4	(0.5)	4	0.3	3	(0.4)	4	0.3
中耳炎	4	(0.5)	6	0.4	1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
眼感染	3	(0.4)	3	0.2	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1
喉頭炎	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	4	(0.5)	4	0.3
気道感染	2	(0.2)	2	0.1	4	(0.5)	5	0.3	2	(0.2)	2	0.1	1	(0.1)	1	0.1
耳感染	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
感染性皮膚潰瘍	0				3	(0.4)	4	0.3	1	(0.1)	1	0.1	4	(0.5)	9	0.6
歯肉炎	4	(0.5)	4	0.3	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0			
爪囲炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
慢性腎盂腎炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	4	0.3	3	(0.4)	3	0.2
急性中耳炎	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
術後創感染	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
敗血症性ショック	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	3	(0.4)	3	0.2
扁桃炎	0				1	(0.1)	1	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1
尿路性敗血症	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
膿瘍	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
皮下組織膿瘍	3	(0.4)	3	0.2	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
皮膚感染	1	(0.1)	1	0.1	0				3	(0.4)	4	0.3	2	(0.2)	2	0.1
咽頭扁桃炎	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
四肢膿瘍	3	(0.4)	4	0.3	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
結膜炎	17	(1.0)	20	0.7	10	(0.6)	10	0.3	27	(0.8)	30	0.5
下気道感染	13	(0.8)	15	0.5	13	(0.8)	14	0.5	26	(0.8)	29	0.5
歯膿瘍	9	(0.5)	10	0.3	14	(0.9)	14	0.5	23	(0.7)	24	0.4
鼻炎	6	(0.4)	6	0.2	17	(1.0)	17	0.6	23	(0.7)	23	0.4
急性副鼻腔炎	10	(0.6)	12	0.4	10	(0.6)	10	0.3	20	(0.6)	22	0.4
敗血症	9	(0.5)	9	0.3	10	(0.6)	10	0.3	19	(0.6)	19	0.3
憩室炎	7	(0.4)	7	0.2	9	(0.5)	11	0.4	16	(0.5)	18	0.3
骨髄炎	6	(0.4)	8	0.3	6	(0.4)	6	0.2	12	(0.4)	14	0.2
外耳炎	8	(0.5)	9	0.3	3	(0.2)	3	0.1	11	(0.3)	12	0.2
創傷感染	4	(0.2)	5	0.2	7	(0.4)	8	0.3	11	(0.3)	13	0.2
中耳炎	5	(0.3)	7	0.2	6	(0.4)	6	0.2	11	(0.3)	13	0.2
眼感染	6	(0.4)	6	0.2	4	(0.2)	4	0.1	10	(0.3)	10	0.2
喉頭炎	4	(0.2)	4	0.1	6	(0.4)	6	0.2	10	(0.3)	10	0.2
気道感染	6	(0.4)	7	0.2	3	(0.2)	3	0.1	9	(0.3)	10	0.2
耳感染	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2
感染性皮膚潰瘍	3	(0.2)	4	0.1	5	(0.3)	10	0.3	8	(0.2)	14	0.2
歯肉炎	7	(0.4)	7	0.2	1	(0.1)	1	<0.1	8	(0.2)	8	0.1
爪囲炎	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
慢性腎盂腎炎	2	(0.1)	2	0.1	6	(0.4)	7	0.2	8	(0.2)	9	0.2
急性中耳炎	1	(0.1)	1	<0.1	6	(0.4)	6	0.2	7	(0.2)	7	0.1
術後創感染	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
敗血症性ショック	1	(0.1)	1	<0.1	6	(0.4)	6	0.2	7	(0.2)	7	0.1
扁桃炎	1	(0.1)	1	<0.1	6	(0.4)	6	0.2	7	(0.2)	7	0.1
尿路性敗血症	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
膿瘍	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
皮下組織膿瘍	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
皮膚感染	1	(0.1)	1	<0.1	5	(0.3)	6	0.2	6	(0.2)	7	0.1
咽頭扁桃炎	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
四肢膿瘍	4	(0.2)	5	0.2	1	(0.1)	1	<0.1	5	(0.2)	6	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
処置後感染	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
腎盂腎炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
精巣上体炎	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
切開部位感染	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
肺感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
迷路炎	1	(0.1)	1	0.1	2	(0.2)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
咬傷感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
医療機器関連感染	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
気管支肺炎	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
歯周炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
赤痢	1	(0.1)	4	0.3	1	(0.1)	4	0.3	1	(0.1)	1	0.1	0			
唾液腺炎	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
大葉性肺炎	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
虫垂炎	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
爪感染	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
軟部組織感染	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
慢性副鼻腔炎	2	(0.2)	3	0.2	0				1	(0.1)	1	0.1	0			
膣感染	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
鼡径部膿瘍	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
感染性大腸炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
感染性皮膚嚢腫	0				0				0				2	(0.2)	2	0.1
気管気管支炎	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
急性腎盂腎炎	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
腎感染	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
糖尿病性足感染	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
膿痂疹	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
麦粒腫	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
腹壁膿瘍	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
腹膜炎	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
処置後感染	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
腎盂腎炎	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
精巣上体炎	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
切開部位感染	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
肺感染	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
迷路炎	3	(0.2)	4	0.1	2	(0.1)	2	0.1	5	(0.2)	6	0.1
咬傷感染	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
医療機器関連感染	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
気管支肺炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
歯周炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
赤痢	2	(0.1)	8	0.3	1	(0.1)	1	<0.1	3	(0.1)	9	0.2
唾液腺炎	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
大葉性肺炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
虫垂炎	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
爪感染	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
軟部組織感染	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
慢性副鼻腔炎	2	(0.1)	3	0.1	1	(0.1)	1	<0.1	3	(0.1)	4	0.1
膣感染	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
鼠径部膿瘍	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
感染性大腸炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
感染性皮膚嚢腫	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
気管気管支炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
急性腎盂腎炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腎感染	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
糖尿病性足感染	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
膿痂疹	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
麦粒腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腹壁膿瘍	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
腹膜炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
埋込み部位感染	0				0				2	(0.2)	2	0.1	0			
カテーテル留置部位膿瘍	1	(0.1)	1	0.1	0				0				0			
医療機器関連敗血症	0				0				1	(0.1)	1	0.1	0			
陰嚢膿瘍	1	(0.1)	1	0.1	0				0				0			
壊死性筋膜炎	0				0				1	(0.1)	1	0.1	0			
外陰部膣炎	0				1	(0.1)	1	0.1	0				0			
感染	1	(0.1)	1	0.1	0				0				0			
感染による慢性閉塞性気道疾患の増悪	1	(0.1)	1	0.1	0				0				0			
感染性関節炎	1	(0.1)	1	0.1	0				0				0			
感染性腸炎	0				0				1	(0.1)	1	0.1	0			
感染性嚢腫	0				0				1	(0.1)	1	0.1	0			
肝膿瘍	1	(0.1)	1	0.1	0				0				0			
寄生虫性胃腸炎	0				1	(0.1)	1	0.1	0				0			
急性扁桃炎	0				0				0				1	(0.1)	1	0.1
筋膿瘍	1	(0.1)	1	0.1	0				0				0			
菌血症	0				0				0				1	(0.1)	1	0.1
口腔感染	0				0				1	(0.1)	1	0.1	0			
口腔膿瘍	0				0				1	(0.1)	1	0.1	0			
脂腺感染	0				0				0				1	(0.1)	1	0.1
歯冠周囲炎	0				0				0				1	(0.1)	1	0.1
歯槽骨炎	0				0				0				1	(0.1)	1	0.1
歯肉膿瘍	0				1	(0.1)	1	0.1	0				0			
耳下腺炎	0				0				0				1	(0.1)	1	0.1
処置後肺炎	1	(0.1)	1	0.1	0				0				0			
消化管感染	0				0				1	(0.1)	1	0.1	0			
心内膜炎	0				0				1	(0.1)	1	0.1	0			
性器感染	0				0				1	(0.1)	1	0.1	0			
性器膿瘍	0				0				0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
埋込み部位感染	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
カテーテル留置部位膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
医療機器関連敗血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
陰嚢膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
壊死性筋膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外陰部膣炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染による慢性閉塞性気道疾患の増悪	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染性関節炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染性腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感染性嚢腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
寄生虫性胃腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
急性扁桃炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
菌血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口腔感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口腔膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脂腺感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯冠周囲炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯槽骨炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯肉膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
耳下腺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
処置後肺炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心内膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
性器感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
性器膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
精巣炎	0				0				0				1	(0.1)	1	0.1
直腸周囲膿瘍	0				1	(0.1)	1	0.1	0				0			
乳房膿瘍	0				0				0				1	(0.1)	1	0.1
尿道炎	0				1	(0.1)	1	0.1	0				0			
熱帯性潰瘍	0				0				1	(0.1)	1	0.1	0			
膿疱性皮疹	0				1	(0.1)	1	0.1	0				0			
肺敗血症	1	(0.1)	1	0.1	0				0				0			
腹部膿瘍	0				0				1	(0.1)	1	0.1	0			
慢性中耳炎	1	(0.1)	1	0.1	0				0				0			
扁桃周囲膿瘍	0				0				0				1	(0.1)	1	0.1
癰	1	(0.1)	1	0.1	0				0				0			
肛門膿瘍	1	(0.1)	2	0.1	0				0				0			
脾臓膿瘍	0				0				0				1	(0.1)	1	0.1
臍帯周囲膿瘍	0				0				0				1	(0.1)	1	0.1
ウイルス感染症	92	(11.2)	113	7.6	81	(9.9)	102	7.1	83	(10.1)	104	6.9	77	(9.3)	98	6.4
インフルエンザ	48	(5.8)	57	3.8	43	(5.3)	52	3.6	47	(5.7)	55	3.6	46	(5.6)	63	4.1
帯状疱疹	15	(1.8)	19	1.3	12	(1.5)	13	0.9	14	(1.7)	14	0.9	12	(1.5)	12	0.8
ウイルス性胃腸炎	9	(1.1)	9	0.6	10	(1.2)	10	0.7	5	(0.6)	5	0.3	7	(0.8)	7	0.5
ウイルス感染	10	(1.2)	11	0.7	9	(1.1)	10	0.7	6	(0.7)	9	0.6	5	(0.6)	5	0.3
ウイルス性上気道感染	0				6	(0.7)	6	0.4	3	(0.4)	4	0.3	1	(0.1)	1	0.1
ウイルス性消化管感染	3	(0.4)	3	0.2	4	(0.5)	4	0.3	0				0			
口腔ヘルペス	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
ウイルス性気道感染	1	(0.1)	1	0.1	0				0				3	(0.4)	3	0.2
単純ヘルペス	2	(0.2)	3	0.2	0				2	(0.2)	2	0.1	0			
アデノウイルス結膜炎	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
ウイルス性気管支炎	1	(0.1)	1	0.1	0				1	(0.1)	2	0.1	0			
ウイルス性耳感染	0				0				2	(0.2)	2	0.1	0			
デング熱	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
ロタウイルス胃腸炎	0				0				2	(0.2)	3	0.2	0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
精巣炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
直腸周囲膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳房膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿道炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
熱帯性潰瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膿疱性皮疹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺敗血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹部膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
慢性中耳炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
扁桃周囲膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
癰	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肛門膿瘍	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
脾臓膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
臍帯周囲膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ウイルス感染症	173	(10.5)	215	7.3	160	(9.7)	202	6.7	333	(10.1)	417	7.0
インフルエンザ	91	(5.5)	109	3.7	93	(5.7)	118	3.9	184	(5.6)	227	3.8
帯状疱疹	27	(1.6)	32	1.1	26	(1.6)	26	0.9	53	(1.6)	58	1.0
ウイルス性胃腸炎	19	(1.2)	19	0.6	12	(0.7)	12	0.4	31	(0.9)	31	0.5
ウイルス感染	19	(1.2)	21	0.7	11	(0.7)	14	0.5	30	(0.9)	35	0.6
ウイルス性上気道感染	6	(0.4)	6	0.2	4	(0.2)	5	0.2	10	(0.3)	11	0.2
ウイルス性消化管感染	7	(0.4)	7	0.2	0				7	(0.2)	7	0.1
口腔ヘルペス	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
ウイルス性気道感染	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
単純ヘルペス	2	(0.1)	3	0.1	2	(0.1)	2	0.1	4	(0.1)	5	0.1
アデノウイルス結膜炎	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
ウイルス性気管支炎	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
ウイルス性耳感染	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
デング熱	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
ロタウイルス胃腸炎	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
Ｂ型肝炎	0				0				0				1	(0.1)	1	0.1
Ｃ型肝炎	0				0				1	(0.1)	1	0.1	0			
インフルエンザ性肺炎	1	(0.1)	1	0.1	0				0				0			
ウイルス性胃炎	0				1	(0.1)	1	0.1	0				0			
ウイルス性咽頭炎	0				0				1	(0.1)	1	0.1	0			
ウイルス性角膜炎	0				1	(0.1)	1	0.1	0				0			
ウイルス性結膜炎	0				1	(0.1)	1	0.1	0				0			
ウイルス性鼻炎	0				0				1	(0.1)	1	0.1	0			
ウイルス性扁桃炎	0				0				1	(0.1)	1	0.1	0			
ウエストナイルウイルス感染	1	(0.1)	1	0.1	0				0				0			
ヘルペスウイルス感染	1	(0.1)	1	0.1	0				0				0			
ヘルペス性皮膚炎	0				1	(0.1)	1	0.1	0				0			
ライノウイルス感染	0				0				0				1	(0.1)	1	0.1
陰部ヘルペス	1	(0.1)	1	0.1	0				0				0			
急性Ｂ型肝炎	1	(0.1)	1	0.1	0				0				0			
細気管支炎	0				0				0				1	(0.1)	1	0.1
水痘	0				1	(0.1)	1	0.1	0				0			
前庭神経炎	1	(0.1)	1	0.1	0				0				0			
慢性Ｃ型肝炎	0				0				0				1	(0.1)	1	0.1
細菌感染症	39	(4.7)	47	3.2	42	(5.1)	45	3.1	45	(5.5)	56	3.7	53	(6.4)	65	4.3
蜂巣炎	20	(2.4)	25	1.7	14	(1.7)	15	1.0	19	(2.3)	21	1.4	25	(3.0)	30	2.0
せつ	4	(0.5)	4	0.3	3	(0.4)	3	0.2	3	(0.4)	3	0.2	4	(0.5)	4	0.3
ヘリコバクター感染	2	(0.2)	2	0.1	6	(0.7)	6	0.4	2	(0.2)	2	0.1	4	(0.5)	4	0.3
ブドウ球菌感染	3	(0.4)	3	0.2	0				0				3	(0.4)	3	0.2
レンサ球菌性咽頭炎	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
壊疽	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	2	(0.2)	2	0.1
丹毒	3	(0.4)	3	0.2	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
毛包炎	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Ｂ型肝炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
Ｃ型肝炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
インフルエンザ性肺炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ウイルス性胃炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ウイルス性咽頭炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ウイルス性角膜炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ウイルス性結膜炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ウイルス性鼻炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ウイルス性扁桃炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ウエストナイルウイルス感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ヘルペスウイルス感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ヘルペス性皮膚炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ライノウイルス感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
陰部ヘルペス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
急性Ｂ型肝炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
細気管支炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
水痘	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
前庭神経炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
慢性Ｃ型肝炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌感染症	81	(4.9)	92	3.1	98	(6.0)	121	4.0	179	(5.4)	213	3.6
蜂巣炎	34	(2.1)	40	1.4	44	(2.7)	51	1.7	78	(2.4)	91	1.5
せつ	7	(0.4)	7	0.2	7	(0.4)	7	0.2	14	(0.4)	14	0.2
ヘリコバクター感染	8	(0.5)	8	0.3	6	(0.4)	6	0.2	14	(0.4)	14	0.2
ブドウ球菌感染	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
レンサ球菌性咽頭炎	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
壊疽	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
丹毒	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
毛包炎	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ヘリコバクター性胃炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
大腸菌性敗血症	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
クロストリジウム・ディフィシレ大腸炎	1	(0.1)	1	0.1	0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
カンピロバクター感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
ブドウ球菌性尿路感染	0				0				0				2	(0.2)	2	0.1
ブドウ球菌性敗血症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
細菌性耳感染	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
細菌性膣症	0				1	(0.1)	2	0.1	0				1	(0.1)	1	0.1
細菌尿	0				0				1	(0.1)	3	0.2	1	(0.1)	1	0.1
小腸内細菌過剰増殖	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
大腸菌性尿路感染	0				0				2	(0.2)	2	0.1	0			
腸球菌感染	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
百日咳	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
無症候性細菌尿	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
カテーテル留置部位蜂巣炎	0				0				1	(0.1)	1	0.1	0			
カンピロバクター胃腸炎	0				1	(0.1)	1	0.1	0				0			
クレブシエラ膀胱炎	0				0				0				1	(0.1)	1	0.1
サルモネラ菌性胃腸炎	0				1	(0.1)	1	0.1	0				0			
シュードモナス性尿路感染	0				1	(0.1)	1	0.1	0				0			
ブドウ球菌性菌血症	0				0				0				1	(0.1)	1	0.1
ブドウ球菌性骨髄炎	0				0				1	(0.1)	1	0.1	0			
ブドウ球菌皮膚感染	0				0				0				1	(0.1)	1	0.1
ライム病	0				0				0				1	(0.1)	1	0.1
偽膜性大腸炎	0				0				1	(0.1)	1	0.1	0			
細菌性咽頭炎	0				1	(0.1)	1	0.1	0				0			
細菌性下痢	0				1	(0.1)	1	0.1	0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ヘリコバクター性胃炎	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
大腸菌性敗血症	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
クロストリジウム・ディフィシレ大腸炎	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
カンピロバクター感染	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
ブドウ球菌性尿路感染	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
ブドウ球菌性敗血症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
細菌性耳感染	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
細菌性膣症	1	(0.1)	2	0.1	1	(0.1)	1	<0.1	2	(0.1)	3	0.1
細菌尿	0				2	(0.1)	4	0.1	2	(0.1)	4	0.1
小腸内細菌過剰増殖	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
大腸菌性尿路感染	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
腸球菌感染	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
百日咳	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
無症候性細菌尿	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
カテーテル留置部位蜂巣炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
カンピロバクター胃腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
クレブシエラ膀胱炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
サルモネラ菌性胃腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
シュードモナス性尿路感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ブドウ球菌性菌血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ブドウ球菌性骨髄炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ブドウ球菌皮膚感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ライム病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
偽膜性大腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性咽頭炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
細菌性下痢	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
細菌性眼感染	0				0				0				1	(0.1)	1	0.1
細菌性気道感染	0				0				0				1	(0.1)	1	0.1
細菌性結膜炎	0				0				0				1	(0.1)	1	0.1
細菌性上気道感染	0				1	(0.1)	1	0.1	0				0			
細菌性髄膜炎	0				1	(0.1)	1	0.1	0				0			
細菌性中耳炎	0				1	(0.1)	1	0.1	0				0			
細菌性爪床感染	0				0				1	(0.1)	1	0.1	0			
細菌性尿路感染	0				0				1	(0.1)	2	0.1	0			
細菌性肺炎	0				0				0				1	(0.1)	1	0.1
細菌性副鼻腔炎	0				0				1	(0.1)	1	0.1	0			
処置後蜂巣炎	0				1	(0.1)	1	0.1	0				0			
大腸菌感染	0				0				0				1	(0.1)	1	0.1
腸球菌性尿路感染	0				1	(0.1)	1	0.1	0				0			
軟骨膜炎	0				0				1	(0.1)	1	0.1	0			
肺炎球菌性肺炎	0				0				1	(0.1)	1	0.1	0			
真菌感染症	25	(3.0)	32	2.2	30	(3.7)	32	2.2	31	(3.8)	42	2.8	34	(4.1)	42	2.8
爪真菌症	9	(1.1)	9	0.6	6	(0.7)	6	0.4	6	(0.7)	6	0.4	7	(0.8)	7	0.5
足部白癬	5	(0.6)	5	0.3	4	(0.5)	4	0.3	6	(0.7)	6	0.4	9	(1.1)	9	0.6
真菌感染	2	(0.2)	2	0.1	4	(0.5)	5	0.3	8	(1.0)	8	0.5	6	(0.7)	6	0.4
外陰部腟カンジダ症	2	(0.2)	2	0.1	2	(0.2)	2	0.1	4	(0.5)	6	0.4	4	(0.5)	4	0.3
外陰腟真菌感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	5	(0.6)	5	0.3	3	(0.4)	4	0.3
カンジダ感染	2	(0.2)	2	0.1	4	(0.5)	4	0.3	0				1	(0.1)	1	0.1
口腔カンジダ症	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	2	(0.2)	3	0.2
皮膚真菌感染	3	(0.4)	5	0.3	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0			
体部白癬	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1	2	(0.2)	2	0.1
癜風	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
カンジダ性亀頭炎	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
股部白癬	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
食道カンジダ症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
細菌性眼感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性気道感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性結膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性上気道感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
細菌性髄膜炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
細菌性中耳炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
細菌性爪床感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性尿路感染	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
細菌性肺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性副鼻腔炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
処置後蜂巣炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大腸菌感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸球菌性尿路感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
軟骨膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺炎球菌性肺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
真菌感染症	55	(3.3)	64	2.2	65	(4.0)	84	2.8	120	(3.7)	148	2.5
爪真菌症	15	(0.9)	15	0.5	13	(0.8)	13	0.4	28	(0.9)	28	0.5
足部白癬	9	(0.5)	9	0.3	15	(0.9)	15	0.5	24	(0.7)	24	0.4
真菌感染	6	(0.4)	7	0.2	14	(0.9)	14	0.5	20	(0.6)	21	0.4
外陰部腟カンジダ症	4	(0.2)	4	0.1	8	(0.5)	10	0.3	12	(0.4)	14	0.2
外陰腟真菌感染	2	(0.1)	2	0.1	8	(0.5)	9	0.3	10	(0.3)	11	0.2
カンジダ感染	6	(0.4)	6	0.2	1	(0.1)	1	<0.1	7	(0.2)	7	0.1
口腔カンジダ症	4	(0.2)	4	0.1	3	(0.2)	4	0.1	7	(0.2)	8	0.1
皮膚真菌感染	4	(0.2)	6	0.2	3	(0.2)	3	0.1	7	(0.2)	9	0.2
体部白癬	3	(0.2)	3	0.1	3	(0.2)	4	0.1	6	(0.2)	7	0.1
癜風	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
カンジダ性亀頭炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
股部白癬	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
食道カンジダ症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
性器カンジダ症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
カンジダ尿	1	(0.1)	1	0.1	0				0				0			
口腔真菌感染	0				0				0				1	(0.1)	1	0.1
手白癬	1	(0.1)	1	0.1	0				0				0			
真菌性口腔咽頭炎	0				0				0				1	(0.1)	1	0.1
真菌性食道炎	0				1	(0.1)	1	0.1	0				0			
真菌性性器感染	0				1	(0.1)	1	0.1	0				0			
真菌性尿路感染	1	(0.1)	1	0.1	0				0				0			
頭部白癬	0				0				0				1	(0.1)	1	0.1
外部寄生生物感染症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
ダニ皮膚炎	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
トコジラミ寄生	0				0				1	(0.1)	1	0.1	0			
マイコバクテリア感染症	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
結核	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
蠕虫感染症	0				2	(0.2)	2	0.1	0				0			
回虫症	0				2	(0.2)	2	0.1	0				0			
リケッチア感染症	0				0				1	(0.1)	1	0.1	0			
ボタン熱	0				0				1	(0.1)	1	0.1	0			
筋骨格系および結合組織障害	218	(26.5)	323	21.7	202	(24.7)	313	21.7	242	(29.5)	423	28.0	232	(28.1)	405	26.5
筋骨格系および結合組織障害ＮＥＣ	106	(12.9)	130	8.7	112	(13.7)	141	9.8	114	(13.9)	159	10.5	121	(14.7)	157	10.3
背部痛	46	(5.6)	46	3.1	48	(5.9)	57	3.9	45	(5.5)	55	3.6	47	(5.7)	49	3.2
四肢痛	35	(4.3)	41	2.8	25	(3.1)	27	1.9	40	(4.9)	44	2.9	38	(4.6)	41	2.7
筋骨格痛	20	(2.4)	21	1.4	25	(3.1)	27	1.9	18	(2.2)	20	1.3	26	(3.2)	31	2.0
筋骨格系胸痛	6	(0.7)	6	0.4	7	(0.9)	7	0.5	18	(2.2)	24	1.6	9	(1.1)	10	0.7
頚部痛	6	(0.7)	6	0.4	8	(1.0)	8	0.6	10	(1.2)	10	0.7	9	(1.1)	9	0.6
側腹部痛	6	(0.7)	6	0.4	4	(0.5)	5	0.3	0				2	(0.2)	2	0.1
足底筋膜炎	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
性器カンジダ症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
カンジダ尿	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔真菌感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
手白癬	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
真菌性口腔咽頭炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
真菌性食道炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
真菌性性器感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
真菌性尿路感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頭部白癬	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外部寄生生物感染症	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
ダニ皮膚炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
トコジラミ寄生	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
マイコバクテリア感染症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
結核	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
蠕虫感染症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
回虫症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
リケッチア感染症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ボタン熱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋骨格系および結合組織障害	420	(25.6)	636	21.7	474	(28.8)	828	27.3	894	(27.2)	1464	24.5
筋骨格系および結合組織障害ＮＥＣ	218	(13.3)	271	9.2	235	(14.3)	316	10.4	453	(13.8)	587	9.8
背部痛	94	(5.7)	103	3.5	92	(5.6)	104	3.4	186	(5.7)	207	3.5
四肢痛	60	(3.7)	68	2.3	78	(4.7)	85	2.8	138	(4.2)	153	2.6
筋骨格痛	45	(2.7)	48	1.6	44	(2.7)	51	1.7	89	(2.7)	99	1.7
筋骨格系胸痛	13	(0.8)	13	0.4	27	(1.6)	34	1.1	40	(1.2)	47	0.8
頚部痛	14	(0.9)	14	0.5	19	(1.2)	19	0.6	33	(1.0)	33	0.6
側腹部痛	10	(0.6)	11	0.4	2	(0.1)	2	0.1	12	(0.4)	13	0.2
足底筋膜炎	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
筋骨格硬直	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
四肢不快感	0				0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
鼡径部痛	0				0				1	(0.1)	1	0.1	3	(0.4)	3	0.2
筋拘縮	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
筋骨格不快感	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
デュプイトラン拘縮	0				0				0				1	(0.1)	1	0.1
運動性低下	0				0				0				1	(0.1)	1	0.1
下肢腫瘤	0				1	(0.1)	1	0.1	0				0			
筋骨格障害	0				1	(0.1)	1	0.1	0				0			
足底腱膜線維腫症	0				0				0				1	(0.1)	1	0.1
軟部組織障害	0				0				0				1	(0.1)	1	0.1
瘻孔	0				0				0				1	(0.1)	1	0.1
鼡径部腫瘤	1	(0.1)	1	0.1	0				0				0			
関節障害	94	(11.4)	112	7.5	68	(8.3)	93	6.4	110	(13.4)	146	9.7	108	(13.1)	145	9.5
関節痛	39	(4.7)	42	2.8	30	(3.7)	35	2.4	56	(6.8)	69	4.6	51	(6.2)	61	4.0
変形性関節症	39	(4.7)	44	3.0	24	(2.9)	27	1.9	25	(3.1)	30	2.0	33	(4.0)	38	2.5
変形性脊椎症	1	(0.1)	1	0.1	5	(0.6)	5	0.3	11	(1.3)	11	0.7	7	(0.8)	9	0.6
関節腫脹	2	(0.2)	2	0.1	4	(0.5)	4	0.3	9	(1.1)	9	0.6	8	(1.0)	8	0.5
関節炎	5	(0.6)	5	0.3	5	(0.6)	7	0.5	5	(0.6)	5	0.3	7	(0.8)	7	0.5
肩回旋筋腱板症候群	3	(0.4)	4	0.3	5	(0.6)	5	0.3	5	(0.6)	5	0.3	3	(0.4)	3	0.2
関節周囲炎	1	(0.1)	1	0.1	0				0				5	(0.6)	6	0.4
顎関節症候群	3	(0.4)	3	0.2	0				2	(0.2)	2	0.1	0			
関節リウマチ	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0			
関節障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
関節滲出液	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
痛風性関節炎	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
関節可動域低下	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
椎間関節症候群	0				1	(0.1)	1	0.1	2	(0.2)	4	0.3	1	(0.1)	1	0.1
関節摩擦音	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
筋骨格硬直	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
四肢不快感	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
鼡径部痛	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
筋拘縮	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
筋骨格不快感	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
デュプイトラン拘縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
運動性低下	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
下肢腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
筋骨格障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
足底腱膜線維腫症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
軟部組織障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
瘻孔	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鼡径部腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
関節障害	162	(9.9)	205	7.0	218	(13.3)	291	9.6	380	(11.6)	496	8.3
関節痛	69	(4.2)	77	2.6	107	(6.5)	130	4.3	176	(5.4)	207	3.5
変形性関節症	63	(3.8)	71	2.4	58	(3.5)	68	2.2	121	(3.7)	139	2.3
変形性脊椎症	6	(0.4)	6	0.2	18	(1.1)	20	0.7	24	(0.7)	26	0.4
関節腫脹	6	(0.4)	6	0.2	17	(1.0)	17	0.6	23	(0.7)	23	0.4
関節炎	10	(0.6)	12	0.4	12	(0.7)	12	0.4	22	(0.7)	24	0.4
肩回旋筋腱板症候群	8	(0.5)	9	0.3	8	(0.5)	8	0.3	16	(0.5)	17	0.3
関節周囲炎	1	(0.1)	1	<0.1	5	(0.3)	6	0.2	6	(0.2)	7	0.1
顎関節症候群	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
関節リウマチ	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
関節障害	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
関節滲出液	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
痛風性関節炎	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
関節可動域低下	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
椎間関節症候群	1	(0.1)	1	<0.1	3	(0.2)	5	0.2	4	(0.1)	6	0.1
関節摩擦音	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
ピロリン酸カルシウム結晶性軟骨石灰化症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
膝蓋大腿関節痛症候群	0				0				0				2	(0.2)	2	0.1
乾癬性関節症	0				1	(0.1)	1	0.1	0				0			
関節拘縮	0				0				0				1	(0.1)	1	0.1
骨関節障害	1	(0.1)	1	0.1	0				0				0			
出血性関節症	0				0				0				1	(0.1)	1	0.1
神経障害性関節症	1	(0.1)	1	0.1	0				0				0			
脊椎炎	1	(0.1)	1	0.1	0				0				0			
脊椎骨棘	1	(0.1)	1	0.1	0				0				0			
仙腸骨炎	0				1	(0.1)	1	0.1	0				0			
多発性関節炎	1	(0.1)	1	0.1	0				0				0			
単関節炎	0				1	(0.1)	1	0.1	0				0			
糖尿病性関節障害	0				0				1	(0.1)	1	0.1	0			
筋障害	26	(3.2)	31	2.1	22	(2.7)	25	1.7	45	(5.5)	56	3.7	30	(3.6)	42	2.8
筋痙縮	14	(1.7)	19	1.3	8	(1.0)	8	0.6	17	(2.1)	19	1.3	11	(1.3)	19	1.2
筋肉痛	7	(0.9)	7	0.5	10	(1.2)	13	0.9	14	(1.7)	18	1.2	15	(1.8)	17	1.1
筋力低下	2	(0.2)	2	0.1	1	(0.1)	1	0.1	5	(0.6)	5	0.3	3	(0.4)	3	0.2
筋炎	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
筋膜疼痛症候群	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
筋攣縮	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
筋萎縮	0				0				0				2	(0.2)	2	0.1
斜頚	0				0				2	(0.2)	2	0.1	0			
線維筋痛	0				0				2	(0.2)	3	0.2	0			
ミオキミア	0				0				1	(0.1)	1	0.1	0			
横紋筋融解症	1	(0.1)	1	0.1	0				0				0			
筋肉疲労	0				0				1	(0.1)	1	0.1	0			
多発性筋炎	1	(0.1)	1	0.1	0				0				0			
腹直筋離開	0				1	(0.1)	1	0.1	0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ピロリン酸カルシウム結晶性軟骨石灰化症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
膝蓋大腿関節痛症候群	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
乾癬性関節症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
関節拘縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
骨関節障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
出血性関節症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経障害性関節症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脊椎炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脊椎骨棘	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
仙腸骨炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
多発性関節炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
単関節炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病性関節障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋障害	48	(2.9)	56	1.9	75	(4.6)	98	3.2	123	(3.7)	154	2.6
筋痙縮	22	(1.3)	27	0.9	28	(1.7)	38	1.3	50	(1.5)	65	1.1
筋肉痛	17	(1.0)	20	0.7	29	(1.8)	35	1.2	46	(1.4)	55	0.9
筋力低下	3	(0.2)	3	0.1	8	(0.5)	8	0.3	11	(0.3)	11	0.2
筋炎	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
筋膜疼痛症候群	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
筋攣縮	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
筋萎縮	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
斜頸	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
線維筋痛	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
ミオキミア	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
横紋筋融解症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
筋肉疲労	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
多発性筋炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹直筋離開	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
筋骨格系および結合組織変形（椎間板障害を含む）	17	(2.1)	19	1.3	13	(1.6)	13	0.9	17	(2.1)	24	1.6	15	(1.8)	20	1.3
椎間板突出	10	(1.2)	10	0.7	2	(0.2)	2	0.1	8	(1.0)	9	0.6	4	(0.5)	4	0.3
腰部脊柱管狭窄症	0				0				3	(0.4)	4	0.3	5	(0.6)	5	0.3
足変形	1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1
椎間板変性症	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2
椎間板障害	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
脊柱管狭窄症	0				1	(0.1)	1	0.1	2	(0.2)	5	0.3	2	(0.2)	2	0.1
側弯症	2	(0.2)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
指変形	0				1	(0.1)	1	0.1	0				0			
脊柱変形	0				1	(0.1)	1	0.1	0				0			
脊椎すべり症	0				0				0				1	(0.1)	1	0.1
椎間板圧迫	0				0				0				1	(0.1)	1	0.1
椎間板線維輪断裂	1	(0.1)	1	0.1	0				0				0			
椎間板偏位	0				0				0				1	(0.1)	1	0.1
膝関節変形	1	(0.1)	1	0.1	0				0				0			
骨障害（先天性障害および骨折を除く）	10	(1.2)	11	0.7	17	(2.1)	19	1.3	14	(1.7)	14	0.9	16	(1.9)	17	1.1
外骨腫	4	(0.5)	4	0.3	0				2	(0.2)	2	0.1	9	(1.1)	9	0.6
骨減少症	2	(0.2)	2	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3	3	(0.4)	3	0.2
骨粗鬆症	0				4	(0.5)	4	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1
顎痛	1	(0.1)	1	0.1	1	(0.1)	2	0.1	0				1	(0.1)	1	0.1
骨痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
脊椎痛	0				3	(0.4)	3	0.2	0				0			
骨壊死	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
骨嚢腫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
尾骨痛	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
顎骨嚢胞	0				1	(0.1)	1	0.1	0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
筋骨格系および結合組織変形（椎間板障害を含む）	30	(1.8)	32	1.1	32	(1.9)	44	1.4	62	(1.9)	76	1.3
椎間板突出	12	(0.7)	12	0.4	12	(0.7)	13	0.4	24	(0.7)	25	0.4
腰部脊柱管狭窄症	0				8	(0.5)	9	0.3	8	(0.2)	9	0.2
足変形	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
椎間板変性症	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
椎間板障害	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
脊柱管狭窄症	1	(0.1)	1	<0.1	4	(0.2)	7	0.2	5	(0.2)	8	0.1
側弯症	3	(0.2)	4	0.1	1	(0.1)	1	<0.1	4	(0.1)	5	0.1
指変形	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脊柱変形	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脊椎すべり症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎間板圧迫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎間板線維輪断裂	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
椎間板偏位	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膝関節変形	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨障害（先天性障害および骨折を除く）	27	(1.6)	30	1.0	30	(1.8)	31	1.0	57	(1.7)	61	1.0
外骨腫	4	(0.2)	4	0.1	11	(0.7)	11	0.4	15	(0.5)	15	0.3
骨減少症	6	(0.4)	6	0.2	7	(0.4)	7	0.2	13	(0.4)	13	0.2
骨粗鬆症	4	(0.2)	4	0.1	6	(0.4)	6	0.2	10	(0.3)	10	0.2
顎痛	2	(0.1)	3	0.1	1	(0.1)	1	<0.1	3	(0.1)	4	0.1
骨痛	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
脊椎痛	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
骨壊死	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
骨嚢腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
尾骨痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
顎骨嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
骨炎	0				0				1	(0.1)	1	0.1	0			
骨障害	0				1	(0.1)	1	0.1	0				0			
骨病変	0				1	(0.1)	1	0.1	0				0			
骨溶解	0				1	(0.1)	1	0.1	0				0			
中足骨痛	1	(0.1)	1	0.1	0				0				0			
脛骨内側過労性症候群	1	(0.1)	1	0.1	0				0				0			
腱、靱帯および軟骨障害	12	(1.5)	12	0.8	11	(1.3)	16	1.1	11	(1.3)	12	0.8	18	(2.2)	18	1.2
弾発指	3	(0.4)	3	0.2	4	(0.5)	7	0.5	3	(0.4)	4	0.3	6	(0.7)	6	0.4
腱炎	2	(0.2)	2	0.1	5	(0.6)	6	0.4	4	(0.5)	4	0.3	3	(0.4)	3	0.2
肋軟骨炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
骨端症	1	(0.1)	1	0.1	0				0				4	(0.5)	4	0.3
腱鞘炎	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
腱障害	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
骨軟骨炎	0				1	(0.1)	2	0.1	0				0			
軟骨溶解	1	(0.1)	1	0.1	0				0				0			
半月板変性	0				0				1	(0.1)	1	0.1	0			
腱石灰化	1	(0.1)	1	0.1	0				0				0			
腱付着部症	0				0				0				1	(0.1)	1	0.1
滑膜および滑液包障害	8	(1.0)	8	0.5	5	(0.6)	5	0.3	10	(1.2)	11	0.7	6	(0.7)	6	0.4
滑液包炎	4	(0.5)	4	0.3	3	(0.4)	3	0.2	8	(1.0)	8	0.5	4	(0.5)	4	0.3
滑液嚢腫	4	(0.5)	4	0.3	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
結合組織障害（先天性障害を除く）	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
シェーグレン症候群	0				1	(0.1)	1	0.1	0				0			
リウマチ性多発筋痛	0				0				1	(0.1)	1	0.1	0			
臨床検査	187	(22.7)	343	23.0	178	(21.7)	347	24.0	172	(21.0)	316	21.0	170	(20.6)	297	19.5
消化管検査	101	(12.3)	153	10.3	98	(12.0)	180	12.5	69	(8.4)	102	6.8	72	(8.7)	113	7.4
リパーゼ増加	87	(10.6)	106	7.1	81	(9.9)	115	8.0	58	(7.1)	68	4.5	62	(7.5)	76	5.0

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
骨炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
骨障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨病変	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨溶解	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
中足骨痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脛骨内側過労性症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腱、靱帯および軟骨障害	23	(1.4)	28	1.0	29	(1.8)	30	1.0	52	(1.6)	58	1.0
弾発指	7	(0.4)	10	0.3	9	(0.5)	10	0.3	16	(0.5)	20	0.3
腱炎	7	(0.4)	8	0.3	7	(0.4)	7	0.2	14	(0.4)	15	0.3
肋軟骨炎	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
骨端症	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
腱鞘炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
腱障害	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
骨軟骨炎	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
軟骨溶解	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
半月板変性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腱石灰化	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腱付着部症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
滑膜および滑液包障害	13	(0.8)	13	0.4	16	(1.0)	17	0.6	29	(0.9)	30	0.5
滑液包炎	7	(0.4)	7	0.2	12	(0.7)	12	0.4	19	(0.6)	19	0.3
滑液嚢腫	6	(0.4)	6	0.2	5	(0.3)	5	0.2	11	(0.3)	11	0.2
結合組織障害（先天性障害を除く）	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
シェーグレン症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
リウマチ性多発筋痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
臨床検査	365	(22.2)	690	23.5	342	(20.8)	613	20.2	707	(21.5)	1303	21.8
消化管検査	199	(12.1)	333	11.4	141	(8.6)	215	7.1	340	(10.3)	548	9.2
リパーゼ増加	168	(10.2)	221	7.5	120	(7.3)	144	4.7	288	(8.8)	365	6.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
アミラーゼ増加	27	(3.3)	32	2.2	44	(5.4)	54	3.7	24	(2.9)	27	1.8	23	(2.8)	28	1.8
膵酵素増加	13	(1.6)	14	0.9	7	(0.9)	9	0.6	6	(0.7)	6	0.4	5	(0.6)	6	0.4
リパーゼ異常	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
便潜血陽性	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
結腸内視鏡検査	0				0				1	(0.1)	1	0.1	0			
便潜血	0				0				0				1	(0.1)	1	0.1
腎尿路系検査および尿検査	28	(3.4)	37	2.5	28	(3.4)	35	2.4	31	(3.8)	44	2.9	29	(3.5)	34	2.2
血中クレアチニン増加	21	(2.6)	23	1.5	12	(1.5)	13	0.9	20	(2.4)	21	1.4	18	(2.2)	20	1.3
血中尿素増加	4	(0.5)	5	0.3	5	(0.6)	5	0.3	3	(0.4)	4	0.3	1	(0.1)	1	0.1
尿中アルブミン／クレアチニン比増加	1	(0.1)	1	0.1	2	(0.2)	2	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3
尿中ブドウ糖陽性	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	4	(0.5)	4	0.3
尿中アルブミン	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
尿検査異常	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
尿中アルブミン陽性	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
尿中ヘモグロビン陽性	0				1	(0.1)	1	0.1	3	(0.4)	4	0.3	0			
血中クレアチン増加	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
糸球体濾過率減少	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
尿蛋白	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
尿中ヘモグロビン	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
尿中血	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
尿中血陽性	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
尿中白血球陽性	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
糸球体濾過率増加	0				1	(0.1)	1	0.1	0				0			
尿中アルブミン／クレアチニン比異常	0				1	(0.1)	1	0.1	0				0			
尿中クレアチニン増加	1	(0.1)	1	0.1	0				0				0			
尿中亜硝酸塩陽性	0				1	(0.1)	1	0.1	0				0			
尿中蛋白陽性	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
アミラーゼ増加	71	(4.3)	86	2.9	47	(2.9)	55	1.8	118	(3.6)	141	2.4
膵酵素増加	20	(1.2)	23	0.8	11	(0.7)	12	0.4	31	(0.9)	35	0.6
リパーゼ異常	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
便潜血陽性	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
結腸内視鏡検査	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
便潜血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎尿路系検査および尿検査	56	(3.4)	72	2.5	60	(3.6)	78	2.6	116	(3.5)	150	2.5
血中クレアチニン増加	33	(2.0)	36	1.2	38	(2.3)	41	1.4	71	(2.2)	77	1.3
血中尿素増加	9	(0.5)	10	0.3	4	(0.2)	5	0.2	13	(0.4)	15	0.3
尿中アルブミン／クレアチニン比増加	3	(0.2)	3	0.1	8	(0.5)	8	0.3	11	(0.3)	11	0.2
尿中ブドウ糖陽性	1	(0.1)	1	<0.1	7	(0.4)	7	0.2	8	(0.2)	8	0.1
尿中アルブミン	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
尿検査異常	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
尿中アルブミン陽性	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
尿中ヘモグロビン陽性	1	(0.1)	1	<0.1	3	(0.2)	4	0.1	4	(0.1)	5	0.1
血中クレアチン増加	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
糸球体濾過率減少	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
尿蛋白	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
尿中ヘモグロビン	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
尿中血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
尿中血陽性	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
尿中白血球陽性	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
糸球体濾過率増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中アルブミン／クレアチニン比異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中クレアチニン増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中亜硝酸塩陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中蛋白陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
心血管系検査（酵素検査を除く）	18	(2.2)	24	1.6	21	(2.6)	25	1.7	27	(3.3)	33	2.2	25	(3.0)	30	2.0
血圧上昇	7	(0.9)	11	0.7	6	(0.7)	7	0.5	7	(0.9)	12	0.8	8	(1.0)	10	0.7
心電図Ｔ波逆転	1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1	3	(0.4)	3	0.2
心拍数増加	2	(0.2)	2	0.1	0				4	(0.5)	4	0.3	0			
駆出率減少	2	(0.2)	2	0.1	0				0				2	(0.2)	2	0.1
心雑音	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
心電図ＱＴ延長	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
心電図変化	0				0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
冠血管造影	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
血圧低下	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
心カテーテル検査	0				2	(0.2)	3	0.2	1	(0.1)	1	0.1	0			
心電図異常ＱＲＳ群	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
ＱＲＳ軸異常	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
血圧異常	0				0				2	(0.2)	2	0.1	0			
心筋虚血の心電図所見	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
心電図ＳＴ部分異常	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
心電図Ｔ波振幅減少	0				0				0				2	(0.2)	2	0.1
心電図異常	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
心電図異常Ｑ波	0				2	(0.2)	2	0.1	0				0			
心電図異常Ｔ波	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
駆出率	1	(0.1)	1	0.1	0				0				0			
頚動脈雑音	0				0				0				1	(0.1)	1	0.1
心電図２相性Ｔ波	0				1	(0.1)	1	0.1	0				0			
心電図ＱＲＳ群延長	0				1	(0.1)	1	0.1	0				0			
心電図Ｑ波	0				0				0				1	(0.1)	1	0.1
心電図ＳＴ部分上昇	0				1	(0.1)	1	0.1	0				0			
心電図Ｔ波	0				0				1	(0.1)	1	0.1	0			
心拍数異常	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心血管系検査（酵素検査を除く）	39	(2.4)	49	1.7	52	(3.2)	63	2.1	91	(2.8)	112	1.9
血圧上昇	13	(0.8)	18	0.6	15	(0.9)	22	0.7	28	(0.9)	40	0.7
心電図Ｔ波逆転	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
心拍数増加	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
駆出率減少	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
心雑音	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
心電図ＱＴ延長	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
心電図変化	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
冠血管造影	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
血圧低下	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
心カテーテル検査	2	(0.1)	3	0.1	1	(0.1)	1	<0.1	3	(0.1)	4	0.1
心電図異常ＱＲＳ群	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
ＱＲＳ軸異常	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血圧異常	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
心筋虚血の心電図所見	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心電図ＳＴ部分異常	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
心電図Ｔ波振幅減少	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
心電図異常	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
心電図異常Ｑ波	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
心電図異常Ｔ波	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
駆出率	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頚動脈雑音	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図２相性Ｔ波	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心電図ＱＲＳ群延長	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心電図Ｑ波	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図ＳＴ部分上昇	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心電図Ｔ波	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心拍数異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
心拍数不整	0				1	(0.1)	1	0.1	0				0			
心房圧上昇	0				0				0				1	(0.1)	1	0.1
足脈拍減少	0				1	(0.1)	1	0.1	0				0			
末梢血管造影	0				0				1	(0.1)	1	0.1	0			
血液学的検査（血液型検査を含む）	12	(1.5)	21	1.4	16	(2.0)	28	1.9	17	(2.1)	31	2.1	19	(2.3)	27	1.8
ヘモグロビン減少	6	(0.7)	7	0.5	4	(0.5)	4	0.3	7	(0.9)	7	0.5	10	(1.2)	10	0.7
白血球数増加	0				5	(0.6)	5	0.3	5	(0.6)	5	0.3	1	(0.1)	1	0.1
ヘマトクリット減少	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2
血小板数減少	1	(0.1)	1	0.1	0				1	(0.1)	2	0.1	4	(0.5)	4	0.3
赤血球分布幅増加	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	3	0.2	1	(0.1)	1	0.1
好中球数増加	0				4	(0.5)	5	0.3	1	(0.1)	1	0.1	0			
赤血球数減少	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
ヘマトクリット増加	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
ヘモグロビン増加	3	(0.4)	3	0.2	0				0				0			
血小板数増加	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
赤血球数増加	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
単球数増加	0				2	(0.2)	3	0.2	0				1	(0.1)	1	0.1
血液学的検査異常	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
国際標準比増加	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
白血球数減少	0				2	(0.2)	2	0.1	0				0			
ヘマトクリット異常	0				0				1	(0.1)	1	0.1	0			
ヘモグロビン異常	0				0				1	(0.1)	1	0.1	0			
血球数異常	0				0				0				1	(0.1)	1	0.1
好塩基球数増加	0				0				0				1	(0.1)	1	0.1
好中球数異常	0				0				1	(0.1)	1	0.1	0			
好中球数減少	0				1	(0.1)	1	0.1	0				0			
平均血小板容積増加	0				1	(0.1)	1	0.1	0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心拍数不整	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心房圧上昇	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
足脈拍減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
末梢血管造影	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血液学的検査（血液型検査を含む）	28	(1.7)	49	1.7	36	(2.2)	58	1.9	64	(1.9)	107	1.8
ヘモグロビン減少	10	(0.6)	11	0.4	17	(1.0)	17	0.6	27	(0.8)	28	0.5
白血球数増加	5	(0.3)	5	0.2	6	(0.4)	6	0.2	11	(0.3)	11	0.2
ヘマトクリット減少	5	(0.3)	5	0.2	5	(0.3)	5	0.2	10	(0.3)	10	0.2
血小板数減少	1	(0.1)	1	<0.1	5	(0.3)	6	0.2	6	(0.2)	7	0.1
赤血球分布幅増加	3	(0.2)	3	0.1	3	(0.2)	4	0.1	6	(0.2)	7	0.1
好中球数増加	4	(0.2)	5	0.2	1	(0.1)	1	<0.1	5	(0.2)	6	0.1
赤血球数減少	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
ヘマトクリット増加	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
ヘモグロビン増加	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
血小板数増加	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
赤血球数増加	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
単球数増加	2	(0.1)	3	0.1	1	(0.1)	1	<0.1	3	(0.1)	4	0.1
血液学的検査異常	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
国際標準比増加	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
白血球数減少	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
ヘマトクリット異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ヘモグロビン異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血球数異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
好塩基球数増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
好中球数異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
好中球数減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
平均血小板容積増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
平均赤血球ヘモグロビン減少	0				0				1	(0.1)	2	0.1	0			
平均赤血球容積減少	0				0				1	(0.1)	1	0.1	0			
平均赤血球容積増加	0				0				0				1	(0.1)	1	0.1
肝胆道系検査	18	(2.2)	33	2.2	8	(1.0)	10	0.7	10	(1.2)	17	1.1	13	(1.6)	17	1.1
アスパラギン酸アミノトランスフェラーゼ増加	10	(1.2)	11	0.7	1	(0.1)	1	0.1	6	(0.7)	6	0.4	5	(0.6)	5	0.3
アラニンアミノトランスフェラーゼ増加	9	(1.1)	11	0.7	3	(0.4)	4	0.3	5	(0.6)	6	0.4	4	(0.5)	4	0.3
血中ビリルビン増加	5	(0.6)	6	0.4	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
肝酵素上昇	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	5	(0.6)	5	0.3
トランスアミナーゼ上昇	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
肝機能検査異常	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
γ－グルタミルトランスフェラーゼ増加	0				0				1	(0.1)	1	0.1	0			
肝酵素異常	0				0				0				1	(0.1)	1	0.1
肝超音波検査異常	1	(0.1)	1	0.1	0				0				0			
血中ビリルビン異常	1	(0.1)	1	0.1	0				0				0			
尿中ビリルビン	0				1	(0.1)	1	0.1	0				0			
水分、電解質および無機質検査	16	(1.9)	17	1.1	12	(1.5)	17	1.2	16	(2.0)	22	1.5	16	(1.9)	19	1.2
血中カリウム増加	6	(0.7)	6	0.4	8	(1.0)	10	0.7	7	(0.9)	9	0.6	8	(1.0)	10	0.7
血中カルシウム増加	5	(0.6)	6	0.4	3	(0.4)	4	0.3	5	(0.6)	8	0.5	4	(0.5)	4	0.3
血中カリウム減少	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	4	0.3	3	(0.4)	3	0.2
血中マグネシウム減少	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
血中ナトリウム増加	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
血中鉄減少	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
血中カルシウム減少	0				1	(0.1)	1	0.1	0				0			
血中亜鉛減少	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
平均赤血球ヘモグロビン減少	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
平均赤血球容積減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
平均赤血球容積増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝胆道系検査	26	(1.6)	43	1.5	23	(1.4)	34	1.1	49	(1.5)	77	1.3
アスパラギン酸アミノトランスフェラーゼ増加	11	(0.7)	12	0.4	11	(0.7)	11	0.4	22	(0.7)	23	0.4
アラニンアミノトランスフェラーゼ増加	12	(0.7)	15	0.5	9	(0.5)	10	0.3	21	(0.6)	25	0.4
血中ビリルビン増加	6	(0.4)	7	0.2	3	(0.2)	3	0.1	9	(0.3)	10	0.2
肝酵素上昇	2	(0.1)	2	0.1	6	(0.4)	6	0.2	8	(0.2)	8	0.1
トランスアミナーゼ上昇	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
肝機能検査異常	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
γ－グルタミルトランスフェラーゼ増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝酵素異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝超音波検査異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中ビリルビン異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中ビリルビン	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
水分、電解質および無機質検査	28	(1.7)	34	1.2	32	(1.9)	41	1.4	60	(1.8)	75	1.3
血中カリウム増加	14	(0.9)	16	0.5	15	(0.9)	19	0.6	29	(0.9)	35	0.6
血中カルシウム増加	8	(0.5)	10	0.3	9	(0.5)	12	0.4	17	(0.5)	22	0.4
血中カリウム減少	2	(0.1)	2	0.1	6	(0.4)	7	0.2	8	(0.2)	9	0.2
血中マグネシウム減少	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
血中ナトリウム増加	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
血中鉄減少	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血中カルシウム減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中亜鉛減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
身体的診察および器官系の状態に関する事項	12	(1.5)	13	0.9	18	(2.2)	19	1.3	11	(1.3)	12	0.8	9	(1.1)	9	0.6
体重減少	9	(1.1)	10	0.7	13	(1.6)	13	0.9	6	(0.7)	6	0.4	3	(0.4)	3	0.2
体重増加	2	(0.2)	2	0.1	3	(0.4)	3	0.2	3	(0.4)	4	0.3	6	(0.7)	6	0.4
体温上昇	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
ウエスト周囲径増加	0				1	(0.1)	1	0.1	0				0			
呼吸音異常	0				1	(0.1)	1	0.1	0				0			
呼吸数増加	1	(0.1)	1	0.1	0				0				0			
脂質検査	9	(1.1)	9	0.6	13	(1.6)	14	1.0	11	(1.3)	15	1.0	10	(1.2)	11	0.7
血中トリグリセリド増加	5	(0.6)	5	0.3	9	(1.1)	9	0.6	6	(0.7)	6	0.4	2	(0.2)	2	0.1
遊離脂肪酸増加	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	4	(0.5)	4	0.3
血中コレステロール増加	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
低比重リポ蛋白増加	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
血中トリグリセリド異常	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
高比重リポ蛋白減少	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
脂質異常	1	(0.1)	1	0.1	0				0				0			
低比重リポ蛋白異常	0				0				1	(0.1)	1	0.1	0			
代謝、栄養学的および血液ガス検査	10	(1.2)	15	1.0	5	(0.6)	5	0.3	13	(1.6)	15	1.0	12	(1.5)	12	0.8
血中ブドウ糖増加	5	(0.6)	10	0.7	2	(0.2)	2	0.1	8	(1.0)	8	0.5	4	(0.5)	4	0.3
グリコヘモグロビン増加	2	(0.2)	2	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1
ビタミンD減少	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
血中尿酸増加	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
血中ブドウ糖減少	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
血中ブドウ糖変動	0				0				0				1	(0.1)	1	0.1
血中葉酸減少	0				0				0				1	(0.1)	1	0.1
内分泌検査（性ホルモン検査を含む）	7	(0.9)	9	0.6	9	(1.1)	10	0.7	11	(1.3)	12	0.8	10	(1.2)	11	0.7
血中カルシトニン増加	4	(0.5)	4	0.3	7	(0.9)	7	0.5	9	(1.1)	9	0.6	4	(0.5)	4	0.3

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
身体的診察および器官系の状態に関する事項	30	(1.8)	32	1.1	20	(1.2)	21	0.7	50	(1.5)	53	0.9
体重減少	22	(1.3)	23	0.8	9	(0.5)	9	0.3	31	(0.9)	32	0.5
体重増加	5	(0.3)	5	0.2	9	(0.5)	10	0.3	14	(0.4)	15	0.3
体温上昇	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
ウエスト周囲径増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
呼吸音異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
呼吸数増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脂質検査	22	(1.3)	23	0.8	21	(1.3)	26	0.9	43	(1.3)	49	0.8
血中トリグリセリド増加	14	(0.9)	14	0.5	8	(0.5)	8	0.3	22	(0.7)	22	0.4
遊離脂肪酸増加	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2
血中コレステロール増加	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
低比重リポ蛋白増加	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
血中トリグリセリド異常	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
高比重リポ蛋白減少	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
脂質異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
低比重リポ蛋白異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
代謝、栄養学的および血液ガス検査	15	(0.9)	20	0.7	25	(1.5)	27	0.9	40	(1.2)	47	0.8
血中ブドウ糖増加	7	(0.4)	12	0.4	12	(0.7)	12	0.4	19	(0.6)	24	0.4
グリコヘモグロビン増加	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2
ビタミンＤ減少	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
血中尿酸増加	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
血中ブドウ糖減少	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
血中ブドウ糖変動	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中葉酸減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
内分泌検査（性ホルモン検査を含む）	16	(1.0)	19	0.6	21	(1.3)	23	0.8	37	(1.1)	42	0.7
血中カルシトニン増加	11	(0.7)	11	0.4	13	(0.8)	13	0.4	24	(0.7)	24	0.4

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
血中プロインスリン増加	0				1	(0.1)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
血中インスリン増加	0				0				0				3	(0.4)	3	0.2
血中テストステロン減少	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
血中エストロゲン増加	1	(0.1)	1	0.1	0				0				0			
血中テストステロン増加	0				0				0				1	(0.1)	1	0.1
血中甲状腺刺激ホルモン減少	0				1	(0.1)	1	0.1	0				0			
血中甲状腺刺激ホルモン増加	1	(0.1)	1	0.1	0				0				0			
血中成長ホルモン増加	0				0				0				1	(0.1)	1	0.1
血中卵胞刺激ホルモン	0				0				0				1	(0.1)	1	0.1
遊離サイロキシン減少	1	(0.1)	1	0.1	0				0				0			
酵素検査ＮＥＣ	4	(0.5)	4	0.3	2	(0.2)	2	0.1	7	(0.9)	7	0.5	5	(0.6)	6	0.4
血中アルカリホスファターゼ増加	2	(0.2)	2	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	2	0.1
トロポニン増加	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
血中クレアチンホスホキナーゼ増加	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
トロポニンＩ増加	0				0				1	(0.1)	1	0.1	0			
血中アルカリホスファターゼ	0				0				1	(0.1)	1	0.1	0			
血中アルカリホスファターゼ異常	1	(0.1)	1	0.1	0				0				0			
神経学、特殊感覚および精神医学的検査	2	(0.2)	2	0.1	0				2	(0.2)	3	0.2	2	(0.2)	2	0.1
つぎ足歩行検査異常	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
眼圧上昇	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
眼圧検査	0				0				1	(0.1)	1	0.1	0			
眼底検査異常	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
血中プロインスリン増加	1	(0.1)	2	0.1	3	(0.2)	3	0.1	4	(0.1)	5	0.1
血中インスリン増加	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
血中テストステロン減少	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
血中エストロゲン増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中テストステロン増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中甲状腺刺激ホルモン減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中甲状腺刺激ホルモン増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中成長ホルモン増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中卵胞刺激ホルモン	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
遊離サイロキシン減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
酵素検査ＮＥＣ	6	(0.4)	6	0.2	12	(0.7)	13	0.4	18	(0.5)	19	0.3
血中アルカリホスファターゼ増加	3	(0.2)	3	0.1	5	(0.3)	6	0.2	8	(0.2)	9	0.2
トロポニン増加	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
血中クレアチンホスホキナーゼ増加	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
トロポニンＩ増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中アルカリホスファターゼ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中アルカリホスファターゼ異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経学、特殊感覚および精神医学的検査	2	(0.1)	2	0.1	4	(0.2)	5	0.2	6	(0.2)	7	0.1
つぎ足歩行検査異常	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
眼圧上昇	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
眼圧検査	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼底検査異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
細胞遺伝学的検査	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
前立腺特異性抗原増加	2	(0.2)	2	0.1	0				0				2	(0.2)	2	0.1
糖鎖抗原１２５増加	0				1	(0.1)	1	0.1	0				0			
糖鎖抗原１９－９増加	1	(0.1)	1	0.1	0				0				0			
検査、画像および病理組織学的検査ＮＥＣ	0				1	(0.1)	1	0.1	1	(0.1)	2	0.1	0			
血液スミア試験異常	0				1	(0.1)	1	0.1	0				0			
血液検査異常	0				0				1	(0.1)	2	0.1	0			
微生物学的および血清学的検査	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
Ｂ型肝炎コア抗体陽性	0				0				1	(0.1)	1	0.1	0			
ヘリコバクター検査陽性	1	(0.1)	1	0.1	0				0				0			
細菌検査陽性	0				0				0				1	(0.1)	1	0.1
呼吸器系検査（血液ガス検査を除く）	0				0				0				2	(0.2)	2	0.1
胸部Ｘ線異常	0				0				0				1	(0.1)	1	0.1
肺活量測定異常	0				0				0				1	(0.1)	1	0.1
筋骨格系および軟部組織検査（酵素検査を除く）	1	(0.1)	1	0.1	0				0				0			
骨密度減少	1	(0.1)	1	0.1	0				0				0			
生殖器および乳房検査（ホルモン検査を除く）	1	(0.1)	1	0.1	0				0				0			
前立腺生検	1	(0.1)	1	0.1	0				0				0			
蛋白および化学的検査ＮＥＣ	0				0				0				1	(0.1)	1	0.1
血中アルブミン増加	0				0				0				1	(0.1)	1	0.1
神経系障害	191	(23.2)	296	19.9	191	(23.3)	302	20.9	209	(25.5)	362	24.0	195	(23.6)	325	21.3
神経学的障害ＮＥＣ	87	(10.6)	109	7.3	93	(11.4)	123	8.5	76	(9.3)	103	6.8	79	(9.6)	101	6.6

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
細胞遺伝学的検査	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
前立腺特異性抗原増加	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
糖鎖抗原１２５増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖鎖抗原１９－９増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
検査、画像および病理組織学的検査ＮＥＣ	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
血液スミア試験異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血液検査異常	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
微生物学的および血清学的検査	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
Ｂ型肝炎コア抗体陽性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ヘリコバクター検査陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
細菌検査陽性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼吸器系検査（血液ガス検査を除く）	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
胸部Ｘ線異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺活量測定異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋骨格系および軟部組織検査（酵素検査を除く）	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨密度減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
生殖器および乳房検査（ホルモン検査を除く）	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
前立腺生検	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
蛋白および化学的検査ＮＥＣ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中アルブミン増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経系障害	382	(23.3)	598	20.4	404	(24.6)	687	22.6	786	(23.9)	1285	21.5
神経学的障害ＮＥＣ	180	(11.0)	232	7.9	155	(9.4)	204	6.7	335	(10.2)	436	7.3

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
浮動性めまい	48	(5.8)	51	3.4	43	(5.3)	49	3.4	38	(4.6)	54	3.6	39	(4.7)	46	3.0
感覚鈍麻	9	(1.1)	11	0.7	8	(1.0)	8	0.6	10	(1.2)	10	0.7	4	(0.5)	4	0.3
失神	8	(1.0)	8	0.5	7	(0.9)	9	0.6	7	(0.9)	8	0.5	8	(1.0)	8	0.5
錯感覚	10	(1.2)	10	0.7	4	(0.5)	4	0.3	4	(0.5)	4	0.3	7	(0.8)	7	0.5
味覚異常	2	(0.2)	2	0.1	10	(1.2)	10	0.7	3	(0.4)	3	0.2	2	(0.2)	2	0.1
低血糖性意識消失	6	(0.7)	6	0.4	4	(0.5)	4	0.3	2	(0.2)	2	0.1	3	(0.4)	9	0.6
傾眠	3	(0.4)	3	0.2	5	(0.6)	6	0.4	2	(0.2)	3	0.2	3	(0.4)	4	0.3
嗜眠	3	(0.4)	4	0.3	7	(0.9)	7	0.5	1	(0.1)	1	0.1	2	(0.2)	2	0.1
失神寸前の状態	2	(0.2)	2	0.1	3	(0.4)	5	0.3	3	(0.4)	3	0.2	3	(0.4)	4	0.3
神経痛	0				4	(0.5)	4	0.3	3	(0.4)	3	0.2	0			
下肢静止不能症候群	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
灼熱感	3	(0.4)	3	0.2	0				2	(0.2)	2	0.1	0			
平衡障害	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
振動覚低下	0				1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
体位性めまい	0				1	(0.1)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
ヘルペス後神経痛	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
意識消失	0				2	(0.2)	2	0.1	0				0			
感覚消失	0				2	(0.2)	2	0.1	0				0			
協調運動異常	0				1	(0.1)	2	0.1	0				1	(0.1)	1	0.1
味覚減退	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
肋間神経痛	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
モートン神経痛	1	(0.1)	1	0.1	0				0				0			
意識変容状態	0				0				1	(0.1)	2	0.1	0			
異常感覚	0				0				0				1	(0.1)	1	0.1
運動失調	0				0				0				1	(0.1)	1	0.1
感覚障害	0				1	(0.1)	1	0.1	0				0			
起立障害	0				0				0				1	(0.1)	1	0.1
蟻走感	0				0				0				1	(0.1)	1	0.1
構語障害	0				0				0				1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
浮動性めまい	91	(5.5)	100	3.4	77	(4.7)	100	3.3	168	(5.1)	200	3.4
感覚鈍麻	17	(1.0)	19	0.6	14	(0.9)	14	0.5	31	(0.9)	33	0.6
失神	15	(0.9)	17	0.6	15	(0.9)	16	0.5	30	(0.9)	33	0.6
錯感覚	14	(0.9)	14	0.5	11	(0.7)	11	0.4	25	(0.8)	25	0.4
味覚異常	12	(0.7)	12	0.4	5	(0.3)	5	0.2	17	(0.5)	17	0.3
低血糖性意識消失	10	(0.6)	10	0.3	5	(0.3)	11	0.4	15	(0.5)	21	0.4
傾眠	8	(0.5)	9	0.3	5	(0.3)	7	0.2	13	(0.4)	16	0.3
嗜眠	10	(0.6)	11	0.4	3	(0.2)	3	0.1	13	(0.4)	14	0.2
失神寸前の状態	5	(0.3)	7	0.2	6	(0.4)	7	0.2	11	(0.3)	14	0.2
神経痛	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
下肢静止不能症候群	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
灼熱感	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
平衡障害	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
振動覚低下	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
体位性めまい	1	(0.1)	2	0.1	3	(0.2)	3	0.1	4	(0.1)	5	0.1
ヘルペス後神経痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
意識消失	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
感覚消失	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
協調運動異常	1	(0.1)	2	0.1	1	(0.1)	1	<0.1	2	(0.1)	3	0.1
味覚減退	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
肋間神経痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
モートン神経痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
意識変容状態	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
異常感覚	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
運動失調	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感覚障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
起立障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
蟻走感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
構語障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
昏睡	0				1	(0.1)	2	0.1	0				0			
失語症	0				1	(0.1)	1	0.1	0				0			
小脳症候群	0				0				1	(0.1)	1	0.1	0			
神経系障害	0				0				1	(0.1)	1	0.1	0			
脳圧低下	0				0				1	(0.1)	1	0.1	0			
脳脊髄液漏	0				0				1	(0.1)	2	0.1	0			
反射減弱	0				0				0				1	(0.1)	1	0.1
味覚消失	1	(0.1)	1	0.1	0				0				0			
頭痛	57	(6.9)	80	5.4	58	(7.1)	91	6.3	67	(8.2)	120	8.0	74	(9.0)	111	7.3
頭痛	54	(6.6)	75	5.0	55	(6.7)	86	6.0	64	(7.8)	111	7.4	74	(9.0)	110	7.2
片頭痛	1	(0.1)	1	0.1	3	(0.4)	3	0.2	5	(0.6)	6	0.4	0			
副鼻腔炎に伴う頭痛	3	(0.4)	3	0.2	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
緊張性頭痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
後頭神経痛	0				0				1	(0.1)	1	0.1	0			
中枢神経系血管障害	29	(3.5)	33	2.2	21	(2.6)	26	1.8	41	(5.0)	52	3.4	32	(3.9)	37	2.4
虚血性脳卒中	8	(1.0)	8	0.5	6	(0.7)	7	0.5	15	(1.8)	15	1.0	4	(0.5)	4	0.3
一過性脳虚血発作	8	(1.0)	9	0.6	6	(0.7)	7	0.5	11	(1.3)	13	0.9	6	(0.7)	6	0.4
頚動脈狭窄	4	(0.5)	4	0.3	2	(0.2)	2	0.1	7	(0.9)	8	0.5	6	(0.7)	6	0.4
脳血管発作	1	(0.1)	1	0.1	3	(0.4)	3	0.2	6	(0.7)	6	0.4	5	(0.6)	5	0.3
脳梗塞	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
出血性卒中	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
脳虚血	0				0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
脳血管障害	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
ラクナ梗塞	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
虚血性脳小血管疾患	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
頭蓋内動脈瘤	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
頚動脈硬化症	1	(0.1)	1	0.1	0				0				1	(0.1)	2	0.1
頚動脈閉塞	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
椎骨脳底動脈不全	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
昏睡	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
失語症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
小脳症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経系障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳圧低下	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳脊髄液漏	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
反射減弱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
味覚消失	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頭痛	115	(7.0)	171	5.8	141	(8.6)	231	7.6	256	(7.8)	402	6.7
頭痛	109	(6.6)	161	5.5	138	(8.4)	221	7.3	247	(7.5)	382	6.4
片頭痛	4	(0.2)	4	0.1	5	(0.3)	6	0.2	9	(0.3)	10	0.2
副鼻腔炎に伴う頭痛	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
緊張性頭痛	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
後頭神経痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
中枢神経系血管障害	50	(3.0)	59	2.0	73	(4.4)	89	2.9	123	(3.7)	148	2.5
虚血性脳卒中	14	(0.9)	15	0.5	19	(1.2)	19	0.6	33	(1.0)	34	0.6
一過性脳虚血発作	14	(0.9)	16	0.5	17	(1.0)	19	0.6	31	(0.9)	35	0.6
頚動脈狭窄	6	(0.4)	6	0.2	13	(0.8)	14	0.5	19	(0.6)	20	0.3
脳血管発作	4	(0.2)	4	0.1	11	(0.7)	11	0.4	15	(0.5)	15	0.3
脳梗塞	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
出血性卒中	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
脳虚血	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
脳血管障害	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
ラクナ梗塞	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
虚血性脳小血管疾患	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
頭蓋内動脈瘤	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
頚動脈硬化症	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
頚動脈閉塞	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
椎骨脳底動脈不全	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
虚血性脳梗塞	0				0				0				1	(0.1)	1	0.1
頚動脈疾患	0				0				0				1	(0.1)	1	0.1
塞栓性脳卒中	0				0				0				1	(0.1)	1	0.1
視床梗塞	0				1	(0.1)	1	0.1	0				0			
小脳出血	0				0				1	(0.1)	1	0.1	0			
椎骨動脈閉塞	1	(0.1)	1	0.1	0				0				0			
頭蓋内出血	0				0				0				1	(0.1)	1	0.1
脳幹梗塞	1	(0.1)	1	0.1	0				0				0			
脳血管不全	0				1	(0.1)	1	0.1	0				0			
脳室内出血	0				0				0				1	(0.1)	1	0.1
脳出血	1	(0.1)	1	0.1	0				0				0			
末梢性ニューロパチー	29	(3.5)	34	2.3	22	(2.7)	24	1.7	33	(4.0)	37	2.5	29	(3.5)	32	2.1
糖尿病性ニューロパチー	11	(1.3)	11	0.7	9	(1.1)	9	0.6	11	(1.3)	11	0.7	12	(1.5)	12	0.8
末梢性ニューロパチー	10	(1.2)	11	0.7	3	(0.4)	5	0.3	7	(0.9)	7	0.5	7	(0.8)	7	0.5
手根管症候群	5	(0.6)	7	0.5	4	(0.5)	4	0.3	6	(0.7)	7	0.5	5	(0.6)	5	0.3
神経圧迫	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
多発ニューロパチー	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
慢性多発ニューロパチー	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1	0			
糖尿病性単ニューロパチー	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
末梢性感覚運動ニューロパチー	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
腓骨神経麻痺	0				0				0				2	(0.2)	2	0.1
感覚異常性大腿神経痛	0				1	(0.1)	1	0.1	0				0			
坐骨神経ニューロパチー	0				0				1	(0.1)	1	0.1	0			
軸索型ニューロパチー	0				0				1	(0.1)	1	0.1	0			
重症疾患多発ニューロパチー	0				0				0				1	(0.1)	1	0.1
神経炎	0				0				1	(0.1)	1	0.1	0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
虚血性脳梗塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頚動脈疾患	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
塞栓性脳卒中	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
視床梗塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
小脳出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎骨動脈閉塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頭蓋内出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳幹梗塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳血管不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳室内出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
末梢性ニューロパチー	51	(3.1)	58	2.0	62	(3.8)	69	2.3	113	(3.4)	127	2.1
糖尿病性ニューロパチー	20	(1.2)	20	0.7	23	(1.4)	23	0.8	43	(1.3)	43	0.7
末梢性ニューロパチー	13	(0.8)	16	0.5	14	(0.9)	14	0.5	27	(0.8)	30	0.5
手根管症候群	9	(0.5)	11	0.4	11	(0.7)	12	0.4	20	(0.6)	23	0.4
神経圧迫	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
多発ニューロパチー	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
慢性多発ニューロパチー	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
糖尿病性単ニューロパチー	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
末梢性感覚運動ニューロパチー	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
腓骨神経麻痺	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
感覚異常性大腿神経痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
坐骨神経ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
軸索型ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
重症疾患多発ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
単ニューロパチー	0				0				0				1	(0.1)	1	0.1
肘部管症候群	0				0				1	(0.1)	2	0.1	0			
末梢性感覚ニューロパチー	0				0				0				1	(0.1)	1	0.1
慢性炎症性脱髄性多発根ニューロパチー	1	(0.1)	1	0.1	0				0				0			
梨状筋症候群	0				0				1	(0.1)	1	0.1	0			
脊髄および神経根障害	13	(1.6)	17	1.1	11	(1.3)	11	0.8	18	(2.2)	18	1.2	14	(1.7)	14	0.9
坐骨神経痛	8	(1.0)	9	0.6	4	(0.5)	4	0.3	7	(0.9)	7	0.5	7	(0.8)	7	0.5
神経根障害	2	(0.2)	2	0.1	1	(0.1)	1	0.1	5	(0.6)	5	0.3	3	(0.4)	3	0.2
腰髄神経根障害	1	(0.1)	1	0.1	2	(0.2)	2	0.1	4	(0.5)	4	0.3	0			
神経根圧迫	1	(0.1)	3	0.2	0				0				2	(0.2)	2	0.1
脊髄症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
頚髄神経根障害	0				2	(0.2)	2	0.1	0				0			
頚髄症	0				0				0				1	(0.1)	1	0.1
頚腕症候群	0				1	(0.1)	1	0.1	0				0			
腰仙部神経根炎	1	(0.1)	1	0.1	0				0				0			
脊髄圧迫	0				0				1	(0.1)	1	0.1	0			
脊髄性跛行症	0				1	(0.1)	1	0.1	0				0			
運動障害（パーキンソニズムを含む）	3	(0.4)	4	0.3	6	(0.7)	8	0.6	8	(1.0)	8	0.5	8	(1.0)	8	0.5
振戦	2	(0.2)	2	0.1	2	(0.2)	3	0.2	3	(0.4)	3	0.2	6	(0.7)	6	0.4
パーキンソン病	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
パーキンソニズム	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
本態性振戦	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
ジスキネジア	0				0				0				1	(0.1)	1	0.1
ジストニア振戦	0				1	(0.1)	1	0.1	0				0			
運動障害	0				0				1	(0.1)	1	0.1	0			
血管性パーキンソニズム	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
単ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肘部管症候群	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
末梢性感覚ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
慢性炎症性脱髄性多発根ニューロパチー	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
梨状筋症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脊髄および神経根障害	24	(1.5)	28	1.0	32	(1.9)	32	1.1	56	(1.7)	60	1.0
坐骨神経痛	12	(0.7)	13	0.4	14	(0.9)	14	0.5	26	(0.8)	27	0.5
神経根障害	3	(0.2)	3	0.1	8	(0.5)	8	0.3	11	(0.3)	11	0.2
腰髄神経根障害	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
神経根圧迫	1	(0.1)	3	0.1	2	(0.1)	2	0.1	3	(0.1)	5	0.1
脊髄症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
頚髄神経根障害	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
頚髄症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頚腕症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腰仙部神経根炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脊髄圧迫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脊髄性跛行症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
運動障害（パーキンソニズムを含む）	9	(0.5)	12	0.4	16	(1.0)	16	0.5	25	(0.8)	28	0.5
振戦	4	(0.2)	5	0.2	9	(0.5)	9	0.3	13	(0.4)	14	0.2
パーキンソン病	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
パーキンソニズム	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
本態性振戦	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
ジスキネジア	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ジストニア振戦	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
運動障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管性パーキンソニズム	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
不全片麻痺	0				0				1	(0.1)	1	0.1	0			
末梢性麻痺	0				0				0				1	(0.1)	1	0.1
精神的機能障害	5	(0.6)	5	0.3	10	(1.2)	10	0.7	4	(0.5)	4	0.3	8	(1.0)	8	0.5
健忘	3	(0.4)	3	0.2	4	(0.5)	4	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1
記憶障害	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
認知障害	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
老年認知症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
アルツハイマー型認知症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
認知症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
注意力障害	0				0				0				1	(0.1)	1	0.1
脳神経障害（新生物を除く）	7	(0.9)	7	0.5	2	(0.2)	2	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3
第７脳神経麻痺	4	(0.5)	4	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
三叉神経痛	0				0				0				1	(0.1)	1	0.1
舌下神経不全麻痺	0				0				0				1	(0.1)	1	0.1
第３脳神経不全麻痺	0				0				0				1	(0.1)	1	0.1
第４脳神経麻痺	0				0				1	(0.1)	1	0.1	0			
第６脳神経障害	1	(0.1)	1	0.1	0				0				0			
第６脳神経不全麻痺	1	(0.1)	1	0.1	0				0				0			
脳神経麻痺	1	(0.1)	1	0.1	0				0				0			
脳症	5	(0.6)	5	0.3	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
代謝性脳症	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
脳症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
肝性脳症	2	(0.2)	2	0.1	0				0				0			
高血圧性脳症	0				0				0				1	(0.1)	1	0.1
低酸素性虚血性脳症	0				0				1	(0.1)	1	0.1	0			
発作（亜型を含む）	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	4	0.3	3	(0.4)	3	0.2
痙攣発作	0				1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
てんかん	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
不全片麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢性麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精神的機能障害	15	(0.9)	15	0.5	12	(0.7)	12	0.4	27	(0.8)	27	0.5
健忘	7	(0.4)	7	0.2	2	(0.1)	2	0.1	9	(0.3)	9	0.2
記憶障害	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
認知障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
老年認知症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
アルツハイマー型認知症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
認知症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
注意力障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳神経障害（新生物を除く）	9	(0.5)	9	0.3	7	(0.4)	7	0.2	16	(0.5)	16	0.3
第７脳神経麻痺	6	(0.4)	6	0.2	3	(0.2)	3	0.1	9	(0.3)	9	0.2
三叉神経痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
舌下神経不全麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
第３脳神経不全麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
第４脳神経麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
第６脳神経障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
第６脳神経不全麻痺	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳神経麻痺	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳症	6	(0.4)	6	0.2	4	(0.2)	4	0.1	10	(0.3)	10	0.2
代謝性脳症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
脳症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
肝性脳症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
高血圧性脳症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
低酸素性虚血性脳症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
発作（亜型を含む）	3	(0.2)	3	0.1	6	(0.4)	7	0.2	9	(0.3)	10	0.2
痙攣発作	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
てんかん	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
部分発作	0				0				2	(0.2)	2	0.1	0			
発作様現象	0				0				1	(0.1)	1	0.1	0			
脳器質性疾患	0				0				3	(0.4)	5	0.3	1	(0.1)	1	0.1
大脳萎縮	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
脳室拡張	0				0				2	(0.2)	2	0.1	0			
硬膜下ヒグローマ	0				0				1	(0.1)	1	0.1	0			
眼部神経学的障害	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
視野欠損	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
トンネル状視野	0				1	(0.1)	1	0.1	0				0			
睡眠障害（亜型を含む）	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
過眠症	0				0				1	(0.1)	1	0.1	0			
概日リズム睡眠障害	0				1	(0.1)	1	0.1	0				0			
周期性四肢運動障害	1	(0.1)	1	0.1	0				0				0			
睡眠時麻痺	0				0				0				1	(0.1)	1	0.1
頭蓋内圧亢進および水頭症	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
水頭症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
脳浮腫	0				0				0				1	(0.1)	1	0.1
良性神経系新生物	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
くも膜嚢胞	0				0				0				1	(0.1)	1	0.1
脊髄髄膜嚢胞	0				0				1	(0.1)	1	0.1	0			
神経筋障害	0				0				1	(0.1)	1	0.1	0			
自律神経失調	0				0				1	(0.1)	1	0.1	0			
脱髄疾患	0				0				1	(0.1)	1	0.1	0			
多発性硬化症	0				0				1	(0.1)	1	0.1	0			
代謝および栄養障害	216	(26.2)	306	20.6	175	(21.4)	235	16.3	198	(24.2)	282	18.7	167	(20.2)	242	15.9
糖代謝障害（糖尿病を含む）	42	(5.1)	60	4.0	24	(2.9)	29	2.0	74	(9.0)	93	6.2	71	(8.6)	85	5.6
高血糖	16	(1.9)	25	1.7	4	(0.5)	4	0.3	26	(3.2)	33	2.2	26	(3.2)	28	1.8

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
部分発作	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
発作様現象	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳器質性疾患	0				4	(0.2)	6	0.2	4	(0.1)	6	0.1
大脳萎縮	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
脳室拡張	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
硬膜下ヒグローマ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼部神経学的障害	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
視野欠損	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
トンネル状視野	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
睡眠障害（亜型を含む）	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
過眠症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
概日リズム睡眠障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
周期性四肢運動障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
睡眠時麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頭蓋内圧亢進および水頭症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
水頭症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
脳浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性神経系新生物	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
くも膜嚢胞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脊髄髄膜嚢胞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経筋障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
自律神経失調	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脱髄疾患	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
多発性硬化症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
代謝および栄養障害	391	(23.8)	541	18.5	365	(22.2)	524	17.3	756	(23.0)	1065	17.8
糖代謝障害（糖尿病を含む）	66	(4.0)	89	3.0	145	(8.8)	178	5.9	211	(6.4)	267	4.5
高血糖	20	(1.2)	29	1.0	52	(3.2)	61	2.0	72	(2.2)	90	1.5

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
コントロール不良の糖尿病	10	(1.2)	10	0.7	7	(0.9)	7	0.5	14	(1.7)	18	1.2	21	(2.5)	23	1.5
糖尿病	9	(1.1)	10	0.7	8	(1.0)	9	0.6	23	(2.8)	26	1.7	11	(1.3)	13	0.9
低血糖症	12	(1.5)	15	1.0	5	(0.6)	9	0.6	10	(1.2)	13	0.9	15	(1.8)	18	1.2
２型糖尿病	0				0				3	(0.4)	3	0.2	3	(0.4)	3	0.2
食欲および総合的栄養摂取障害	85	(10.3)	100	6.7	84	(10.3)	98	6.8	23	(2.8)	25	1.7	11	(1.3)	13	0.9
食欲減退	84	(10.2)	94	6.3	76	(9.3)	89	6.2	19	(2.3)	21	1.4	9	(1.1)	10	0.7
食欲亢進	6	(0.7)	6	0.4	5	(0.6)	5	0.3	3	(0.4)	3	0.2	1	(0.1)	1	0.1
肥満	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
悪液質	0				1	(0.1)	1	0.1	0				0			
過小食	0				0				0				1	(0.1)	1	0.1
拒食	0				1	(0.1)	1	0.1	0				0			
成長障害	0				0				0				1	(0.1)	1	0.1
電解質および水分バランス異常	39	(4.7)	44	3.0	30	(3.7)	33	2.3	51	(6.2)	61	4.0	38	(4.6)	50	3.3
高カリウム血症	23	(2.8)	26	1.7	11	(1.3)	12	0.8	23	(2.8)	25	1.7	20	(2.4)	24	1.6
低カリウム血症	7	(0.9)	7	0.5	12	(1.5)	13	0.9	15	(1.8)	15	1.0	6	(0.7)	8	0.5
脱水	4	(0.5)	4	0.3	4	(0.5)	4	0.3	4	(0.5)	4	0.3	8	(1.0)	9	0.6
低ナトリウム血症	2	(0.2)	2	0.1	2	(0.2)	2	0.1	9	(1.1)	10	0.7	2	(0.2)	2	0.1
水分過負荷	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1	1	(0.1)	1	0.1
高ナトリウム血症	0				0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
電解質失調	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
血液量減少症	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
体液貯留	0				0				0				2	(0.2)	2	0.1
水分摂取量減少	0				0				1	(0.1)	1	0.1	0			
多飲症	1	(0.1)	2	0.1	0				0				0			
脂質代謝障害	28	(3.4)	32	2.2	27	(3.3)	29	2.0	43	(5.3)	48	3.2	45	(5.5)	48	3.1
脂質異常症	16	(1.9)	16	1.1	20	(2.4)	20	1.4	26	(3.2)	26	1.7	17	(2.1)	18	1.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
コントロール不良の糖尿病	17	(1.0)	17	0.6	35	(2.1)	41	1.4	52	(1.6)	58	1.0
糖尿病	17	(1.0)	19	0.6	34	(2.1)	39	1.3	51	(1.6)	58	1.0
低血糖症	17	(1.0)	24	0.8	25	(1.5)	31	1.0	42	(1.3)	55	0.9
２型糖尿病	0				6	(0.4)	6	0.2	6	(0.2)	6	0.1
食欲および総合的栄養摂取障害	169	(10.3)	198	6.8	34	(2.1)	38	1.3	203	(6.2)	236	4.0
食欲減退	160	(9.7)	183	6.2	28	(1.7)	31	1.0	188	(5.7)	214	3.6
食欲亢進	11	(0.7)	11	0.4	4	(0.2)	4	0.1	15	(0.5)	15	0.3
肥満	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
悪液質	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
過小食	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
拒食	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
成長障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
電解質および水分バランス異常	69	(4.2)	77	2.6	89	(5.4)	111	3.7	158	(4.8)	188	3.2
高カリウム血症	34	(2.1)	38	1.3	43	(2.6)	49	1.6	77	(2.3)	87	1.5
低カリウム血症	19	(1.2)	20	0.7	21	(1.3)	23	0.8	40	(1.2)	43	0.7
脱水	8	(0.5)	8	0.3	12	(0.7)	13	0.4	20	(0.6)	21	0.4
低ナトリウム血症	4	(0.2)	4	0.1	11	(0.7)	12	0.4	15	(0.5)	16	0.3
水分過負荷	3	(0.2)	3	0.1	2	(0.1)	3	0.1	5	(0.2)	6	0.1
高ナトリウム血症	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
電解質失調	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
血液量減少症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
体液貯留	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
水分摂取量減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
多飲症	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
脂質代謝障害	55	(3.3)	61	2.1	88	(5.4)	96	3.2	143	(4.4)	157	2.6
脂質異常症	36	(2.2)	36	1.2	43	(2.6)	44	1.4	79	(2.4)	80	1.3

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
高トリグリセリド血症	13	(1.6)	14	0.9	6	(0.7)	6	0.4	11	(1.3)	13	0.9	19	(2.3)	20	1.3
高脂血症	2	(0.2)	2	0.1	1	(0.1)	1	0.1	6	(0.7)	6	0.4	6	(0.7)	6	0.4
高コレステロール血症	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3
プリンおよびピリミジン代謝障害	22	(2.7)	27	1.8	9	(1.1)	10	0.7	14	(1.7)	16	1.1	12	(1.5)	14	0.9
痛風	20	(2.4)	24	1.6	8	(1.0)	9	0.6	10	(1.2)	12	0.8	12	(1.5)	14	0.9
高尿酸血症	2	(0.2)	3	0.2	1	(0.1)	1	0.1	4	(0.5)	4	0.3	0			
骨、カルシウム、マグネシウムおよびリン代謝障害	16	(1.9)	17	1.1	15	(1.8)	17	1.2	15	(1.8)	16	1.1	13	(1.6)	15	1.0
高カルシウム血症	11	(1.3)	12	0.8	8	(1.0)	8	0.6	7	(0.9)	7	0.5	10	(1.2)	12	0.8
低マグネシウム血症	4	(0.5)	4	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1
低カルシウム血症	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
マグネシウム欠乏	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
低リン酸血症	0				0				2	(0.2)	2	0.1	0			
カルシウム欠乏	0				0				1	(0.1)	1	0.1	0			
高カルシトニン血症	0				0				1	(0.1)	1	0.1	0			
高マグネシウム血症	0				1	(0.1)	1	0.1	0				0			
高リン酸塩血症	0				1	(0.1)	1	0.1	0				0			
ビタミン関連障害	13	(1.6)	14	0.9	15	(1.8)	17	1.2	15	(1.8)	15	1.0	10	(1.2)	12	0.8
ビタミンＤ欠乏	11	(1.3)	11	0.7	10	(1.2)	10	0.7	11	(1.3)	11	0.7	8	(1.0)	8	0.5
ビタミンＢ１２欠乏	3	(0.4)	3	0.2	7	(0.9)	7	0.5	3	(0.4)	3	0.2	2	(0.2)	2	0.1
葉酸欠乏	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
ビタミン欠乏症	0				0				0				1	(0.1)	1	0.1
代謝障害ＮＥＣ	3	(0.4)	5	0.3	0				5	(0.6)	5	0.3	2	(0.2)	2	0.1
高リパーゼ血症	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
高アミラーゼ血症	2	(0.2)	3	0.2	0				2	(0.2)	2	0.1	0			
代謝障害	0				0				1	(0.1)	1	0.1	0			
酸・アルカリ障害	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
高トリグリセリド血症	19	(1.2)	20	0.7	30	(1.8)	33	1.1	49	(1.5)	53	0.9
高脂血症	3	(0.2)	3	0.1	12	(0.7)	12	0.4	15	(0.5)	15	0.3
高コレステロール血症	2	(0.1)	2	0.1	7	(0.4)	7	0.2	9	(0.3)	9	0.2
プリンおよびピリミジン代謝障害	31	(1.9)	37	1.3	26	(1.6)	30	1.0	57	(1.7)	67	1.1
痛風	28	(1.7)	33	1.1	22	(1.3)	26	0.9	50	(1.5)	59	1.0
高尿酸血症	3	(0.2)	4	0.1	4	(0.2)	4	0.1	7	(0.2)	8	0.1
骨、カルシウム、マグネシウムおよびリン代謝障害	31	(1.9)	34	1.2	28	(1.7)	31	1.0	59	(1.8)	65	1.1
高カルシウム血症	19	(1.2)	20	0.7	17	(1.0)	19	0.6	36	(1.1)	39	0.7
低マグネシウム血症	8	(0.5)	8	0.3	4	(0.2)	4	0.1	12	(0.4)	12	0.2
低カルシウム血症	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
マグネシウム欠乏	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
低リン酸血症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
カルシウム欠乏	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高カルシトニン血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高マグネシウム血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高リン酸塩血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ビタミン関連障害	28	(1.7)	31	1.1	25	(1.5)	27	0.9	53	(1.6)	58	1.0
ビタミンＤ欠乏	21	(1.3)	21	0.7	19	(1.2)	19	0.6	40	(1.2)	40	0.7
ビタミンＢ１２欠乏	10	(0.6)	10	0.3	5	(0.3)	5	0.2	15	(0.5)	15	0.3
葉酸欠乏	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
ビタミン欠乏症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
代謝障害ＮＥＣ	3	(0.2)	5	0.2	7	(0.4)	7	0.2	10	(0.3)	12	0.2
高リパーゼ血症	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
高アミラーゼ血症	2	(0.1)	3	0.1	2	(0.1)	2	0.1	4	(0.1)	5	0.1
代謝障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
酸・アルカリ障害	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
乳酸アシドーシス	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
アシドーシス	1	(0.1)	1	0.1	0				0				0			
ケトーシス	1	(0.1)	1	0.1	0				0				0			
糖尿病合併症	1	(0.1)	2	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
糖尿病性ケトアシドーシス	1	(0.1)	2	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
食物不耐性症候群	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
アルコール不耐性	1	(0.1)	1	0.1	0				0				0			
ラクトース不耐性	0				1	(0.1)	1	0.1	0				0			
蛋白およびアミノ酸代謝障害ＮＥＣ	0				0				0				1	(0.1)	1	0.1
低アルブミン血症	0				0				0				1	(0.1)	1	0.1
鉄および微量金属代謝障害	1	(0.1)	1	0.1	0				0				0			
鉄欠乏	1	(0.1)	1	0.1	0				0				0			
心臓障害	151	(18.3)	236	15.9	120	(14.7)	227	15.7	172	(21.0)	271	18.0	155	(18.8)	266	17.4
冠動脈障害	64	(7.8)	76	5.1	53	(6.5)	67	4.6	81	(9.9)	101	6.7	81	(9.8)	109	7.1
狭心症	17	(2.1)	17	1.1	12	(1.5)	13	0.9	24	(2.9)	28	1.9	25	(3.0)	31	2.0
不安定狭心症	10	(1.2)	13	0.9	12	(1.5)	15	1.0	19	(2.3)	21	1.4	23	(2.8)	24	1.6
急性心筋梗塞	13	(1.6)	14	0.9	9	(1.1)	9	0.6	15	(1.8)	15	1.0	23	(2.8)	24	1.6
冠動脈疾患	13	(1.6)	13	0.9	10	(1.2)	10	0.7	10	(1.2)	12	0.8	4	(0.5)	4	0.3
心筋梗塞	4	(0.5)	4	0.3	10	(1.2)	10	0.7	10	(1.2)	12	0.8	13	(1.6)	14	0.9
心筋虚血	7	(0.9)	7	0.5	3	(0.4)	3	0.2	4	(0.5)	4	0.3	4	(0.5)	4	0.3
冠動脈狭窄	4	(0.5)	4	0.3	3	(0.4)	3	0.2	5	(0.6)	5	0.3	3	(0.4)	3	0.2
急性冠動脈症候群	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
冠動脈硬化症	0				0				0				3	(0.4)	3	0.2
冠動脈閉塞	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
無症候性心筋梗塞	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
冠動脈入口部狭窄	0				0				1	(0.1)	1	0.1	0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
乳酸アシドーシス	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
アシドーシス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ケトーシス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病合併症	1	(0.1)	2	0.1	3	(0.2)	3	0.1	4	(0.1)	5	0.1
糖尿病性ケトアシドーシス	1	(0.1)	2	0.1	3	(0.2)	3	0.1	4	(0.1)	5	0.1
食物不耐性症候群	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
アルコール不耐性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ラクトース不耐性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
蛋白およびアミノ酸代謝障害ＮＥＣ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
低アルブミン血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鉄および微量金属代謝障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鉄欠乏	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心臓障害	271	(16.5)	463	15.8	327	(19.9)	537	17.7	598	(18.2)	1000	16.8
冠動脈障害	117	(7.1)	143	4.9	162	(9.9)	210	6.9	279	(8.5)	353	5.9
狭心症	29	(1.8)	30	1.0	49	(3.0)	59	1.9	78	(2.4)	89	1.5
不安定狭心症	22	(1.3)	28	1.0	42	(2.6)	45	1.5	64	(1.9)	73	1.2
急性心筋梗塞	22	(1.3)	23	0.8	38	(2.3)	39	1.3	60	(1.8)	62	1.0
冠動脈疾患	23	(1.4)	23	0.8	14	(0.9)	16	0.5	37	(1.1)	39	0.7
心筋梗塞	14	(0.9)	14	0.5	23	(1.4)	26	0.9	37	(1.1)	40	0.7
心筋虚血	10	(0.6)	10	0.3	8	(0.5)	8	0.3	18	(0.5)	18	0.3
冠動脈狭窄	7	(0.4)	7	0.2	8	(0.5)	8	0.3	15	(0.5)	15	0.3
急性冠動脈症候群	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
冠動脈硬化症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
冠動脈閉塞	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
無症候性心筋梗塞	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
冠動脈入口部狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
冠動脈不全	1	(0.1)	1	0.1	0				0				0			
不整脈	62	(7.5)	75	5.0	65	(7.9)	86	6.0	72	(8.8)	93	6.2	75	(9.1)	94	6.2
心房細動	20	(2.4)	21	1.4	19	(2.3)	26	1.8	30	(3.7)	34	2.3	26	(3.2)	30	2.0
心室性期外収縮	6	(0.7)	7	0.5	6	(0.7)	6	0.4	3	(0.4)	3	0.2	7	(0.8)	7	0.5
右脚ブロック	6	(0.7)	6	0.4	6	(0.7)	6	0.4	4	(0.5)	4	0.3	3	(0.4)	3	0.2
左脚ブロック	4	(0.5)	4	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1	6	(0.7)	7	0.5
徐脈	2	(0.2)	3	0.2	2	(0.2)	2	0.1	7	(0.9)	7	0.5	5	(0.6)	5	0.3
第一度房室ブロック	4	(0.5)	4	0.3	4	(0.5)	4	0.3	3	(0.4)	3	0.2	5	(0.6)	5	0.3
不整脈	2	(0.2)	3	0.2	3	(0.4)	3	0.2	2	(0.2)	2	0.1	8	(1.0)	8	0.5
頻脈	4	(0.5)	5	0.3	5	(0.6)	5	0.3	4	(0.5)	4	0.3	1	(0.1)	1	0.1
心室性頻脈	1	(0.1)	1	0.1	7	(0.9)	7	0.5	3	(0.4)	3	0.2	1	(0.1)	1	0.1
心房粗動	1	(0.1)	1	0.1	2	(0.2)	2	0.1	7	(0.9)	7	0.5	2	(0.2)	2	0.1
上室性期外収縮	1	(0.1)	1	0.1	5	(0.6)	5	0.3	3	(0.4)	3	0.2	1	(0.1)	1	0.1
心停止	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
洞性徐脈	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	5	(0.6)	6	0.4
上室性頻脈	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	4	0.3	1	(0.1)	1	0.1
洞性頻脈	3	(0.4)	3	0.2	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
完全房室ブロック	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2
心室細動	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
洞結節機能不全	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
心室内伝導障害	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
第二度房室ブロック	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
房室ブロック	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
期外収縮	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
結節性不整脈	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
心室性頻脈性不整脈	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
心室性不整脈	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
心肺停止	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
洞性不整脈	0				0				2	(0.2)	2	0.1	0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
冠動脈不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
不整脈	127	(7.7)	161	5.5	147	(8.9)	187	6.2	274	(8.3)	348	5.8
心房細動	39	(2.4)	47	1.6	56	(3.4)	64	2.1	95	(2.9)	111	1.9
心室性期外収縮	12	(0.7)	13	0.4	10	(0.6)	10	0.3	22	(0.7)	23	0.4
右脚ブロック	12	(0.7)	12	0.4	7	(0.4)	7	0.2	19	(0.6)	19	0.3
左脚ブロック	8	(0.5)	8	0.3	8	(0.5)	9	0.3	16	(0.5)	17	0.3
徐脈	4	(0.2)	5	0.2	12	(0.7)	12	0.4	16	(0.5)	17	0.3
第一度房室ブロック	8	(0.5)	8	0.3	8	(0.5)	8	0.3	16	(0.5)	16	0.3
不整脈	5	(0.3)	6	0.2	10	(0.6)	10	0.3	15	(0.5)	16	0.3
頻脈	9	(0.5)	10	0.3	5	(0.3)	5	0.2	14	(0.4)	15	0.3
心室性頻脈	8	(0.5)	8	0.3	4	(0.2)	4	0.1	12	(0.4)	12	0.2
心房粗動	3	(0.2)	3	0.1	9	(0.5)	9	0.3	12	(0.4)	12	0.2
上室性期外収縮	6	(0.4)	6	0.2	4	(0.2)	4	0.1	10	(0.3)	10	0.2
心停止	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
洞性徐脈	2	(0.1)	2	0.1	6	(0.4)	7	0.2	8	(0.2)	9	0.2
上室性頻脈	3	(0.2)	3	0.1	4	(0.2)	5	0.2	7	(0.2)	8	0.1
洞性頻脈	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
完全房室ブロック	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
心室細動	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
洞結節機能不全	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
心室内伝導障害	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
第二度房室ブロック	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
房室ブロック	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
期外収縮	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
結節性不整脈	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心室性頻脈性不整脈	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心室性不整脈	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心肺停止	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
洞性不整脈	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
結節性調律	0				1	(0.1)	1	0.1	0				0			
上室性頻脈性不整脈	0				0				0				1	(0.1)	1	0.1
心室無収縮	0				0				0				1	(0.1)	1	0.1
心粗動	0				1	(0.1)	1	0.1	0				0			
心房頻脈	0				0				1	(0.1)	1	0.1	0			
伝導障害	0				1	(0.1)	1	0.1	0				0			
発作性頻脈	0				0				0				1	(0.1)	1	0.1
両側性脚ブロック	1	(0.1)	1	0.1	0				0				0			
心不全	38	(4.6)	45	3.0	24	(2.9)	30	2.1	34	(4.2)	43	2.9	31	(3.8)	36	2.4
うっ血性心不全	14	(1.7)	17	1.1	11	(1.3)	14	1.0	16	(2.0)	22	1.5	20	(2.4)	23	1.5
心不全	13	(1.6)	15	1.0	10	(1.2)	10	0.7	9	(1.1)	9	0.6	5	(0.6)	5	0.3
慢性心不全	8	(1.0)	8	0.5	5	(0.6)	5	0.3	5	(0.6)	5	0.3	3	(0.4)	3	0.2
急性心不全	2	(0.2)	2	0.1	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
心原性ショック	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
右室不全	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
左室不全	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
急性左室不全	0				0				0				1	(0.1)	1	0.1
心臓性喘息	1	(0.1)	1	0.1	0				0				0			
心肺不全	0				0				1	(0.1)	1	0.1	0			
心筋障害	10	(1.2)	12	0.8	11	(1.3)	14	1.0	11	(1.3)	20	1.3	14	(1.7)	19	1.2
左室機能不全	4	(0.5)	4	0.3	1	(0.1)	1	0.1	5	(0.6)	5	0.3	4	(0.5)	4	0.3
左室肥大	0				4	(0.5)	4	0.3	4	(0.5)	4	0.3	4	(0.5)	4	0.3
心拡大	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
拡張機能障害	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
虚血性心筋症	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
高血圧性心筋症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
左房拡張	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
心筋症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
心筋線維症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
結節性調律	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
上室性頻脈性不整脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心室無収縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心粗動	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心房頻脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
伝導障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
発作性頻脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
両側性脚ブロック	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心不全	62	(3.8)	75	2.6	65	(4.0)	79	2.6	127	(3.9)	154	2.6
うっ血性心不全	25	(1.5)	31	1.1	36	(2.2)	45	1.5	61	(1.9)	76	1.3
心不全	23	(1.4)	25	0.9	14	(0.9)	14	0.5	37	(1.1)	39	0.7
慢性心不全	13	(0.8)	13	0.4	8	(0.5)	8	0.3	21	(0.6)	21	0.4
急性心不全	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
心原性ショック	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
右室不全	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
左室不全	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
急性左室不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心臓性喘息	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心肺不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心筋障害	21	(1.3)	26	0.9	25	(1.5)	39	1.3	46	(1.4)	65	1.1
左室機能不全	5	(0.3)	5	0.2	9	(0.5)	9	0.3	14	(0.4)	14	0.2
左室肥大	4	(0.2)	4	0.1	8	(0.5)	8	0.3	12	(0.4)	12	0.2
心拡大	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
拡張機能障害	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
虚血性心筋症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
高血圧性心筋症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
左房拡張	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
心筋症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
心筋線維症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心室壁運動低下	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
うっ血性心筋症	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
右房拡張	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
収縮機能障害	0				0				1	(0.1)	1	0.1	0			
心筋炎	1	(0.1)	1	0.1	0				0				0			
心室拡張	0				0				1	(0.1)	1	0.1	0			
心室肥大	0				1	(0.1)	1	0.1	0				0			
心臓瘤	0				0				0				1	(0.1)	1	0.1
心肥大	0				0				1	(0.1)	1	0.1	0			
心房拡張	1	(0.1)	1	0.1	0				0				0			
糖尿病性心筋症	0				0				0				1	(0.1)	1	0.1
心臓弁膜障害	11	(1.3)	17	1.1	10	(1.2)	20	1.4	6	(0.7)	7	0.5	6	(0.7)	7	0.5
僧帽弁閉鎖不全症	8	(1.0)	8	0.5	4	(0.5)	4	0.3	3	(0.4)	3	0.2	2	(0.2)	2	0.1
三尖弁閉鎖不全症	6	(0.7)	6	0.4	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1
大動脈弁閉鎖不全症	1	(0.1)	1	0.1	4	(0.5)	4	0.3	0				3	(0.4)	3	0.2
大動脈弁狭窄	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
肺動脈弁閉鎖不全症	0				2	(0.2)	2	0.1	0				0			
心臓弁石灰化	0				1	(0.1)	1	0.1	0				0			
心臓弁膜疾患	0				1	(0.1)	1	0.1	0				0			
僧帽弁狭窄症	0				1	(0.1)	1	0.1	0				0			
僧帽弁疾患	0				1	(0.1)	1	0.1	0				0			
僧帽弁石灰化	0				0				1	(0.1)	1	0.1	0			
大動脈弁硬化症	0				0				1	(0.1)	1	0.1	0			
大動脈弁疾患	1	(0.1)	1	0.1	0				0				0			
変性僧帽弁疾患	0				1	(0.1)	1	0.1	0				0			
変性大動脈弁疾患	0				1	(0.1)	1	0.1	0				0			
心障害徴候および症状	7	(0.9)	8	0.5	7	(0.9)	9	0.6	6	(0.7)	7	0.5	1	(0.1)	1	0.1
動悸	6	(0.7)	7	0.5	6	(0.7)	7	0.5	5	(0.6)	6	0.4	0			
心室血栓症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心室壁運動低下	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
うっ血性心筋症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
右房拡張	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
収縮機能障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心筋炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心室拡張	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心室肥大	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心臓瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心肥大	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心房拡張	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病性心筋症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心臓弁膜障害	21	(1.3)	37	1.3	12	(0.7)	14	0.5	33	(1.0)	51	0.9
僧帽弁閉鎖不全症	12	(0.7)	12	0.4	5	(0.3)	5	0.2	17	(0.5)	17	0.3
三尖弁閉鎖不全症	9	(0.5)	9	0.3	4	(0.2)	4	0.1	13	(0.4)	13	0.2
大動脈弁閉鎖不全症	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
大動脈弁狭窄	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
肺動脈弁閉鎖不全症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
心臓弁石灰化	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心臓弁膜疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
僧帽弁狭窄症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
僧帽弁疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
僧帽弁石灰化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大動脈弁硬化症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大動脈弁疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
変性僧帽弁疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
変性大動脈弁疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心障害徴候および症状	14	(0.9)	17	0.6	7	(0.4)	8	0.3	21	(0.6)	25	0.4
動悸	12	(0.7)	14	0.5	5	(0.3)	6	0.2	17	(0.5)	20	0.3
心室血栓症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
高血圧性心疾患	1	(0.1)	1	0.1	0				0				0			
心血管不全	0				1	(0.1)	1	0.1	0				0			
心房血栓症	0				1	(0.1)	1	0.1	0				0			
心膜障害	2	(0.2)	3	0.2	1	(0.1)	1	0.1	0				0			
心タンポナーデ	1	(0.1)	1	0.1	0				0				0			
心嚢液貯留	1	(0.1)	1	0.1	0				0				0			
心膜炎	1	(0.1)	1	0.1	0				0				0			
心膜石灰化	0				1	(0.1)	1	0.1	0				0			
腎および尿路障害	131	(15.9)	164	11.0	124	(15.1)	165	11.4	173	(21.1)	246	16.3	159	(19.3)	225	14.7
尿路系徴候および症状	55	(6.7)	66	4.4	66	(8.1)	76	5.3	74	(9.0)	99	6.6	84	(10.2)	105	6.9
ミクロアルブミン尿	22	(2.7)	23	1.5	24	(2.9)	25	1.7	37	(4.5)	41	2.7	35	(4.2)	36	2.4
蛋白尿	14	(1.7)	14	0.9	8	(1.0)	8	0.6	15	(1.8)	16	1.1	16	(1.9)	16	1.0
血尿	3	(0.4)	3	0.2	6	(0.7)	7	0.5	5	(0.6)	5	0.3	13	(1.6)	13	0.9
排尿困難	4	(0.5)	4	0.3	6	(0.7)	6	0.4	6	(0.7)	6	0.4	6	(0.7)	6	0.4
尿失禁	4	(0.5)	4	0.3	8	(1.0)	8	0.6	4	(0.5)	4	0.3	4	(0.5)	4	0.3
糖尿	1	(0.1)	1	0.1	1	(0.1)	1	0.1	6	(0.7)	6	0.4	5	(0.6)	5	0.3
夜間頻尿	1	(0.1)	1	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3	3	(0.4)	3	0.2
尿閉	2	(0.2)	4	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1
白血球尿	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3
尿異常	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
頻尿	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
腎仙痛	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0				2	(0.2)	2	0.1
アルブミン尿	2	(0.2)	2	0.1	0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
ケトン尿	0				1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
腎臓痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
多尿	1	(0.1)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
失禁	2	(0.2)	2	0.1	0				0				0			
着色尿	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
高血圧性心疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心血管不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心房血栓症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心膜障害	3	(0.2)	4	0.1	0				3	(0.1)	4	0.1
心タンポナーデ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心嚢液貯留	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心膜炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心膜石灰化	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎および尿路障害	255	(15.5)	329	11.2	332	(20.2)	471	15.5	587	(17.9)	800	13.4
尿路系徴候および症状	121	(7.4)	142	4.8	158	(9.6)	204	6.7	279	(8.5)	346	5.8
ミクロアルブミン尿	46	(2.8)	48	1.6	72	(4.4)	77	2.5	118	(3.6)	125	2.1
蛋白尿	22	(1.3)	22	0.8	31	(1.9)	32	1.1	53	(1.6)	54	0.9
血尿	9	(0.5)	10	0.3	18	(1.1)	18	0.6	27	(0.8)	28	0.5
排尿困難	10	(0.6)	10	0.3	12	(0.7)	12	0.4	22	(0.7)	22	0.4
尿失禁	12	(0.7)	12	0.4	8	(0.5)	8	0.3	20	(0.6)	20	0.3
糖尿	2	(0.1)	2	0.1	11	(0.7)	11	0.4	13	(0.4)	13	0.2
夜間頻尿	4	(0.2)	4	0.1	7	(0.4)	7	0.2	11	(0.3)	11	0.2
尿閉	6	(0.4)	8	0.3	4	(0.2)	4	0.1	10	(0.3)	12	0.2
白血球尿	3	(0.2)	3	0.1	7	(0.4)	7	0.2	10	(0.3)	10	0.2
尿異常	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2
頻尿	1	(0.1)	1	<0.1	6	(0.4)	6	0.2	7	(0.2)	7	0.1
腎仙痛	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
アルブミン尿	2	(0.1)	2	0.1	2	(0.1)	3	0.1	4	(0.1)	5	0.1
ケトン尿	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
腎臓痛	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
多尿	2	(0.1)	3	0.1	1	(0.1)	1	<0.1	3	(0.1)	4	0.1
失禁	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
着色尿	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
腹圧性尿失禁	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
下部尿路症状	0				0				1	(0.1)	1	0.1	0			
気尿症	0				0				0				1	(0.1)	1	0.1
切迫性尿失禁	0				1	(0.1)	1	0.1	0				0			
尿意切迫	0				0				0				1	(0.1)	1	0.1
排尿異常	0				1	(0.1)	1	0.1	0				0			
膀胱痛	0				0				1	(0.1)	1	0.1	0			
膀胱痙縮	0				0				1	(0.1)	1	0.1	0			
腎障害（腎症を除く）	60	(7.3)	67	4.5	44	(5.4)	51	3.5	73	(8.9)	90	6.0	68	(8.2)	81	5.3
腎嚢胞	16	(1.9)	16	1.1	14	(1.7)	15	1.0	22	(2.7)	23	1.5	19	(2.3)	20	1.3
急性腎不全	16	(1.9)	18	1.2	10	(1.2)	11	0.8	21	(2.6)	22	1.5	20	(2.4)	21	1.4
慢性腎臓病	14	(1.7)	14	0.9	8	(1.0)	8	0.6	26	(3.2)	32	2.1	17	(2.1)	17	1.1
腎機能障害	10	(1.2)	10	0.7	6	(0.7)	6	0.4	5	(0.6)	5	0.3	4	(0.5)	4	0.3
腎不全	5	(0.6)	5	0.3	4	(0.5)	4	0.3	3	(0.4)	3	0.2	4	(0.5)	5	0.3
水腎症	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1
腎腫瘤	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
腎盂腎杯拡張症	0				0				1	(0.1)	2	0.1	2	(0.2)	2	0.1
急性腎前性腎不全	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
高窒素血症	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
腎下垂症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
腎拡張症	0				0				0				1	(0.1)	1	0.1
腎梗塞	0				0				0				1	(0.1)	1	0.1
腎脂肪腫症	0				1	(0.1)	1	0.1	0				0			
腎障害	0				1	(0.1)	1	0.1	0				0			
腎損傷	0				0				0				1	(0.1)	1	0.1
腎動脈の動脈硬化症	0				1	(0.1)	1	0.1	0				0			
腎動脈瘤	0				0				0				1	(0.1)	1	0.1
腎嚢胞出血	0				0				0				1	(0.1)	1	0.1
無尿	0				0				0				1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腹圧性尿失禁	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
下部尿路症状	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
気尿症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
切迫性尿失禁	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿意切迫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
排尿異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膀胱痙縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎障害（腎症を除く）	104	(6.3)	118	4.0	141	(8.6)	171	5.6	245	(7.5)	289	4.8
腎嚢胞	30	(1.8)	31	1.1	41	(2.5)	43	1.4	71	(2.2)	74	1.2
急性腎不全	26	(1.6)	29	1.0	41	(2.5)	43	1.4	67	(2.0)	72	1.2
慢性腎臓病	22	(1.3)	22	0.8	43	(2.6)	49	1.6	65	(2.0)	71	1.2
腎機能障害	16	(1.0)	16	0.5	9	(0.5)	9	0.3	25	(0.8)	25	0.4
腎不全	9	(0.5)	9	0.3	7	(0.4)	8	0.3	16	(0.5)	17	0.3
水腎症	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
腎腫瘤	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
腎盂腎杯拡張症	0				3	(0.2)	4	0.1	3	(0.1)	4	0.1
急性腎前性腎不全	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
高窒素血症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腎下垂症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腎拡張症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎梗塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎脂肪腫症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎動脈の動脈硬化症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎動脈瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎嚢胞出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
無尿	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
尿石症	13	(1.6)	16	1.1	20	(2.4)	21	1.5	17	(2.1)	22	1.5	15	(1.8)	15	1.0
腎結石症	9	(1.1)	11	0.7	17	(2.1)	17	1.2	15	(1.8)	20	1.3	11	(1.3)	11	0.7
尿管結石	3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
尿路結石	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
鹿角状結石	0				1	(0.1)	1	0.1	0				0			
膀胱結石	1	(0.1)	1	0.1	0				0				0			
腎症	12	(1.5)	12	0.8	14	(1.7)	14	1.0	26	(3.2)	27	1.8	19	(2.3)	20	1.3
腎症	5	(0.6)	5	0.3	6	(0.7)	6	0.4	14	(1.7)	14	0.9	9	(1.1)	9	0.6
糖尿病性腎症	5	(0.6)	5	0.3	7	(0.9)	7	0.5	10	(1.2)	10	0.7	9	(1.1)	9	0.6
ネフローゼ症候群	1	(0.1)	1	0.1	0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
腎硬化症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
慢性糸球体腎炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
膀胱および膀胱頚部障害（結石を除く）	3	(0.4)	3	0.2	2	(0.2)	2	0.1	7	(0.9)	7	0.5	2	(0.2)	2	0.1
緊張性膀胱	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
膀胱憩室	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
膀胱ポリープ	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
膀胱肉柱形成	0				0				2	(0.2)	2	0.1	0			
間質性膀胱炎	0				0				0				1	(0.1)	1	0.1
出血性膀胱炎	1	(0.1)	1	0.1	0				0				0			
尿道障害（結石を除く）	0				0				0				2	(0.2)	2	0.1
尿道狭窄	0				0				0				2	(0.2)	2	0.1
尿管障害	0				1	(0.1)	1	0.1	0				0			
尿管狭窄	0				1	(0.1)	1	0.1	0				0			
泌尿生殖器系障害ＮＥＣ	0				0				1	(0.1)	1	0.1	0			
尿路障害	0				0				1	(0.1)	1	0.1	0			
眼障害	149	(18.1)	199	13.4	143	(17.5)	209	14.5	133	(16.2)	175	11.6	139	(16.8)	192	12.6

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
尿石症	33	(2.0)	37	1.3	32	(1.9)	37	1.2	65	(2.0)	74	1.2
腎結石症	26	(1.6)	28	1.0	26	(1.6)	31	1.0	52	(1.6)	59	1.0
尿管結石	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
尿路結石	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
鹿角状結石	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱結石	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎症	26	(1.6)	26	0.9	45	(2.7)	47	1.5	71	(2.2)	73	1.2
腎症	11	(0.7)	11	0.4	23	(1.4)	23	0.8	34	(1.0)	34	0.6
糖尿病性腎症	12	(0.7)	12	0.4	19	(1.2)	19	0.6	31	(0.9)	31	0.5
ネフローゼ症候群	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
腎硬化症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
慢性糸球体腎炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
膀胱および膀胱頚部障害（結石を除く）	5	(0.3)	5	0.2	9	(0.5)	9	0.3	14	(0.4)	14	0.2
緊張性膀胱	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
膀胱憩室	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
膀胱ポリープ	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
膀胱肉柱形成	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
間質性膀胱炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性膀胱炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿道障害（結石を除く）	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
尿道狭窄	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
尿管障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿管狭窄	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
泌尿生殖器系障害ＮＥＣ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿路障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼障害	292	(17.8)	408	13.9	272	(16.5)	367	12.1	564	(17.2)	775	13.0

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
網膜、脈絡膜および硝子体の出血および血管障害	56	(6.8)	62	4.2	68	(8.3)	81	5.6	50	(6.1)	53	3.5	60	(7.3)	71	4.7
糖尿病網膜症	42	(5.1)	44	3.0	48	(5.9)	56	3.9	36	(4.4)	36	2.4	39	(4.7)	43	2.8
網膜症	6	(0.7)	6	0.4	7	(0.9)	7	0.5	5	(0.6)	5	0.3	6	(0.7)	6	0.4
高血圧性網膜症	2	(0.2)	2	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2	10	(1.2)	10	0.7
硝子体出血	3	(0.4)	3	0.2	6	(0.7)	6	0.4	1	(0.1)	1	0.1	2	(0.2)	2	0.1
網膜出血	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	4	(0.5)	4	0.3
網膜血管瘤	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	2	(0.2)	2	0.1
出血性網膜症	3	(0.4)	3	0.2	0				0				0			
増殖性網膜症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
動脈硬化性網膜症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
網膜静脈血栓症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
網膜動脈閉塞	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
網膜滲出物	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
網膜血管障害	1	(0.1)	1	0.1	0				0				0			
網膜血管新生	0				1	(0.1)	1	0.1	0				0			
網膜静脈閉塞	0				1	(0.1)	1	0.1	0				0			
眼前方部構造変化、沈着および変性	57	(6.9)	63	4.2	43	(5.3)	48	3.3	39	(4.8)	44	2.9	50	(6.1)	53	3.5
白内障	51	(6.2)	54	3.6	41	(5.0)	46	3.2	34	(4.2)	36	2.4	45	(5.5)	48	3.1
核性白内障	2	(0.2)	3	0.2	0				2	(0.2)	2	0.1	0			
角膜混濁	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
皮質白内障	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
翼状片	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
嚢下白内障	0				0				2	(0.2)	2	0.1	0			
角膜リポイド環	0				0				0				1	(0.1)	1	0.1
眼の変色	1	(0.1)	1	0.1	0				0				0			
眼瞼皮膚のたるみ	1	(0.1)	1	0.1	0				0				0			
後天性涙道狭窄	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
網膜、脈絡膜および硝子体の出血および血管障害	124	(7.6)	143	4.9	110	(6.7)	124	4.1	234	(7.1)	267	4.5
糖尿病網膜症	90	(5.5)	100	3.4	75	(4.6)	79	2.6	165	(5.0)	179	3.0
網膜症	13	(0.8)	13	0.4	11	(0.7)	11	0.4	24	(0.7)	24	0.4
高血圧性網膜症	6	(0.4)	6	0.2	13	(0.8)	13	0.4	19	(0.6)	19	0.3
硝子体出血	9	(0.5)	9	0.3	3	(0.2)	3	0.1	12	(0.4)	12	0.2
網膜出血	5	(0.3)	5	0.2	6	(0.4)	6	0.2	11	(0.3)	11	0.2
網膜血管瘤	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
出血性網膜症	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
増殖性網膜症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
動脈硬化性網膜症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
網膜静脈血栓症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
網膜動脈閉塞	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
網膜滲出物	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
網膜血管障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
網膜血管新生	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
網膜静脈閉塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼前方部構造変化、沈着および変性	100	(6.1)	111	3.8	89	(5.4)	97	3.2	189	(5.8)	208	3.5
白内障	92	(5.6)	100	3.4	79	(4.8)	84	2.8	171	(5.2)	184	3.1
核性白内障	2	(0.1)	3	0.1	2	(0.1)	2	0.1	4	(0.1)	5	0.1
角膜混濁	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
皮質白内障	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
翼状片	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
嚢下白内障	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
角膜リポイド環	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼の変色	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼瞼皮膚のたるみ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
後天性涙道狭窄	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
前房狭隅角	0				0				1	(0.1)	1	0.1	0			
糖尿病性白内障	0				1	(0.1)	1	0.1	0				0			
落屑症候群	0				0				1	(0.1)	1	0.1	0			
涙器構造障害	0				0				1	(0.1)	1	0.1	0			
視覚障害	19	(2.3)	20	1.3	21	(2.6)	24	1.7	18	(2.2)	20	1.3	17	(2.1)	21	1.4
霧視	7	(0.9)	7	0.5	7	(0.9)	7	0.5	4	(0.5)	4	0.3	3	(0.4)	3	0.2
老視	3	(0.4)	3	0.2	3	(0.4)	3	0.2	1	(0.1)	1	0.1	4	(0.5)	4	0.3
遠視	1	(0.1)	1	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1	3	(0.4)	3	0.2
視力低下	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3
乱視	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
視力障害	2	(0.2)	2	0.1	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
複視	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
近視	0				1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
光視症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
一過性黒内障	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
屈折障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
失明	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
弱視	0				0				1	(0.1)	1	0.1	0			
調節障害	0				1	(0.1)	1	0.1	0				0			
片側失明	0				1	(0.1)	1	0.1	0				0			
眼部構造変化、沈着および変性ＮＥＣ	14	(1.7)	16	1.1	13	(1.6)	13	0.9	15	(1.8)	17	1.1	15	(1.8)	15	1.0
網膜剥離	3	(0.4)	4	0.3	0				0				5	(0.6)	5	0.3
黄斑症	2	(0.2)	2	0.1	0				4	(0.5)	4	0.3	0			
黄斑線維症	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2	0			
黄斑変性	0				0				5	(0.6)	5	0.3	0			
加齢黄斑変性	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
硝子体浮遊物	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
網膜変性	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
前房狭隅角	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糖尿病性白内障	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
落屑症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
涙器構造障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
視覚障害	40	(2.4)	44	1.5	35	(2.1)	41	1.4	75	(2.3)	85	1.4
霧視	14	(0.9)	14	0.5	7	(0.4)	7	0.2	21	(0.6)	21	0.4
老視	6	(0.4)	6	0.2	5	(0.3)	5	0.2	11	(0.3)	11	0.2
遠視	5	(0.3)	5	0.2	5	(0.3)	5	0.2	10	(0.3)	10	0.2
視力低下	4	(0.2)	4	0.1	5	(0.3)	5	0.2	9	(0.3)	9	0.2
乱視	2	(0.1)	2	0.1	5	(0.3)	5	0.2	7	(0.2)	7	0.1
視力障害	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
複視	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
近視	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
光視症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
一過性黒内障	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
屈折障害	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
失明	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
弱視	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
調節障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
片側失明	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼部構造変化、沈着および変性ＮＥＣ	27	(1.6)	29	1.0	30	(1.8)	32	1.1	57	(1.7)	61	1.0
網膜剥離	3	(0.2)	4	0.1	5	(0.3)	5	0.2	8	(0.2)	9	0.2
黄斑症	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
黄斑線維症	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
黄斑変性	0				5	(0.3)	5	0.2	5	(0.2)	5	0.1
加齢黄斑変性	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
硝子体浮遊物	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
網膜変性	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
硝子体剥離	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
網膜裂孔	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
網脈絡膜症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
新生血管加齢黄斑変性	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
黄斑円孔	0				0				1	(0.1)	1	0.1	0			
乾性加齢黄斑変性	0				1	(0.1)	1	0.1	0				0			
眼球突出症	0				0				0				1	(0.1)	1	0.1
眼沈着物	0				1	(0.1)	1	0.1	0				0			
視神経萎縮	0				0				1	(0.1)	1	0.1	0			
視神経乳頭障害	1	(0.1)	1	0.1	0				0				0			
視神経乳頭浮腫	0				1	(0.1)	1	0.1	0				0			
硝子体混濁	1	(0.1)	1	0.1	0				0				0			
硝子体変性	0				0				0				1	(0.1)	1	0.1
星状硝子体症	0				1	(0.1)	1	0.1	0				0			
網膜色素上皮症	0				0				0				1	(0.1)	1	0.1
網脈絡膜萎縮	0				0				0				1	(0.1)	1	0.1
眼部感染、刺激症状および炎症	13	(1.6)	14	0.9	11	(1.3)	14	1.0	14	(1.7)	16	1.1	11	(1.3)	12	0.8
黄斑浮腫	2	(0.2)	2	0.1	5	(0.6)	6	0.4	6	(0.7)	6	0.4	2	(0.2)	2	0.1
糖尿病性網膜浮腫	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
眼そう痒症	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
眼刺激	3	(0.4)	3	0.2	0				0				1	(0.1)	1	0.1
眼瞼炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
嚢胞様黄斑浮腫	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
アレルギー性結膜炎	0				1	(0.1)	1	0.1	2	(0.2)	3	0.2	0			
眼瞼浮腫	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
眼充血	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
虹彩炎	1	(0.1)	1	0.1	0				0				1	(0.1)	2	0.1
虹彩毛様体炎	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
硝子体剥離	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
網膜裂孔	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
網脈絡膜症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
新生血管加齢黄斑変性	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
黄斑円孔	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乾性加齢黄斑変性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼球突出症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼沈着物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
視神経萎縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
視神経乳頭障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
視神経乳頭浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
硝子体混濁	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
硝子体変性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
星状硝子体症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
網膜色素上皮症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
網脈絡膜萎縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼部感染、刺激症状および炎症	24	(1.5)	28	1.0	25	(1.5)	28	0.9	49	(1.5)	56	0.9
黄斑浮腫	7	(0.4)	8	0.3	8	(0.5)	8	0.3	15	(0.5)	16	0.3
糖尿病性網膜浮腫	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
眼そう痒症	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
眼刺激	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
眼瞼炎	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
嚢胞様黄斑浮腫	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
アレルギー性結膜炎	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
眼瞼浮腫	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
眼充血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
虹彩炎	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
虹彩毛様体炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
アレルギー性眼瞼炎	0				0				0				1	(0.1)	1	0.1
マイボーム腺機能不全	0				1	(0.1)	1	0.1	0				0			
結膜刺激	0				0				0				1	(0.1)	1	0.1
結膜充血	1	(0.1)	1	0.1	0				0				0			
霰粒腫	1	(0.1)	1	0.1	0				0				0			
緑内障および高眼圧症	7	(0.9)	7	0.5	8	(1.0)	9	0.6	8	(1.0)	9	0.6	8	(1.0)	9	0.6
緑内障	6	(0.7)	6	0.4	6	(0.7)	6	0.4	7	(0.9)	7	0.5	7	(0.8)	7	0.5
開放隅角緑内障	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1
高眼圧症	0				0				1	(0.1)	1	0.1	0			
閉塞隅角緑内障	0				1	(0.1)	2	0.1	0				0			
眼部障害ＮＥＣ	9	(1.1)	10	0.7	11	(1.3)	11	0.8	7	(0.9)	7	0.5	5	(0.6)	5	0.3
眼乾燥	5	(0.6)	5	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
眼痛	3	(0.4)	3	0.2	4	(0.5)	4	0.3	1	(0.1)	1	0.1	0			
網膜障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
流涙増加	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
眼の障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
眼球浮腫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
眼部腫脹	0				0				1	(0.1)	1	0.1	0			
眼部不快感	0				0				0				1	(0.1)	1	0.1
硝子体障害	0				0				0				1	(0.1)	1	0.1
涙液分泌低下	0				1	(0.1)	1	0.1	0				0			
眼部出血および血管障害ＮＥＣ	5	(0.6)	5	0.3	6	(0.7)	6	0.4	4	(0.5)	5	0.3	4	(0.5)	5	0.3
眼出血	2	(0.2)	2	0.1	1	(0.1)	1	0.1	4	(0.5)	5	0.3	3	(0.4)	4	0.3
結膜出血	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
虚血性視神経症	0				2	(0.2)	2	0.1	0				0			
視神経乳頭出血	0				1	(0.1)	1	0.1	0				0			
前房出血	1	(0.1)	1	0.1	0				0				0			
眼神経筋障害	2	(0.2)	2	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3	1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
アレルギー性眼瞼炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
マイボーム腺機能不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
結膜刺激	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結膜充血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
霰粒腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
緑内障および高眼圧症	15	(0.9)	16	0.5	16	(1.0)	18	0.6	31	(0.9)	34	0.6
緑内障	12	(0.7)	12	0.4	14	(0.9)	14	0.5	26	(0.8)	26	0.4
開放隅角緑内障	2	(0.1)	2	0.1	2	(0.1)	3	0.1	4	(0.1)	5	0.1
高眼圧症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
閉塞隅角緑内障	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
眼部障害ＮＥＣ	20	(1.2)	21	0.7	12	(0.7)	12	0.4	32	(1.0)	33	0.6
眼乾燥	7	(0.4)	7	0.2	3	(0.2)	3	0.1	10	(0.3)	10	0.2
眼痛	7	(0.4)	7	0.2	1	(0.1)	1	<0.1	8	(0.2)	8	0.1
網膜障害	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
流涙増加	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
眼の障害	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
眼球浮腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
眼部腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼部不快感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
硝子体障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
涙液分泌低下	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼部出血および血管障害ＮＥＣ	11	(0.7)	11	0.4	8	(0.5)	10	0.3	19	(0.6)	21	0.4
眼出血	3	(0.2)	3	0.1	7	(0.4)	9	0.3	10	(0.3)	12	0.2
結膜出血	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
虚血性視神経症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
視神経乳頭出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
前房出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼神経筋障害	5	(0.3)	5	0.2	5	(0.3)	5	0.2	10	(0.3)	10	0.2

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
眼瞼下垂	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	0			
眼筋麻痺	1	(0.1)	1	0.1	0				0				0			
眼瞼痙攣	0				1	(0.1)	1	0.1	0				0			
斜視	0				0				1	(0.1)	1	0.1	0			
瞳孔障害	0				0				0				1	(0.1)	1	0.1
傷害、中毒および処置合併症	122	(14.8)	168	11.3	122	(14.9)	168	11.6	155	(18.9)	230	15.3	146	(17.7)	205	13.4
損傷ＮＥＣ	86	(10.4)	109	7.3	95	(11.6)	121	8.4	116	(14.2)	164	10.9	96	(11.6)	125	8.2
転倒	25	(3.0)	27	1.8	22	(2.7)	29	2.0	27	(3.3)	35	2.3	32	(3.9)	41	2.7
挫傷	5	(0.6)	5	0.3	13	(1.6)	13	0.9	21	(2.6)	23	1.5	9	(1.1)	9	0.6
創傷	9	(1.1)	10	0.7	9	(1.1)	9	0.6	14	(1.7)	14	0.9	7	(0.8)	8	0.5
靭帯捻挫	5	(0.6)	6	0.4	10	(1.2)	10	0.7	8	(1.0)	9	0.6	8	(1.0)	8	0.5
四肢損傷	9	(1.1)	12	0.8	3	(0.4)	3	0.2	10	(1.2)	12	0.8	6	(0.7)	6	0.4
交通事故	5	(0.6)	7	0.5	11	(1.3)	11	0.8	7	(0.9)	8	0.5	4	(0.5)	5	0.3
肉離れ	9	(1.1)	9	0.6	5	(0.6)	5	0.3	6	(0.7)	7	0.5	3	(0.4)	3	0.2
裂傷	7	(0.9)	7	0.5	4	(0.5)	4	0.3	3	(0.4)	4	0.3	6	(0.7)	6	0.4
皮膚擦過傷	2	(0.2)	2	0.1	3	(0.4)	4	0.3	9	(1.1)	10	0.7	5	(0.6)	5	0.3
節足動物咬傷	3	(0.4)	3	0.2	4	(0.5)	4	0.3	7	(0.9)	7	0.5	3	(0.4)	4	0.3
歯牙破折	5	(0.6)	6	0.4	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
動物咬傷	1	(0.1)	1	0.1	3	(0.4)	3	0.2	5	(0.6)	5	0.3	1	(0.1)	1	0.1
腱断裂	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0				4	(0.5)	4	0.3
頭部損傷	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	3	0.2	2	(0.2)	2	0.1
体内異物	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
筋断裂	0				2	(0.2)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
上顆炎	0				0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
損傷	0				2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
胸部損傷	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
硬膜下血腫	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
骨格損傷	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
眼瞼下垂	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
眼筋麻痺	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼瞼痙攣	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
斜視	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
瞳孔障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
傷害、中毒および処置合併症	244	(14.9)	336	11.5	301	(18.3)	435	14.3	545	(16.6)	771	12.9
損傷ＮＥＣ	181	(11.0)	230	7.8	212	(12.9)	289	9.5	393	(12.0)	519	8.7
転倒	47	(2.9)	56	1.9	59	(3.6)	76	2.5	106	(3.2)	132	2.2
挫傷	18	(1.1)	18	0.6	30	(1.8)	32	1.1	48	(1.5)	50	0.8
創傷	18	(1.1)	19	0.6	21	(1.3)	22	0.7	39	(1.2)	41	0.7
靭帯捻挫	15	(0.9)	16	0.5	16	(1.0)	17	0.6	31	(0.9)	33	0.6
四肢損傷	12	(0.7)	15	0.5	16	(1.0)	18	0.6	28	(0.9)	33	0.6
交通事故	16	(1.0)	18	0.6	11	(0.7)	13	0.4	27	(0.8)	31	0.5
肉離れ	14	(0.9)	14	0.5	9	(0.5)	10	0.3	23	(0.7)	24	0.4
裂傷	11	(0.7)	11	0.4	9	(0.5)	10	0.3	20	(0.6)	21	0.4
皮膚擦過傷	5	(0.3)	6	0.2	14	(0.9)	15	0.5	19	(0.6)	21	0.4
節足動物咬傷	7	(0.4)	7	0.2	10	(0.6)	11	0.4	17	(0.5)	18	0.3
歯牙破折	7	(0.4)	8	0.3	4	(0.2)	4	0.1	11	(0.3)	12	0.2
動物咬傷	4	(0.2)	4	0.1	6	(0.4)	6	0.2	10	(0.3)	10	0.2
腱断裂	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
頭部損傷	3	(0.2)	3	0.1	4	(0.2)	5	0.2	7	(0.2)	8	0.1
体内異物	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
筋断裂	2	(0.1)	3	0.1	2	(0.1)	2	0.1	4	(0.1)	5	0.1
上顎炎	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
損傷	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
胸部損傷	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
硬膜下血腫	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
骨格損傷	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
背部損傷	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
靱帯断裂	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
外傷性潰瘍	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
眼外傷	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
眼挫傷	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
眼窩周囲出血	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
節足動物刺傷	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
創部炎症	0				0				0				2	(0.2)	2	0.1
腸脛靱帯症候群	0				1	(0.1)	1	0.1	1	(0.1)	2	0.1	0			
軟部組織損傷	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
皮膚損傷	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
労働災害	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
引っかき傷	0				0				0				1	(0.1)	1	0.1
外陰膣損傷	1	(0.1)	1	0.1	0				0				0			
外傷後疼痛	0				0				1	(0.1)	1	0.1	0			
外傷性血胸	0				0				1	(0.1)	1	0.1	0			
外傷性血腫	0				0				0				1	(0.1)	1	0.1
角膜擦過傷	0				1	(0.1)	1	0.1	0				0			
角膜損傷	0				0				1	(0.1)	1	0.1	0			
眼の擦過傷	0				1	(0.1)	1	0.1	0				0			
口腔内損傷	0				1	(0.1)	1	0.1	0				0			
口唇損傷	0				0				1	(0.1)	1	0.1	0			
坐骨神経損傷	0				0				0				1	(0.1)	1	0.1
擦過傷	0				0				0				1	(0.1)	1	0.1
脂肪塞栓症	0				0				0				1	(0.1)	1	0.1
事故	0				0				1	(0.1)	1	0.1	0			
蛇咬傷	0				0				1	(0.1)	1	0.1	0			
創壊死	0				0				1	(0.1)	1	0.1	0			
創傷血腫	0				1	(0.1)	1	0.1	0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
背部損傷	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
靱帯断裂	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
外傷性潰瘍	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
眼外傷	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
眼挫傷	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
眼窩周囲出血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
節足動物刺傷	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
創部炎症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
腸脛靱帯症候群	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
軟部組織損傷	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
皮膚損傷	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
労働災害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
引っかき傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外陰膣損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
外傷後疼痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外傷性血胸	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外傷性血腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
角膜擦過傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
角膜損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼の擦過傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔内損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口唇損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
坐骨神経損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
擦過傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脂肪塞栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
事故	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
蛇咬傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
創壊死	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
創傷血腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
創傷出血	0				0				1	(0.1)	1	0.1	0			
爪損傷	0				0				1	(0.1)	1	0.1	0			
脳振盪	1	(0.1)	2	0.1	0				0				0			
皮下血腫	0				0				0				1	(0.1)	1	0.1
靱帯損傷	0				0				0				1	(0.1)	1	0.1
骨および関節損傷	32	(3.9)	35	2.4	14	(1.7)	17	1.2	23	(2.8)	24	1.6	27	(3.3)	31	2.0
肋骨骨折	1	(0.1)	1	0.1	1	(0.1)	1	0.1	5	(0.6)	5	0.3	6	(0.7)	6	0.4
関節損傷	2	(0.2)	2	0.1	1	(0.1)	1	0.1	4	(0.5)	5	0.3	3	(0.4)	3	0.2
半月板損傷	5	(0.6)	5	0.3	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
手首関節骨折	4	(0.5)	4	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
足骨折	2	(0.2)	3	0.2	0				3	(0.4)	3	0.2	3	(0.4)	3	0.2
上腕骨骨折	1	(0.1)	1	0.1	2	(0.2)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	3	0.2
橈骨骨折	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
手骨折	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
上肢骨折	2	(0.2)	2	0.1	0				0				2	(0.2)	2	0.1
脊椎圧迫骨折	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
関節脱臼	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
足関節部骨折	3	(0.4)	3	0.2	0				0				0			
下肢骨折	2	(0.2)	2	0.1	0				0				0			
胸椎骨折	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
肩甲骨骨折	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
大腿骨骨折	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
膝蓋骨骨折	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
粉砕骨折	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
脛骨骨折	2	(0.2)	2	0.1	0				0				0			
腓骨骨折	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
ストレス骨折	0				0				1	(0.1)	1	0.1	0			
外傷性骨折	1	(0.1)	1	0.1	0				0				0			
顔面骨骨折	1	(0.1)	1	0.1	0				0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
創傷出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
爪損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳振盪	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
皮下血腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
靱帯損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
骨および関節損傷	46	(2.8)	52	1.8	50	(3.0)	55	1.8	96	(2.9)	107	1.8
肋骨骨折	2	(0.1)	2	0.1	11	(0.7)	11	0.4	13	(0.4)	13	0.2
関節損傷	3	(0.2)	3	0.1	7	(0.4)	8	0.3	10	(0.3)	11	0.2
半月板損傷	7	(0.4)	7	0.2	2	(0.1)	2	0.1	9	(0.3)	9	0.2
手首関節骨折	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
足骨折	2	(0.1)	3	0.1	6	(0.4)	6	0.2	8	(0.2)	9	0.2
上腕骨骨折	3	(0.2)	4	0.1	4	(0.2)	4	0.1	7	(0.2)	8	0.1
橈骨骨折	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
手骨折	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
上肢骨折	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
脊椎圧迫骨折	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
関節脱臼	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
足関節部骨折	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
下肢骨折	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
胸椎骨折	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
肩甲骨骨折	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
大腿骨骨折	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
膝蓋骨骨折	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
粉砕骨折	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
脛骨骨折	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
腓骨骨折	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
ストレス骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外傷性骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
顔面骨骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
頚椎骨折	0				0				1	(0.1)	1	0.1	0			
腰椎骨折	0				1	(0.1)	1	0.1	0				0			
骨亀裂	1	(0.1)	1	0.1	0				0				0			
尺骨骨折	0				0				0				1	(0.1)	1	0.1
頭蓋骨骨折	0				0				0				1	(0.1)	1	0.1
軟骨損傷	1	(0.1)	1	0.1	0				0				0			
処置による損傷および合併症ＮＥＣ	6	(0.7)	6	0.4	8	(1.0)	9	0.6	21	(2.6)	26	1.7	16	(1.9)	19	1.2
処置による疼痛	1	(0.1)	1	0.1	5	(0.6)	5	0.3	9	(1.1)	9	0.6	6	(0.7)	7	0.5
術後貧血	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	0			
切開部位痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
処置後浮腫	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
ワクチン接種合併症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
処置による悪心	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
処置後甲状腺機能低下症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
処置後出血	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
漿液腫	0				0				2	(0.2)	2	0.1	0			
移植血管合併症	0				0				1	(0.1)	1	0.1	0			
移植血管閉塞	0				0				1	(0.1)	1	0.1	0			
栄養補給チューブ合併症	0				1	(0.1)	1	0.1	0				0			
頚動脈再狭窄	1	(0.1)	1	0.1	0				0				0			
血管偽動脈瘤	1	(0.1)	1	0.1	0				0				0			
硬膜裂傷	0				0				1	(0.1)	1	0.1	0			
術後イレウス	0				1	(0.1)	1	0.1	0				0			
術後呼吸不全	1	(0.1)	1	0.1	0				0				0			
術後創合併症	0				0				0				1	(0.1)	1	0.1
処置後血腫	0				0				0				1	(0.1)	1	0.1
処置後合併症	0				0				0				1	(0.1)	1	0.1
処置後便秘	0				1	(0.1)	1	0.1	0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
頚椎骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腰椎骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨亀裂	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尺骨骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頭蓋骨骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
軟骨損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
処置による損傷および合併症ＮＥＣ	14	(0.9)	15	0.5	37	(2.3)	45	1.5	51	(1.6)	60	1.0
処置による疼痛	6	(0.4)	6	0.2	15	(0.9)	16	0.5	21	(0.6)	22	0.4
術後貧血	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
切開部位痛	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
処置後浮腫	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
ワクチン接種合併症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
処置による悪心	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
処置後甲状腺機能低下症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
処置後出血	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
漿液腫	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
移植血管合併症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
移植血管閉塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
栄養補給チューブ合併症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頚動脈再狭窄	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管偽動脈瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
硬膜裂傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
術後イレウス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
術後呼吸不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
術後創合併症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
処置後血腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
処置後合併症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
処置後便秘	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
心臓処置合併症	0				0				0				1	(0.1)	1	0.1
椎弓切除後症候群	0				0				1	(0.1)	1	0.1	0			
白内障手術合併症	0				0				0				1	(0.1)	1	0.1
吻合不全	0				0				0				1	(0.1)	1	0.1
末梢動脈再狭窄	0				0				1	(0.1)	1	0.1	0			
投薬過誤	6	(0.7)	7	0.5	9	(1.1)	9	0.6	9	(1.1)	10	0.7	10	(1.2)	15	1.0
偶発的過量投与	3	(0.4)	3	0.2	2	(0.2)	2	0.1	6	(0.7)	7	0.5	9	(1.1)	13	0.9
不適切な投与計画での薬剤の投与	0				3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1
誤薬投与	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
誤った投与期間	0				1	(0.1)	1	0.1	0				0			
誤った投与経路	0				1	(0.1)	1	0.1	0				0			
誤用量投与	1	(0.1)	2	0.1	0				0				0			
投薬過誤	0				1	(0.1)	1	0.1	0				0			
薬剤誤投与	1	(0.1)	1	0.1	0				0				0			
物理的要因による損傷	10	(1.2)	10	0.7	5	(0.6)	5	0.3	4	(0.5)	4	0.3	6	(0.7)	8	0.5
熱傷	7	(0.9)	7	0.5	3	(0.4)	3	0.2	2	(0.2)	2	0.1	4	(0.5)	4	0.3
第２度熱傷	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1
凍瘡	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
気圧性中耳炎	1	(0.1)	1	0.1	0				0				0			
食道熱傷	1	(0.1)	1	0.1	0				0				0			
第１度熱傷	0				0				0				1	(0.1)	1	0.1
凍傷	0				0				1	(0.1)	1	0.1	0			
熱射病	0				0				0				1	(0.1)	1	0.1
製品使用に関する問題	0				6	(0.7)	7	0.5	0				6	(0.7)	6	0.4
過量投与	0				6	(0.7)	7	0.5	0				5	(0.6)	5	0.3
企図的過量投与	0				0				0				1	(0.1)	1	0.1
曝露、化学的損傷および中毒	1	(0.1)	1	0.1	0				1	(0.1)	2	0.1	1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心臓処置合併症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎弓切除後症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
白内障手術合併症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
吻合不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈再狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
投薬過誤	15	(0.9)	16	0.5	19	(1.2)	25	0.8	34	(1.0)	41	0.7
偶発的過量投与	5	(0.3)	5	0.2	15	(0.9)	20	0.7	20	(0.6)	25	0.4
不適切な投与計画での薬剤の投与	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
誤薬投与	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
誤った投与期間	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
誤った投与経路	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
誤用量投与	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
投薬過誤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
薬剤誤投与	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
物理的要因による損傷	15	(0.9)	15	0.5	10	(0.6)	12	0.4	25	(0.8)	27	0.5
熱傷	10	(0.6)	10	0.3	6	(0.4)	6	0.2	16	(0.5)	16	0.3
第２度熱傷	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
凍瘡	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
気圧性中耳炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
食道熱傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
第１度熱傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
凍傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
熱射病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
製品使用に関する問題	6	(0.4)	7	0.2	6	(0.4)	6	0.2	12	(0.4)	13	0.2
過量投与	6	(0.4)	7	0.2	5	(0.3)	5	0.2	11	(0.3)	12	0.2
企図的過量投与	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
曝露、化学的損傷および中毒	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
各種物質毒性	0				0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
中毒	1	(0.1)	1	0.1	0				0				0			
呼吸器、胸郭および縦隔障害	127	(15.4)	173	11.6	114	(13.9)	173	12.0	132	(16.1)	187	12.4	145	(17.6)	229	15.0
呼吸器系障害ＮＥＣ	88	(10.7)	112	7.5	77	(9.4)	104	7.2	93	(11.4)	116	7.7	102	(12.4)	137	9.0
咳嗽	32	(3.9)	36	2.4	27	(3.3)	28	1.9	37	(4.5)	37	2.5	41	(5.0)	43	2.8
呼吸困難	15	(1.8)	20	1.3	19	(2.3)	26	1.8	18	(2.2)	20	1.3	26	(3.2)	27	1.8
口腔咽頭痛	8	(1.0)	8	0.5	5	(0.6)	6	0.4	10	(1.2)	10	0.7	15	(1.8)	18	1.2
睡眠時無呼吸症候群	3	(0.4)	3	0.2	2	(0.2)	2	0.1	10	(1.2)	10	0.7	14	(1.7)	14	0.9
肺腫瘤	7	(0.9)	7	0.5	4	(0.5)	4	0.3	8	(1.0)	8	0.5	6	(0.7)	6	0.4
しゃっくり	5	(0.6)	8	0.5	8	(1.0)	8	0.6	0				2	(0.2)	2	0.1
鼻漏	5	(0.6)	5	0.3	3	(0.4)	3	0.2	5	(0.6)	6	0.4	2	(0.2)	2	0.1
労作性呼吸困難	1	(0.1)	1	0.1	5	(0.6)	5	0.3	6	(0.7)	6	0.4	3	(0.4)	3	0.2
呼吸不全	2	(0.2)	2	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2	4	(0.5)	4	0.3
呼吸障害	2	(0.2)	3	0.2	0				4	(0.5)	4	0.3	2	(0.2)	2	0.1
発声障害	0				4	(0.5)	4	0.3	0				2	(0.2)	2	0.1
湿性咳嗽	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
上気道うっ血	0				2	(0.2)	4	0.3	0				3	(0.4)	5	0.3
くしゃみ	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
気道うっ血	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
急性呼吸不全	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
低酸素症	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
咽喉刺激感	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
胸膜痛	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
上気道咳症候群	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
肺障害	1	(0.1)	1	0.1	0				0				2	(0.2)	3	0.2
咽喉乾燥	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
いびき	1	(0.1)	1	0.1	0				0				0			
カタル	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
各種物質毒性	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
中毒	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
呼吸器、胸郭および縦隔障害	241	(14.7)	346	11.8	277	(16.8)	416	13.7	518	(15.8)	762	12.8
呼吸器系障害ＮＥＣ	165	(10.0)	216	7.4	195	(11.9)	253	8.3	360	(11.0)	469	7.9
咳嗽	59	(3.6)	64	2.2	78	(4.7)	80	2.6	137	(4.2)	144	2.4
呼吸困難	34	(2.1)	46	1.6	44	(2.7)	47	1.5	78	(2.4)	93	1.6
口腔咽頭痛	13	(0.8)	14	0.5	25	(1.5)	28	0.9	38	(1.2)	42	0.7
睡眠時無呼吸症候群	5	(0.3)	5	0.2	24	(1.5)	24	0.8	29	(0.9)	29	0.5
肺腫瘤	11	(0.7)	11	0.4	14	(0.9)	14	0.5	25	(0.8)	25	0.4
しゃっくり	13	(0.8)	16	0.5	2	(0.1)	2	0.1	15	(0.5)	18	0.3
鼻漏	8	(0.5)	8	0.3	7	(0.4)	8	0.3	15	(0.5)	16	0.3
労作性呼吸困難	6	(0.4)	6	0.2	9	(0.5)	9	0.3	15	(0.5)	15	0.3
呼吸不全	6	(0.4)	6	0.2	7	(0.4)	7	0.2	13	(0.4)	13	0.2
呼吸障害	2	(0.1)	3	0.1	6	(0.4)	6	0.2	8	(0.2)	9	0.2
発声障害	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
湿性咳嗽	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
上気道うっ血	2	(0.1)	4	0.1	3	(0.2)	5	0.2	5	(0.2)	9	0.2
くしゃみ	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
気道うっ血	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
急性呼吸不全	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
低酸素症	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
咽喉刺激感	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
胸膜痛	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
上気道咳症候群	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
肺障害	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
咽喉乾燥	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
いびき	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
カタル	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
ピックウィック症候群	1	(0.1)	1	0.1	0				0				0			
安静時呼吸困難	0				0				1	(0.1)	1	0.1	0			
過換気	0				1	(0.1)	1	0.1	0				0			
呼吸窮迫	0				0				1	(0.1)	1	0.1	0			
呼吸停止	0				0				1	(0.1)	1	0.1	0			
高炭酸ガス血症	1	(0.1)	1	0.1	0				0				0			
徐呼吸	1	(0.1)	1	0.1	0				0				0			
息詰まり	1	(0.1)	1	0.1	0				0				0			
副鼻腔不快感	0				0				0				1	(0.1)	1	0.1
喀血	0				1	(0.1)	3	0.2	0				0			
上気道障害（感染を除く）	18	(2.2)	22	1.5	21	(2.6)	23	1.6	23	(2.8)	29	1.9	21	(2.5)	26	1.7
アレルギー性鼻炎	5	(0.6)	5	0.3	8	(1.0)	8	0.6	6	(0.7)	6	0.4	5	(0.6)	10	0.7
鼻閉	4	(0.5)	7	0.5	2	(0.2)	2	0.1	5	(0.6)	5	0.3	5	(0.6)	5	0.3
鼻出血	4	(0.5)	5	0.3	3	(0.4)	3	0.2	4	(0.5)	9	0.6	4	(0.5)	4	0.3
副鼻腔うっ血	1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	4	0.3	2	(0.2)	2	0.1
鼻茸	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
副鼻腔障害	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
副鼻腔分泌過多	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
逆流性喉頭炎	0				1	(0.1)	1	0.1	0				0			
喉頭狭窄	0				0				1	(0.1)	1	0.1	0			
声帯の炎症	0				0				0				1	(0.1)	1	0.1
声帯障害	0				0				1	(0.1)	1	0.1	0			
鼻そう痒症	1	(0.1)	1	0.1	0				0				0			
鼻の炎症	0				1	(0.1)	1	0.1	0				0			
鼻乾燥	0				0				1	(0.1)	1	0.1	0			
鼻甲介肥大	0				0				0				1	(0.1)	1	0.1
鼻中隔障害	0				1	(0.1)	1	0.1	0				0			
鼻中隔穿孔	0				1	(0.1)	1	0.1	0				0			
鼻中隔彎曲	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ピックウィック症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
安静時呼吸困難	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
過換気	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
呼吸窮迫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼吸停止	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高炭酸ガス血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
徐呼吸	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
息詰まり	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
副鼻腔不快感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
喀血	1	(0.1)	3	0.1	0				1	(<0.1)	3	0.1
上気道障害（感染を除く）	39	(2.4)	45	1.5	44	(2.7)	55	1.8	83	(2.5)	100	1.7
アレルギー性鼻炎	13	(0.8)	13	0.4	11	(0.7)	16	0.5	24	(0.7)	29	0.5
鼻閉	6	(0.4)	9	0.3	10	(0.6)	10	0.3	16	(0.5)	19	0.3
鼻出血	7	(0.4)	8	0.3	8	(0.5)	13	0.4	15	(0.5)	21	0.4
副鼻腔うっ血	4	(0.2)	4	0.1	5	(0.3)	6	0.2	9	(0.3)	10	0.2
鼻茸	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
副鼻腔障害	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
副鼻腔分泌過多	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
逆流性喉頭炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
喉頭狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
声帯の炎症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
声帯障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鼻そう痒症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻の炎症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻乾燥	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鼻甲介肥大	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鼻中隔障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻中隔穿孔	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻中隔彎曲	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
鼻浮腫	0				1	(0.1)	2	0.1	0				0			
気管支障害（新生物を除く）	14	(1.7)	16	1.1	17	(2.1)	20	1.4	16	(2.0)	21	1.4	27	(3.3)	35	2.3
慢性閉塞性肺疾患	5	(0.6)	6	0.4	8	(1.0)	11	0.8	11	(1.3)	15	1.0	15	(1.8)	21	1.4
喘息	5	(0.6)	6	0.4	5	(0.6)	5	0.3	3	(0.4)	3	0.2	4	(0.5)	6	0.4
慢性気管支炎	2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	3	0.2
気管支反応性亢進	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
気管支痙攣	0				0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
喘息クリーゼ	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
気管支拡張症	0				0				0				1	(0.1)	1	0.1
気管支壁肥厚	0				0				0				1	(0.1)	1	0.1
喘鳴	1	(0.1)	1	0.1	0				0				0			
下気道障害（閉塞および感染を除く）	13	(1.6)	14	0.9	8	(1.0)	11	0.8	11	(1.3)	12	0.8	14	(1.7)	21	1.4
無気肺	5	(0.6)	5	0.3	1	(0.1)	1	0.1	6	(0.7)	6	0.4	3	(0.4)	4	0.3
肺水腫	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	5	(0.6)	6	0.4
急性肺水腫	3	(0.4)	3	0.2	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
肺うっ血	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
肺気腫	0				2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
誤嚥性肺炎	0				2	(0.2)	3	0.2	0				1	(0.1)	1	0.1
拘束性肺疾患	2	(0.2)	2	0.1	0				0				0			
肺線維症	0				0				0				2	(0.2)	2	0.1
肺肉芽腫	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
間質性肺疾患	0				0				0				1	(0.1)	1	0.1
器質化肺炎	0				0				0				1	(0.1)	1	0.1
肺浸潤	0				0				1	(0.1)	1	0.1	0			
肺嚢胞	1	(0.1)	1	0.1	0				0				0			
胸膜障害	4	(0.5)	4	0.3	6	(0.7)	7	0.5	6	(0.7)	7	0.5	5	(0.6)	5	0.3
胸水	0				4	(0.5)	4	0.3	4	(0.5)	5	0.3	1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
鼻浮腫	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
気管支障害（新生物を除く）	31	(1.9)	36	1.2	43	(2.6)	56	1.8	74	(2.3)	92	1.5
慢性閉塞性肺疾患	13	(0.8)	17	0.6	26	(1.6)	36	1.2	39	(1.2)	53	0.9
喘息	10	(0.6)	11	0.4	7	(0.4)	9	0.3	17	(0.5)	20	0.3
慢性気管支炎	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
気管支反応性亢進	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
気管支痙攣	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
喘息クリーゼ	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
気管支拡張症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
気管支壁肥厚	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
喘鳴	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
下気道障害（閉塞および感染を除く）	21	(1.3)	25	0.9	25	(1.5)	33	1.1	46	(1.4)	58	1.0
無気肺	6	(0.4)	6	0.2	9	(0.5)	10	0.3	15	(0.5)	16	0.3
肺水腫	5	(0.3)	5	0.2	7	(0.4)	8	0.3	12	(0.4)	13	0.2
急性肺水腫	5	(0.3)	5	0.2	2	(0.1)	2	0.1	7	(0.2)	7	0.1
肺うっ血	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
肺気腫	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
誤嚥性肺炎	2	(0.1)	3	0.1	1	(0.1)	1	<0.1	3	(0.1)	4	0.1
拘束性肺疾患	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
肺線維症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
肺肉芽腫	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
間質性肺疾患	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
器質化肺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺浸潤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胸膜障害	10	(0.6)	11	0.4	11	(0.7)	12	0.4	21	(0.6)	23	0.4
胸水	4	(0.2)	4	0.1	5	(0.3)	6	0.2	9	(0.3)	10	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
気胸	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
胸水症	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
胸膜炎	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
胸膜線維症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
胸膜障害	1	(0.1)	1	0.1	0				0				0			
肺血管障害	4	(0.5)	4	0.3	8	(1.0)	8	0.6	2	(0.2)	2	0.1	5	(0.6)	5	0.3
肺塞栓症	2	(0.2)	2	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1	3	(0.4)	3	0.2
肺高血圧症	2	(0.2)	2	0.1	4	(0.5)	4	0.3	0				2	(0.2)	2	0.1
肺動脈性肺高血圧症	0				0				1	(0.1)	1	0.1	0			
胸郭障害（肺および胸膜を除く）	1	(0.1)	1	0.1	0				0				0			
後天性横隔膜性内臓転位	1	(0.1)	1	0.1	0				0				0			
一般・全身障害および投与部位の状態	118	(14.3)	160	10.8	133	(16.2)	194	13.4	133	(16.2)	182	12.1	132	(16.0)	173	11.3
全身障害ＮＥＣ	97	(11.8)	126	8.5	114	(13.9)	157	10.9	111	(13.6)	149	9.9	113	(13.7)	147	9.6
疲労	22	(2.7)	25	1.7	37	(4.5)	43	3.0	14	(1.7)	15	1.0	24	(2.9)	25	1.6
末梢性浮腫	15	(1.8)	16	1.1	9	(1.1)	9	0.6	28	(3.4)	32	2.1	24	(2.9)	26	1.7
無力症	16	(1.9)	17	1.1	25	(3.1)	29	2.0	10	(1.2)	11	0.7	15	(1.8)	17	1.1
非心臓性胸痛	16	(1.9)	16	1.1	13	(1.6)	13	0.9	18	(2.2)	18	1.2	12	(1.5)	13	0.9
胸痛	4	(0.5)	4	0.3	11	(1.3)	20	1.4	12	(1.5)	14	0.9	15	(1.8)	16	1.0
末梢腫脹	12	(1.5)	14	0.9	4	(0.5)	4	0.3	14	(1.7)	18	1.2	6	(0.7)	6	0.4
胸部不快感	6	(0.7)	8	0.5	6	(0.7)	6	0.4	5	(0.6)	5	0.3	12	(1.5)	12	0.8
疼痛	1	(0.1)	1	0.1	8	(1.0)	8	0.6	10	(1.2)	13	0.9	6	(0.7)	7	0.5
悪寒	4	(0.5)	4	0.3	2	(0.2)	3	0.2	3	(0.4)	4	0.3	3	(0.4)	4	0.3
インフルエンザ様疾患	2	(0.2)	2	0.1	2	(0.2)	3	0.2	3	(0.4)	4	0.3	3	(0.4)	3	0.2
倦怠感	4	(0.5)	4	0.3	2	(0.2)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
歩行障害	0				3	(0.4)	3	0.2	2	(0.2)	2	0.1	3	(0.4)	3	0.2
浮腫	3	(0.4)	3	0.2	0				1	(0.1)	2	0.1	2	(0.2)	2	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
気胸	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
胸水症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
胸膜炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胸膜線維症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
胸膜障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺血管障害	12	(0.7)	12	0.4	7	(0.4)	7	0.2	19	(0.6)	19	0.3
肺塞栓症	6	(0.4)	6	0.2	4	(0.2)	4	0.1	10	(0.3)	10	0.2
肺高血圧症	6	(0.4)	6	0.2	2	(0.1)	2	0.1	8	(0.2)	8	0.1
肺動脈性肺高血圧症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胸郭障害（肺および胸膜を除く）	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
後天性横隔膜性内臓転位	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
一般・全身障害および投与部位の状態	251	(15.3)	354	12.1	265	(16.1)	355	11.7	516	(15.7)	709	11.9
全身障害ＮＥＣ	211	(12.9)	283	9.7	224	(13.6)	296	9.8	435	(13.2)	579	9.7
疲労	59	(3.6)	68	2.3	38	(2.3)	40	1.3	97	(3.0)	108	1.8
末梢性浮腫	24	(1.5)	25	0.9	52	(3.2)	58	1.9	76	(2.3)	83	1.4
無力症	41	(2.5)	46	1.6	25	(1.5)	28	0.9	66	(2.0)	74	1.2
非心臓性胸痛	29	(1.8)	29	1.0	30	(1.8)	31	1.0	59	(1.8)	60	1.0
胸痛	15	(0.9)	24	0.8	27	(1.6)	30	1.0	42	(1.3)	54	0.9
末梢腫脹	16	(1.0)	18	0.6	20	(1.2)	24	0.8	36	(1.1)	42	0.7
胸部不快感	12	(0.7)	14	0.5	17	(1.0)	17	0.6	29	(0.9)	31	0.5
疼痛	9	(0.5)	9	0.3	16	(1.0)	20	0.7	25	(0.8)	29	0.5
悪寒	6	(0.4)	7	0.2	6	(0.4)	8	0.3	12	(0.4)	15	0.3
インフルエンザ様疾患	4	(0.2)	5	0.2	6	(0.4)	7	0.2	10	(0.3)	12	0.2
倦怠感	6	(0.4)	7	0.2	2	(0.1)	2	0.1	8	(0.2)	9	0.2
歩行障害	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
浮腫	3	(0.2)	3	0.1	3	(0.2)	4	0.1	6	(0.2)	7	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
早期満腹	2	(0.2)	2	0.1	3	(0.4)	3	0.2	0				0			
ポリープ	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
熱感	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1	0			
炎症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
口渇	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
全身性浮腫	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
多臓器不全	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
圧痛	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
空腹	0				0				2	(0.2)	2	0.1	0			
限局性浮腫	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
先行疾患の改善	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
不快感	0				2	(0.2)	2	0.1	0				0			
ヘルニア	0				1	(0.1)	1	0.1	0				0			
顔面痛	1	(0.1)	1	0.1	0				0				0			
局所腫脹	0				0				1	(0.1)	1	0.1	0			
硬結	1	(0.1)	2	0.1	0				0				0			
腫脹	1	(0.1)	1	0.1	0				0				0			
重力性浮腫	0				0				0				1	(0.1)	1	0.1
軟部組織の炎症	0				0				0				1	(0.1)	1	0.1
捻髪音	0				0				0				1	(0.1)	1	0.1
粘膜過形成	0				0				0				1	(0.1)	1	0.1
微石症	0				0				1	(0.1)	1	0.1	0			
冷感	0				0				0				1	(0.1)	1	0.1
体温異常	12	(1.5)	12	0.8	9	(1.1)	10	0.7	15	(1.8)	16	1.1	9	(1.1)	9	0.6
発熱	12	(1.5)	12	0.8	8	(1.0)	9	0.6	15	(1.8)	16	1.1	9	(1.1)	9	0.6
悪性高熱	0				1	(0.1)	1	0.1	0				0			
投与部位反応	6	(0.7)	7	0.5	10	(1.2)	12	0.8	9	(1.1)	11	0.7	11	(1.3)	11	0.7
注射部位内出血	1	(0.1)	1	0.1	4	(0.5)	4	0.3	6	(0.7)	7	0.5	4	(0.5)	4	0.3
注射部位出血	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
早期満腹	5	(0.3)	5	0.2	0				5	(0.2)	5	0.1
ポリープ	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
熱感	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
炎症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
口渇	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
全身性浮腫	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
多臓器不全	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
圧痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
空腹	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
限局性浮腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
先行疾患の改善	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
不快感	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
ヘルニア	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
顔面痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
局所腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
硬結	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
腫脹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
重力性浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
軟部組織の炎症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
捻髪音	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
粘膜過形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
微石症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
冷感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
体温異常	21	(1.3)	22	0.8	24	(1.5)	25	0.8	45	(1.4)	47	0.8
発熱	20	(1.2)	21	0.7	24	(1.5)	25	0.8	44	(1.3)	46	0.8
悪性高熱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
投与部位反応	16	(1.0)	19	0.6	20	(1.2)	22	0.7	36	(1.1)	41	0.7
注射部位内出血	5	(0.3)	5	0.2	10	(0.6)	11	0.4	15	(0.5)	16	0.3
注射部位出血	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
注射部位疼痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
注射部位反応	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1	0			
注射部位血腫	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
注射部位腫瘤	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
カテーテル留置部位炎症	0				1	(0.1)	1	0.1	0				0			
血管穿刺部位内出血	0				0				0				1	(0.1)	1	0.1
注射部位萎縮	0				0				1	(0.1)	1	0.1	0			
注射部位結節	0				0				0				1	(0.1)	1	0.1
注射部位硬結	1	(0.1)	1	0.1	0				0				0			
注射部位熱感	0				0				1	(0.1)	1	0.1	0			
注射部位不快感	0				1	(0.1)	2	0.1	0				0			
注射部位変色	1	(0.1)	1	0.1	0				0				0			
組織障害ＮＥＣ	7	(0.9)	9	0.6	9	(1.1)	9	0.6	2	(0.2)	2	0.1	3	(0.4)	3	0.2
嚢胞	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
小結節	1	(0.1)	3	0.2	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
化生	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
治癒不良	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
腫瘤	0				2	(0.2)	2	0.1	0				0			
石灰沈着症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
潰瘍	0				2	(0.2)	2	0.1	0				0			
壊死	1	(0.1)	1	0.1	0				0				0			
線維症	1	(0.1)	1	0.1	0				0				0			
致命的転帰	4	(0.5)	4	0.3	2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
死亡	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
突然死	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
心突然死	1	(0.1)	1	0.1	0				0				0			
治療的効果および非治療的効果（毒性を除く）	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
医薬品副作用	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
注射部位疼痛	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
注射部位反応	2	(0.1)	2	0.1	1	(0.1)	2	0.1	3	(0.1)	4	0.1
注射部位血腫	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
注射部位腫瘤	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
カテーテル留置部位炎症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管穿刺部位内出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
注射部位萎縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
注射部位結節	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
注射部位硬結	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
注射部位熱感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
注射部位不快感	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
注射部位変色	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
組織障害ＮＥＣ	16	(1.0)	18	0.6	5	(0.3)	5	0.2	21	(0.6)	23	0.4
嚢胞	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
小結節	2	(0.1)	4	0.1	2	(0.1)	2	0.1	4	(0.1)	6	0.1
化生	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
治癒不良	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腫瘤	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
石灰沈着症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
潰瘍	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
壊死	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
線維症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
致命的転帰	6	(0.4)	6	0.2	4	(0.2)	4	0.1	10	(0.3)	10	0.2
死亡	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
突然死	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心突然死	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
治療的効果および非治療的効果（毒性を除く）	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
医薬品副作用	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
薬剤離脱症候群	0				1	(0.1)	1	0.1	0				0			
薬物特異体質反応	0				1	(0.1)	1	0.1	0				0			
薬物不耐性	0				0				1	(0.1)	1	0.1	0			
医療機器に関する問題	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
医療機器機能不良	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
医療機器関連の血栓症	0				0				0				1	(0.1)	1	0.1
皮膚および皮下組織障害	89	(10.8)	124	8.3	90	(11.0)	126	8.7	95	(11.6)	124	8.2	120	(14.5)	159	10.4
表皮および皮膚異常	52	(6.3)	63	4.2	56	(6.8)	71	4.9	56	(6.8)	66	4.4	71	(8.6)	90	5.9
発疹	12	(1.5)	13	0.9	11	(1.3)	11	0.8	10	(1.2)	10	0.7	15	(1.8)	16	1.0
そう痒症	11	(1.3)	13	0.9	10	(1.2)	14	1.0	9	(1.1)	9	0.6	9	(1.1)	10	0.7
湿疹	2	(0.2)	2	0.1	3	(0.4)	3	0.2	8	(1.0)	9	0.6	3	(0.4)	4	0.3
皮膚炎	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	5	(0.6)	5	0.3
皮膚病変	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	3	0.2	7	(0.8)	8	0.5
皮膚乾燥	0				5	(0.6)	5	0.3	2	(0.2)	2	0.1	4	(0.5)	4	0.3
紅斑	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2
接触性皮膚炎	3	(0.4)	3	0.2	0				2	(0.2)	2	0.1	5	(0.6)	5	0.3
間擦疹	2	(0.2)	2	0.1	3	(0.4)	4	0.3	1	(0.1)	1	0.1	3	(0.4)	4	0.3
褥瘡性潰瘍	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
乾癬	1	(0.1)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
水疱	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
脂漏性皮膚炎	4	(0.5)	4	0.3	2	(0.2)	3	0.2	0				0			
全身性そう痒症	0				0				3	(0.4)	3	0.2	3	(0.4)	3	0.2
アトピー性皮膚炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
全身性皮疹	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
アレルギー性皮膚炎	0				2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
紅斑性皮疹	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	0			
皮膚剥脱	0				3	(0.4)	3	0.2	0				1	(0.1)	1	0.1
血性水疱	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
薬剤離脱症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
薬物特異体質反応	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
薬物不耐性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
医療機器に関する問題	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
医療機器機能不良	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
医療機器関連の血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚および皮下組織障害	179	(10.9)	250	8.5	215	(13.1)	283	9.3	394	(12.0)	533	8.9
表皮および皮膚異常	108	(6.6)	134	4.6	127	(7.7)	156	5.1	235	(7.2)	290	4.9
発疹	23	(1.4)	24	0.8	25	(1.5)	26	0.9	48	(1.5)	50	0.8
そう痒症	21	(1.3)	27	0.9	18	(1.1)	19	0.6	39	(1.2)	46	0.8
湿疹	5	(0.3)	5	0.2	11	(0.7)	13	0.4	16	(0.5)	18	0.3
皮膚炎	5	(0.3)	5	0.2	7	(0.4)	7	0.2	12	(0.4)	12	0.2
皮膚病変	3	(0.2)	3	0.1	9	(0.5)	11	0.4	12	(0.4)	14	0.2
皮膚乾燥	5	(0.3)	5	0.2	6	(0.4)	6	0.2	11	(0.3)	11	0.2
紅斑	5	(0.3)	5	0.2	5	(0.3)	5	0.2	10	(0.3)	10	0.2
接触性皮膚炎	3	(0.2)	3	0.1	7	(0.4)	7	0.2	10	(0.3)	10	0.2
間擦疹	5	(0.3)	6	0.2	4	(0.2)	5	0.2	9	(0.3)	11	0.2
褥瘡性潰瘍	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
乾癬	3	(0.2)	4	0.1	4	(0.2)	4	0.1	7	(0.2)	8	0.1
水疱	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
脂漏性皮膚炎	6	(0.4)	7	0.2	0				6	(0.2)	7	0.1
全身性そう痒症	0				6	(0.4)	6	0.2	6	(0.2)	6	0.1
アトピー性皮膚炎	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
全身性皮疹	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
アレルギー性皮膚炎	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
紅斑性皮疹	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
皮膚剥脱	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
血性水疱	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
皮膚障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
うっ滞性皮膚炎	0				0				2	(0.2)	2	0.1	0			
そう痒性皮疹	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
丘疹	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
丘疹性皮疹	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
神経皮膚炎	0				0				0				2	(0.2)	2	0.1
水疱性皮膚炎	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
斑状皮疹	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
皮脂欠乏性湿疹	1	(0.1)	1	0.1	0				0				1	(0.1)	2	0.1
皮膚壊死	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
皮膚弛緩症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
スティーブンス・ジョンソン症候群	1	(0.1)	1	0.1	0				0				0			
環状肉芽腫	0				1	(0.1)	1	0.1	0				0			
血管周囲細胞浸潤性皮膚炎	0				0				1	(0.1)	1	0.1	0			
光線過敏性反応	0				0				1	(0.1)	2	0.1	0			
硬化性苔癬	0				1	(0.1)	1	0.1	0				0			
中毒性皮疹	1	(0.1)	1	0.1	0				0				0			
斑状丘疹状皮疹	0				0				0				1	(0.1)	1	0.1
皮膚亀裂	0				0				1	(0.1)	1	0.1	0			
皮膚局面	0				1	(0.1)	2	0.1	0				0			
皮膚筋炎	1	(0.1)	3	0.2	0				0				0			
皮膚刺激	0				1	(0.1)	1	0.1	0				0			
皮膚灼熱感	0				0				1	(0.1)	1	0.1	0			
皮膚反応	0				0				1	(0.1)	1	0.1	0			
皮膚変色	0				0				0				1	(0.1)	1	0.1
薬疹	0				0				0				1	(0.1)	2	0.1
扁平苔癬	0				0				0				1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
皮膚障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
うっ滞性皮膚炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
そう痒性皮疹	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
丘疹	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
丘疹性皮疹	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
神経皮膚炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
水疱性皮膚炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
斑状皮疹	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
皮脂欠乏性湿疹	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
皮膚壊死	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
皮膚弛緩症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
スティーブンス・ジョンソン症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
環状肉芽腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管周囲細胞浸潤性皮膚炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
光線過敏性反応	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
硬化性苔癬	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
中毒性皮疹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
斑状丘疹状皮疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚亀裂	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚局面	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
皮膚筋炎	1	(0.1)	3	0.1	0				1	(<0.1)	3	0.1
皮膚刺激	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮膚灼熱感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚反応	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚変色	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
薬疹	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
扁平苔癬	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
痂皮	0				1	(0.1)	1	0.1	0				0			
痒疹	0				0				0				1	(0.1)	1	0.1
皮膚および皮下組織障害ＮＥＣ	19	(2.3)	30	2.0	16	(2.0)	16	1.1	24	(2.9)	30	2.0	26	(3.2)	34	2.2
皮膚潰瘍	13	(1.6)	16	1.1	8	(1.0)	8	0.6	11	(1.3)	15	1.0	13	(1.6)	17	1.1
糖尿病性足病変	9	(1.1)	14	0.9	6	(0.7)	6	0.4	8	(1.0)	8	0.5	9	(1.1)	13	0.9
脂肪肥大症	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
皮膚腫瘤	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
糖尿病性潰瘍	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
後天性リポジストロフィー	0				0				1	(0.1)	1	0.1	0			
手掌・足底発赤知覚不全症候群	0				1	(0.1)	1	0.1	0				0			
神経障害性潰瘍	0				0				1	(0.1)	1	0.1	0			
皮下気腫	0				0				0				1	(0.1)	1	0.1
皮膚アミロイドーシス	0				0				1	(0.1)	1	0.1	0			
皮膚付属器状態	16	(1.9)	18	1.2	13	(1.6)	13	0.9	11	(1.3)	11	0.7	9	(1.1)	9	0.6
多汗症	3	(0.4)	3	0.2	5	(0.6)	5	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1
嵌入爪	2	(0.2)	2	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1
脱毛症	3	(0.4)	3	0.2	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
ざ瘡	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
寝汗	3	(0.4)	5	0.3	1	(0.1)	1	0.1	0				0			
爪の障害	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
汗疹	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
酒さ	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
びまん性脱毛症	0				0				0				1	(0.1)	1	0.1
脂漏	0				0				1	(0.1)	1	0.1	0			
爪変色	0				0				0				1	(0.1)	1	0.1
内方発育毛	0				0				0				1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
痂皮	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
痒疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚および皮下組織障害ＮＥＣ	35	(2.1)	46	1.6	50	(3.0)	64	2.1	85	(2.6)	110	1.8
皮膚潰瘍	21	(1.3)	24	0.8	24	(1.5)	32	1.1	45	(1.4)	56	0.9
糖尿病性足病変	15	(0.9)	20	0.7	17	(1.0)	21	0.7	32	(1.0)	41	0.7
脂肪肥大症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
皮膚腫瘤	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
糖尿病性潰瘍	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
後天性リポジストロフィー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
手掌・足底発赤知覚不全症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経障害性潰瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮下気腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚アミロイドーシス	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚付属器状態	29	(1.8)	31	1.1	20	(1.2)	20	0.7	49	(1.5)	51	0.9
多汗症	8	(0.5)	8	0.3	4	(0.2)	4	0.1	12	(0.4)	12	0.2
嵌入爪	6	(0.4)	6	0.2	3	(0.2)	3	0.1	9	(0.3)	9	0.2
脱毛症	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
ざ瘡	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
寝汗	4	(0.2)	6	0.2	0				4	(0.1)	6	0.1
爪の障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
汗疹	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
酒さ	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
びまん性脱毛症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脂漏	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
爪変色	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
内方発育毛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
冷汗	0				1	(0.1)	1	0.1	0				0			
角化および皮膚異栄養性障害	3	(0.4)	3	0.2	8	(1.0)	11	0.8	7	(0.9)	7	0.5	11	(1.3)	13	0.9
日光角化症	2	(0.2)	2	0.1	5	(0.6)	8	0.6	1	(0.1)	1	0.1	8	(1.0)	10	0.7
過角化	1	(0.1)	1	0.1	1	(0.1)	1	0.1	6	(0.7)	6	0.4	3	(0.4)	3	0.2
乾皮症	0				1	(0.1)	1	0.1	0				0			
掌蹠角皮症	0				1	(0.1)	1	0.1	0				0			
血管浮腫および蕁麻疹	5	(0.6)	6	0.4	9	(1.1)	10	0.7	4	(0.5)	4	0.3	7	(0.8)	7	0.5
蕁麻疹	4	(0.5)	4	0.3	6	(0.7)	7	0.5	4	(0.5)	4	0.3	5	(0.6)	5	0.3
血管浮腫	0				2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
顔面腫脹	1	(0.1)	2	0.1	1	(0.1)	1	0.1	0				0			
皮膚血管異常	3	(0.4)	3	0.2	2	(0.2)	2	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1
斑状出血	2	(0.2)	2	0.1	0				4	(0.5)	4	0.3	1	(0.1)	1	0.1
点状出血	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
紫斑	0				1	(0.1)	1	0.1	0				0			
良性皮膚新生物	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	4	(0.5)	5	0.3
皮膚嚢腫	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	4	(0.5)	5	0.3
色素沈着性疾患	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
日光黒子	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
血管障害	92	(11.2)	110	7.4	92	(11.2)	114	7.9	99	(12.1)	131	8.7	108	(13.1)	135	8.8
高血圧性血管障害	33	(4.0)	34	2.3	35	(4.3)	43	3.0	46	(5.6)	56	3.7	42	(5.1)	48	3.1
高血圧	26	(3.2)	26	1.7	30	(3.7)	38	2.6	39	(4.8)	47	3.1	36	(4.4)	40	2.6
高血圧クリーゼ	4	(0.5)	4	0.3	4	(0.5)	4	0.3	4	(0.5)	6	0.4	6	(0.7)	8	0.5
高血圧緊急症	3	(0.4)	3	0.2	0				0				0			
高血圧性血管障害	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
起立性高血圧	0				1	(0.1)	1	0.1	0				0			
収縮期高血圧	0				0				1	(0.1)	1	0.1	0			
本態性高血圧症	0				0				1	(0.1)	1	0.1	0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
冷汗	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
角化および皮膚異栄養性障害	11	(0.7)	14	0.5	18	(1.1)	20	0.7	29	(0.9)	34	0.6
日光角化症	7	(0.4)	10	0.3	9	(0.5)	11	0.4	16	(0.5)	21	0.4
過角化	2	(0.1)	2	0.1	9	(0.5)	9	0.3	11	(0.3)	11	0.2
乾皮症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
掌蹠角皮症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管浮腫および蕁麻疹	14	(0.9)	16	0.5	11	(0.7)	11	0.4	25	(0.8)	27	0.5
蕁麻疹	10	(0.6)	11	0.4	9	(0.5)	9	0.3	19	(0.6)	20	0.3
血管浮腫	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
顔面腫脹	2	(0.1)	3	0.1	0				2	(0.1)	3	0.1
皮膚血管異常	5	(0.3)	5	0.2	5	(0.3)	5	0.2	10	(0.3)	10	0.2
斑状出血	2	(0.1)	2	0.1	5	(0.3)	5	0.2	7	(0.2)	7	0.1
点状出血	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
紫斑	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性皮膚新生物	2	(0.1)	2	0.1	6	(0.4)	7	0.2	8	(0.2)	9	0.2
皮膚嚢腫	2	(0.1)	2	0.1	6	(0.4)	7	0.2	8	(0.2)	9	0.2
色素沈着性疾患	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
日光黒子	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
血管障害	184	(11.2)	224	7.6	207	(12.6)	266	8.8	391	(11.9)	490	8.2
高血圧性血管障害	68	(4.1)	77	2.6	88	(5.4)	104	3.4	156	(4.7)	181	3.0
高血圧	56	(3.4)	64	2.2	75	(4.6)	87	2.9	131	(4.0)	151	2.5
高血圧クリーゼ	8	(0.5)	8	0.3	10	(0.6)	14	0.5	18	(0.5)	22	0.4
高血圧緊急症	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
高血圧性血管障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
起立性高血圧	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
収縮期高血圧	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
本態性高血圧症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
動脈硬化、狭窄、血流障害および壊死	25	(3.0)	25	1.7	19	(2.3)	21	1.5	22	(2.7)	24	1.6	30	(3.6)	33	2.2
末梢動脈閉塞性疾患	4	(0.5)	4	0.3	8	(1.0)	8	0.6	6	(0.7)	6	0.4	10	(1.2)	10	0.7
大動脈硬化症	2	(0.2)	2	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1	5	(0.6)	5	0.3
末梢静脈疾患	1	(0.1)	1	0.1	2	(0.2)	2	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2
間欠性跛行	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	5	(0.6)	5	0.3
大動脈狭窄	6	(0.7)	6	0.4	0				1	(0.1)	1	0.1	0			
動脈硬化症	4	(0.5)	4	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
糖尿病性血管障害	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
末梢動脈狭窄	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
虚血	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
血行不全	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
鎖骨下動脈狭窄	0				0				0				2	(0.2)	2	0.1
四肢壊死	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
大腿動脈閉塞	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
動脈閉塞性疾患	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
末梢冷感	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
糖尿病性大血管障害	0				0				0				1	(0.1)	1	0.1
糖尿病性微小血管症	0				0				1	(0.1)	1	0.1	0			
動脈不全	0				0				1	(0.1)	1	0.1	0			
末梢性虚血	0				0				1	(0.1)	1	0.1	0			
腕頭動脈硬化症	0				1	(0.1)	1	0.1	0				0			
血圧低下、非特異的血圧障害およびショック	21	(2.6)	23	1.5	21	(2.6)	22	1.5	21	(2.6)	29	1.9	17	(2.1)	19	1.2
低血圧	15	(1.8)	16	1.1	15	(1.8)	15	1.0	15	(1.8)	22	1.5	15	(1.8)	17	1.1
起立性低血圧	6	(0.7)	6	0.4	7	(0.9)	7	0.5	3	(0.4)	4	0.3	2	(0.2)	2	0.1
コントロール不良の血圧	0				0				1	(0.1)	1	0.1	0			
出血性ショック	0				0				1	(0.1)	1	0.1	0			
循環虚脱	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
動脈硬化、狭窄、血流障害および壊死	44	(2.7)	46	1.6	52	(3.2)	57	1.9	96	(2.9)	103	1.7
末梢動脈閉塞性疾患	12	(0.7)	12	0.4	16	(1.0)	16	0.5	28	(0.9)	28	0.5
大動脈硬化症	6	(0.4)	6	0.2	7	(0.4)	7	0.2	13	(0.4)	13	0.2
末梢静脈疾患	3	(0.2)	3	0.1	7	(0.4)	7	0.2	10	(0.3)	10	0.2
間欠性跛行	1	(0.1)	1	<0.1	6	(0.4)	6	0.2	7	(0.2)	7	0.1
大動脈狭窄	6	(0.4)	6	0.2	1	(0.1)	1	<0.1	7	(0.2)	7	0.1
動脈硬化症	5	(0.3)	5	0.2	2	(0.1)	2	0.1	7	(0.2)	7	0.1
糖尿病性血管障害	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
末梢動脈狭窄	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
虚血	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
血行不全	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
鎖骨下動脈狭窄	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
四肢壊死	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
大腿動脈閉塞	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
動脈閉塞性疾患	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
末梢冷感	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
糖尿病性大血管障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糖尿病性微小血管症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
動脈不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢性虚血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腕頭動脈硬化症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血圧低下、非特異的血圧障害およびショック	42	(2.6)	45	1.5	38	(2.3)	48	1.6	80	(2.4)	93	1.6
低血圧	30	(1.8)	31	1.1	30	(1.8)	39	1.3	60	(1.8)	70	1.2
起立性低血圧	13	(0.8)	13	0.4	5	(0.3)	6	0.2	18	(0.5)	19	0.3
コントロール不良の血圧	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性ショック	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
循環虚脱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
低潅流	0				0				1	(0.1)	1	0.1	0			
血管障害ＮＥＣ	4	(0.5)	4	0.3	7	(0.9)	9	0.6	6	(0.7)	6	0.4	16	(1.9)	18	1.2
末梢血管障害	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	7	(0.8)	8	0.5
ほてり	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
血管石灰化	0				0				0				3	(0.4)	3	0.2
大動脈拡張	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
大動脈障害	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
潮紅	0				1	(0.1)	3	0.2	0				1	(0.1)	1	0.1
血管拡張	0				0				0				1	(0.1)	1	0.1
血管障害	1	(0.1)	1	0.1	0				0				0			
血管破裂	0				0				0				1	(0.1)	1	0.1
紅痛症	1	(0.1)	1	0.1	0				0				0			
蒼白	0				1	(0.1)	1	0.1	0				0			
微小血管症	0				0				0				1	(0.1)	1	0.1
毛細血管脆弱	0				0				1	(0.1)	1	0.1	0			
塞栓症および血栓症	8	(1.0)	8	0.5	7	(0.9)	7	0.5	5	(0.6)	5	0.3	6	(0.7)	8	0.5
深部静脈血栓症	4	(0.5)	4	0.3	3	(0.4)	3	0.2	0				3	(0.4)	4	0.3
血栓性静脈炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
末梢動脈血栓症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
表在性血栓性静脈炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
静脈血栓症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
血栓症	0				0				1	(0.1)	1	0.1	0			
四肢静脈血栓症	0				0				0				1	(0.1)	1	0.1
大動脈血栓症	0				0				0				1	(0.1)	1	0.1
血管性出血障害	5	(0.6)	6	0.4	2	(0.2)	2	0.1	4	(0.5)	5	0.3	1	(0.1)	1	0.1
血腫	5	(0.6)	5	0.3	2	(0.2)	2	0.1	3	(0.4)	4	0.3	1	(0.1)	1	0.1
腹腔内血腫	1	(0.1)	1	0.1	0				0				0			
帽状腱膜下血腫	0				0				1	(0.1)	1	0.1	0			
瘤および動脈解離	2	(0.2)	3	0.2	6	(0.7)	6	0.4	1	(0.1)	1	0.1	4	(0.5)	4	0.3

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
低潅流	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管障害ＮＥＣ	11	(0.7)	13	0.4	22	(1.3)	24	0.8	33	(1.0)	37	0.6
末梢血管障害	5	(0.3)	5	0.2	9	(0.5)	10	0.3	14	(0.4)	15	0.3
ほてり	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
血管石灰化	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
大動脈拡張	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
大動脈障害	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
潮紅	1	(0.1)	3	0.1	1	(0.1)	1	<0.1	2	(0.1)	4	0.1
血管拡張	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管破裂	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
紅痛症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
蒼白	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
微小血管症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
毛細血管脆弱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
塞栓症および血栓症	15	(0.9)	15	0.5	11	(0.7)	13	0.4	26	(0.8)	28	0.5
深部静脈血栓症	7	(0.4)	7	0.2	3	(0.2)	4	0.1	10	(0.3)	11	0.2
血栓性静脈炎	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
末梢動脈血栓症	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
表在性血栓性静脈炎	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
静脈血栓症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
四肢静脈血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大動脈血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管性出血障害	7	(0.4)	8	0.3	5	(0.3)	6	0.2	12	(0.4)	14	0.2
血腫	7	(0.4)	7	0.2	4	(0.2)	5	0.2	11	(0.3)	12	0.2
腹腔内血腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
帽状腱膜下血腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
瘤および動脈解離	8	(0.5)	9	0.3	5	(0.3)	5	0.2	13	(0.4)	14	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
大動脈瘤	2	(0.2)	2	0.1	5	(0.6)	5	0.3	0				3	(0.4)	3	0.2
末梢動脈瘤	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
大動脈解離	0				0				0				1	(0.1)	1	0.1
動脈瘤	0				0				1	(0.1)	1	0.1	0			
静脈瘤	3	(0.4)	3	0.2	3	(0.4)	3	0.2	3	(0.4)	3	0.2	2	(0.2)	2	0.1
静脈瘤	2	(0.2)	2	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2	1	(0.1)	1	0.1
静脈瘤性潰瘍	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
血管の炎症	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
静脈炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
血管炎	0				0				1	(0.1)	1	0.1	0			
側頭動脈炎	1	(0.1)	1	0.1	0				0				0			
リンパ管障害	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
リンパ浮腫	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
リンパうっ滞	0				0				0				1	(0.1)	1	0.1
外科および内科処置	51	(6.2)	62	4.2	53	(6.5)	58	4.0	82	(10.0)	102	6.8	75	(9.1)	94	6.2
血管治療手技	40	(4.9)	46	3.1	30	(3.7)	32	2.2	61	(7.4)	69	4.6	61	(7.4)	73	4.8
冠動脈ステント挿入	11	(1.3)	13	0.9	9	(1.1)	10	0.7	15	(1.8)	17	1.1	17	(2.1)	19	1.2
冠動脈血行再建	14	(1.7)	15	1.0	7	(0.9)	7	0.5	15	(1.8)	17	1.1	9	(1.1)	10	0.7
冠動脈バイパス	8	(1.0)	8	0.5	4	(0.5)	4	0.3	13	(1.6)	13	0.9	8	(1.0)	8	0.5
末梢血行再建	2	(0.2)	2	0.1	2	(0.2)	2	0.1	6	(0.7)	6	0.4	11	(1.3)	12	0.8
冠動脈形成	1	(0.1)	1	0.1	1	(0.1)	1	0.1	4	(0.5)	5	0.3	5	(0.6)	5	0.3
経皮的冠インターベンション	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	4	0.3	4	(0.5)	5	0.3
末梢動脈形成	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
末梢動脈ステント挿入	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				3	(0.4)	3	0.2
頚動脈内膜剥離術	0				0				3	(0.4)	3	0.2	2	(0.2)	2	0.1
頚動脈血行再建	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
血管形成	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
大動脈瘤	7	(0.4)	7	0.2	3	(0.2)	3	0.1	10	(0.3)	10	0.2
末梢動脈瘤	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
大動脈解離	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
動脈瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
静脈瘤	6	(0.4)	6	0.2	5	(0.3)	5	0.2	11	(0.3)	11	0.2
静脈瘤	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
静脈瘤性潰瘍	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血管の炎症	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
静脈炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
血管炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
側頭動脈炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
リンパ管障害	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
リンパ浮腫	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
リンパうっ滞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外科および内科処置	104	(6.3)	120	4.1	157	(9.5)	196	6.5	261	(7.9)	316	5.3
血管治療手技	70	(4.3)	78	2.7	122	(7.4)	142	4.7	192	(5.8)	220	3.7
冠動脈ステント挿入	20	(1.2)	23	0.8	32	(1.9)	36	1.2	52	(1.6)	59	1.0
冠動脈血行再建	21	(1.3)	22	0.8	24	(1.5)	27	0.9	45	(1.4)	49	0.8
冠動脈バイパス	12	(0.7)	12	0.4	21	(1.3)	21	0.7	33	(1.0)	33	0.6
末梢血行再建	4	(0.2)	4	0.1	17	(1.0)	18	0.6	21	(0.6)	22	0.4
冠動脈形成	2	(0.1)	2	0.1	9	(0.5)	10	0.3	11	(0.3)	12	0.2
経皮的冠インターベンション	3	(0.2)	3	0.1	7	(0.4)	9	0.3	10	(0.3)	12	0.2
末梢動脈形成	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
末梢動脈ステント挿入	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
頚動脈内膜剥離術	0				5	(0.3)	5	0.2	5	(0.2)	5	0.1
頚動脈血行再建	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
血管形成	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
動静脈瘻手術	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
末梢動脈バイパス	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
頚動脈ステント挿入	0				1	(0.1)	1	0.1	0				0			
頚動脈形成	0				0				0				1	(0.1)	1	0.1
静脈切除術	0				0				0				1	(0.1)	1	0.1
末梢動脈内膜剥離術	0				1	(0.1)	1	0.1	0				0			
眼科治療手技	4	(0.5)	6	0.4	12	(1.5)	14	1.0	13	(1.6)	17	1.1	8	(1.0)	10	0.7
白内障手術	4	(0.5)	5	0.3	10	(1.2)	11	0.8	11	(1.3)	15	1.0	7	(0.8)	9	0.6
網膜レーザー凝固	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
眼レーザー手術	0				0				1	(0.1)	1	0.1	0			
眼内レンズ挿入	0				1	(0.1)	2	0.1	0				0			
眼瞼形成	0				0				0				1	(0.1)	1	0.1
翼状片手術	1	(0.1)	1	0.1	0				0				0			
頭頚部治療手技	4	(0.5)	4	0.3	5	(0.6)	5	0.3	6	(0.7)	9	0.6	6	(0.7)	7	0.5
抜歯	2	(0.2)	2	0.1	4	(0.5)	4	0.3	5	(0.6)	8	0.5	5	(0.6)	6	0.4
歯内療法	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
口腔手術	1	(0.1)	1	0.1	0				0				0			
鼻ポリープ切除	0				0				0				1	(0.1)	1	0.1
鼻手術	0				0				1	(0.1)	1	0.1	0			
治療的手技および補助療法ＮＥＣ	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
ステント装着	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
近距離照射療法	0				0				0				1	(0.1)	1	0.1
入院	1	(0.1)	1	0.1	0				0				0			
瘻修復	0				0				1	(0.1)	1	0.1	0			
消化管治療手技	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
開腹	1	(0.1)	1	0.1	0				0				0			
消化管拡張術	0				0				1	(0.1)	1	0.1	0			
腹部ヘルニア修復	0				1	(0.1)	1	0.1	0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
動静脈瘻手術	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
末梢動脈バイパス	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
頚動脈ステント挿入	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頚動脈形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
静脈切除術	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈内膜剥離術	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼科治療手技	16	(1.0)	20	0.7	21	(1.3)	27	0.9	37	(1.1)	47	0.8
白内障手術	14	(0.9)	16	0.5	18	(1.1)	24	0.8	32	(1.0)	40	0.7
網膜レーザー凝固	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
眼レーザー手術	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼内レンズ挿入	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
眼瞼形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
翼状片手術	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頭頚部治療手技	9	(0.5)	9	0.3	12	(0.7)	16	0.5	21	(0.6)	25	0.4
抜歯	6	(0.4)	6	0.2	10	(0.6)	14	0.5	16	(0.5)	20	0.3
歯内療法	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
口腔手術	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻ポリープ切除	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鼻手術	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
治療的手技および補助療法ＮＥＣ	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
ステント装着	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
近距離照射療法	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
入院	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
瘻修復	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
消化管治療手技	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
開腹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管拡張術	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腹部ヘルニア修復	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
臍ヘルニア修復	0				1	(0.1)	1	0.1	0				0			
骨および関節治療手技	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
肩回旋筋腱板修復	1	(0.1)	1	0.1	0				0				0			
内固定除去	0				0				1	(0.1)	1	0.1	0			
膝関節形成	0				0				1	(0.1)	1	0.1	0			
神経系、頭蓋骨および脊椎治療手技	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
外科的脊椎固定	0				0				0				1	(0.1)	1	0.1
手根管除圧	0				0				0				1	(0.1)	1	0.1
椎間板手術	0				0				1	(0.1)	1	0.1	0			
心臓治療手技	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
心臓ペースメーカー挿入	0				0				0				1	(0.1)	1	0.1
心房中隔欠損修復	0				0				1	(0.1)	1	0.1	0			
呼吸器系治療手技	1	(0.1)	1	0.1	0				0				0			
機械的換気	1	(0.1)	1	0.1	0				0				0			
男性生殖器系治療手技	0				1	(0.1)	1	0.1	0				0			
水瘤手術	0				1	(0.1)	1	0.1	0				0			
内分泌腺治療手技	0				1	(0.1)	1	0.1	0				0			
性転換ホルモン療法	0				1	(0.1)	1	0.1	0				0			
皮膚および皮下組織治療手技	0				1	(0.1)	1	0.1	0				0			
植皮	0				1	(0.1)	1	0.1	0				0			
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	58	(7.0)	71	4.8	76	(9.3)	98	6.8	62	(7.6)	71	4.7	62	(7.5)	72	4.7
良性神経系新生物	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
良性髄膜腫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
良性皮膚新生物	3	(0.4)	3	0.2	10	(1.2)	11	0.8	3	(0.4)	3	0.2	5	(0.6)	6	0.4

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
臍ヘルニア修復	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨および関節治療手技	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
肩回旋筋腱板修復	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
内固定除去	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膝関節形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経系、頭蓋骨および脊椎治療手技	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
外科的脊椎固定	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
手根管除圧	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎間板手術	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心臓治療手技	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
心臓ペースメーカー挿入	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心房中隔欠損修復	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼吸器系治療手技	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
機械的換気	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
男性生殖器系治療手技	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
水瘤手術	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
内分泌腺治療手技	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
性転換ホルモン療法	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮膚および皮下組織治療手技	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
植皮	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	134	(8.2)	169	5.8	124	(7.5)	143	4.7	258	(7.9)	312	5.2
良性神経系新生物	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
良性髄膜腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
良性皮膚新生物	13	(0.8)	14	0.5	8	(0.5)	9	0.3	21	(0.6)	23	0.4

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
皮膚乳頭腫	2	(0.2)	2	0.1	5	(0.6)	5	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1
脂漏性角化症	0				3	(0.4)	3	0.2	0				2	(0.2)	2	0.1
アクロコルドン	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
肛門性器疣贅	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
メラノサイト性母斑	1	(0.1)	1	0.1	0				0				0			
異形成母斑	0				1	(0.1)	1	0.1	0				0			
棘細胞腫	0				0				1	(0.1)	1	0.1	0			
悪性および詳細不明の皮膚新生物	9	(1.1)	11	0.7	13	(1.6)	22	1.5	5	(0.6)	5	0.3	8	(1.0)	10	0.7
基底細胞癌	6	(0.7)	6	0.4	10	(1.2)	18	1.2	4	(0.5)	4	0.3	7	(0.8)	8	0.5
皮膚有棘細胞癌	2	(0.2)	3	0.2	2	(0.2)	2	0.1	0				0			
ボーエン病	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
皮膚の新生物	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
悪性黒色腫	1	(0.1)	1	0.1	0				0				0			
消化器の良性新生物	4	(0.5)	4	0.3	11	(1.3)	11	0.8	10	(1.2)	11	0.7	5	(0.6)	6	0.4
大腸腺腫	3	(0.4)	3	0.2	10	(1.2)	10	0.7	9	(1.1)	10	0.7	4	(0.5)	5	0.3
口腔線維腫	0				0				1	(0.1)	1	0.1	0			
十二指腸の良性新生物	1	(0.1)	1	0.1	0				0				0			
直腸腺腫	0				1	(0.1)	1	0.1	0				0			
膵管内乳頭粘液性腫瘍	0				0				0				1	(0.1)	1	0.1
悪性および詳細不明の内分泌新生物	6	(0.7)	8	0.5	7	(0.9)	7	0.5	9	(1.1)	9	0.6	7	(0.8)	7	0.5
甲状腺新生物	5	(0.6)	6	0.4	5	(0.6)	5	0.3	7	(0.9)	7	0.5	6	(0.7)	6	0.4
成長ホルモン産生性下垂体腫瘍	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
カルチノイド腫瘍	0				1	(0.1)	1	0.1	0				0			
褐色細胞腫	1	(0.1)	1	0.1	0				0				0			
乳頭様甲状腺癌	0				0				1	(0.1)	1	0.1	0			
副腎新生物	0				0				1	(0.1)	1	0.1	0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
皮膚乳頭腫	7	(0.4)	7	0.2	3	(0.2)	3	0.1	10	(0.3)	10	0.2
脂漏性角化症	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
アクロコルドン	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
肛門性器疣贅	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
メラノサイト性母斑	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
異形成母斑	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
棘細胞腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
悪性および詳細不明の皮膚新生物	22	(1.3)	33	1.1	13	(0.8)	15	0.5	35	(1.1)	48	0.8
基底細胞癌	16	(1.0)	24	0.8	11	(0.7)	12	0.4	27	(0.8)	36	0.6
皮膚有棘細胞癌	4	(0.2)	5	0.2	0				4	(0.1)	5	0.1
ボーエン病	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
皮膚の新生物	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
悪性黒色腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化器の良性新生物	15	(0.9)	15	0.5	15	(0.9)	17	0.6	30	(0.9)	32	0.5
大腸腺腫	13	(0.8)	13	0.4	13	(0.8)	15	0.5	26	(0.8)	28	0.5
口腔線維腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
十二指腸の良性新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
直腸腺腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵管内乳頭粘液性腫瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
悪性および詳細不明の内分泌新生物	13	(0.8)	15	0.5	16	(1.0)	16	0.5	29	(0.9)	31	0.5
甲状腺新生物	10	(0.6)	11	0.4	13	(0.8)	13	0.4	23	(0.7)	24	0.4
成長ホルモン産生性下垂体腫瘍	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
カルチノイド腫瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
褐色細胞腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳頭様甲状腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副腎新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
傍神経節新生物	1	(0.1)	1	0.1	0				0				0			
良性内分泌新生物	6	(0.7)	7	0.5	5	(0.6)	5	0.3	6	(0.7)	6	0.4	5	(0.6)	5	0.3
甲状腺の良性新生物	2	(0.2)	2	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3	3	(0.4)	3	0.2
良性副甲状腺腫瘍	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
副腎の良性新生物	2	(0.2)	2	0.1	0				0				0			
甲状腺腺腫	0				0				1	(0.1)	1	0.1	0			
副腎腺腫	1	(0.1)	1	0.1	0				0				0			
悪性および詳細不明の消化管新生物	7	(0.9)	7	0.5	3	(0.4)	3	0.2	6	(0.7)	6	0.4	6	(0.7)	6	0.4
結腸腺癌	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
胃腺癌	2	(0.2)	2	0.1	0				0				0			
結腸癌	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
直腸癌	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
胃癌	1	(0.1)	1	0.1	0				0				0			
遠隔転移を伴う胃癌	1	(0.1)	1	0.1	0				0				0			
遠隔転移を伴う結腸癌	0				0				0				1	(0.1)	1	0.1
遠隔転移を伴う膵癌	0				0				1	(0.1)	1	0.1	0			
結腸新生物	0				0				1	(0.1)	1	0.1	0			
結腸直腸癌	0				0				1	(0.1)	1	0.1	0			
口唇の悪性新生物、病期不明	1	(0.1)	1	0.1	0				0				0			
十二指腸新生物	0				0				0				1	(0.1)	1	0.1
消化管粘膜下腫瘍	1	(0.1)	1	0.1	0				0				0			
消化器新生物	0				0				0				1	(0.1)	1	0.1
虫垂新生物	0				1	(0.1)	1	0.1	0				0			
膵癌	0				0				0				1	(0.1)	1	0.1
膵腺癌	0				0				0				1	(0.1)	1	0.1
悪性および詳細不明の呼吸器系および縦隔新生物	2	(0.2)	2	0.1	6	(0.7)	6	0.4	5	(0.6)	5	0.3	4	(0.5)	4	0.3

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
傍神経節新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性内分泌新生物	11	(0.7)	12	0.4	11	(0.7)	11	0.4	22	(0.7)	23	0.4
甲状腺の良性新生物	5	(0.3)	5	0.2	7	(0.4)	7	0.2	12	(0.4)	12	0.2
良性副甲状腺腫瘍	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
副腎の良性新生物	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
甲状腺腺腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副腎腺腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
悪性および詳細不明の消化管新生物	10	(0.6)	10	0.3	12	(0.7)	12	0.4	22	(0.7)	22	0.4
結腸腺癌	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
胃腺癌	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
結腸癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
直腸癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胃癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う胃癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う結腸癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
遠隔転移を伴う膵癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結腸新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結腸直腸癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口唇の悪性新生物、病期不明	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
十二指腸新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
消化管粘膜下腫瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化器新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
虫垂新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膵腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
悪性および詳細不明の呼吸器系および縦隔新生物	8	(0.5)	8	0.3	9	(0.5)	9	0.3	17	(0.5)	17	0.3

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
小細胞肺癌	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
気管支癌	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
喉頭扁平上皮癌	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
肺の悪性新生物	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
肺腺癌	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
肺癌第４期、細胞タイプ不明	0				1	(0.1)	1	0.1	0				0			
肺新生物	0				1	(0.1)	1	0.1	0				0			
肺腺癌第４期	0				1	(0.1)	1	0.1	0				0			
肺扁平上皮癌	0				0				0				1	(0.1)	1	0.1
非小細胞肺癌	0				0				0				1	(0.1)	1	0.1
悪性および詳細不明の男性生殖器系新生物	5	(0.6)	5	0.3	3	(0.4)	3	0.2	4	(0.5)	4	0.3	5	(0.6)	5	0.3
前立腺癌	4	(0.5)	4	0.3	2	(0.2)	2	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1
遠隔転移を伴う前立腺癌	0				1	(0.1)	1	0.1	0				0			
再発前立腺癌	0				0				0				1	(0.1)	1	0.1
前立腺癌第１期	0				0				0				1	(0.1)	1	0.1
前立腺癌第３期	0				0				0				1	(0.1)	1	0.1
前立腺新生物	1	(0.1)	1	0.1	0				0				0			
悪性および詳細不明の腎尿路系新生物	2	(0.2)	2	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2	4	(0.5)	5	0.3
膀胱移行上皮癌	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
膀胱新生物	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
移行上皮癌	1	(0.1)	1	0.1	0				0				0			
遠隔転移を伴う腎癌	1	(0.1)	1	0.1	0				0				0			
再発膀胱移行上皮癌	0				0				0				1	(0.1)	1	0.1
腎癌第１期	0				0				0				1	(0.1)	1	0.1
腎細胞癌	0				1	(0.1)	1	0.1	0				0			
腎明細胞癌	0				0				0				1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
小細胞肺癌	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
気管支癌	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
喉頭扁平上皮癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肺の悪性新生物	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肺腺癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肺癌第４期、細胞タイプ不明	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺腺癌第４期	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺扁平上皮癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
非小細胞肺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
悪性および詳細不明の男性生殖器系新生物	8	(0.5)	8	0.3	9	(0.5)	9	0.3	17	(0.5)	17	0.3
前立腺癌	6	(0.4)	6	0.2	6	(0.4)	6	0.2	12	(0.4)	12	0.2
遠隔転移を伴う前立腺癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
再発前立腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
前立腺癌第１期	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
前立腺癌第３期	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
前立腺新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
悪性および詳細不明の腎尿路系新生物	6	(0.4)	6	0.2	7	(0.4)	8	0.3	13	(0.4)	14	0.2
膀胱移行上皮癌	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
膀胱新生物	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
移行上皮癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う腎癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
再発膀胱移行上皮癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎癌第１期	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎細胞癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎明細胞癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
尿管癌	0				1	(0.1)	1	0.1	0				0			
膀胱移行上皮癌第２期	0				1	(0.1)	1	0.1	0				0			
良性軟部組織新生物	4	(0.5)	4	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2
脂肪腫	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
血管筋脂肪腫	2	(0.2)	2	0.1	0				0				0			
グロームス腫瘍	0				1	(0.1)	1	0.1	0				0			
平滑筋腫	0				0				0				1	(0.1)	1	0.1
その他および部位不明の良性新生物	0				5	(0.6)	5	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1
真珠腫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
血管の良性新生物	0				1	(0.1)	1	0.1	0				0			
血管腫	0				1	(0.1)	1	0.1	0				0			
線維腫	0				1	(0.1)	1	0.1	0				0			
良性新生物	0				0				0				1	(0.1)	1	0.1
良性腺腫	0				1	(0.1)	1	0.1	0				0			
良性女性生殖器系新生物	3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
子宮平滑筋腫	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
卵巣良性腫瘍	0				0				0				1	(0.1)	1	0.1
卵巣胚細胞良性奇形腫	1	(0.1)	1	0.1	0				0				0			
悪性および詳細不明の肝胆道系新生物	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	3	0.2	0			
肝新生物	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
肝癌	1	(0.1)	1	0.1	0				0				0			
肝内胆管癌	0				0				1	(0.1)	2	0.1	0			
胆嚢腺癌	0				0				1	(0.1)	1	0.1	0			
悪性および詳細不明の乳房新生物（乳頭を含む）	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
浸潤性乳管癌	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
乳癌	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
尿管癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱移行上皮癌第２期	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性軟部組織新生物	5	(0.3)	5	0.2	5	(0.3)	5	0.2	10	(0.3)	10	0.2
脂肪腫	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
血管筋脂肪腫	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
グロームス腫瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
平滑筋腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
その他および部位不明の良性新生物	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
真珠腫	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
血管の良性新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
線維腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性腺腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性女性生殖器系新生物	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
子宮平滑筋腫	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
卵巣良性腫瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
卵巣胚細胞良性奇形腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
悪性および詳細不明の肝胆道系新生物	3	(0.2)	3	0.1	2	(0.1)	3	0.1	5	(0.2)	6	0.1
肝新生物	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
肝癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝内胆管癌	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
胆嚢腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
悪性および詳細不明の乳房新生物（乳頭を含む）	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
浸潤性乳管癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
乳癌	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
乳癌第３期	0				0				0				1	(0.1)	1	0.1
乳房の上皮内癌	0				1	(0.1)	1	0.1	0				0			
眼球新生物	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
眼の母斑	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
眼瞼乳頭腫	0				0				1	(0.1)	1	0.1	0			
脈絡膜黒色腫	1	(0.1)	1	0.1	0				0				0			
涙管の良性新生物	1	(0.1)	1	0.1	0				0				0			
非ホジキンＢ細胞性リンパ腫	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
Ｂ細胞性リンパ腫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
Ｂ細胞性小リンパ球性リンパ腫	0				0				1	(0.1)	1	0.1	0			
節外周辺帯Ｂ細胞リンパ腫（ＭＡＬＴ型）	1	(0.1)	1	0.1	0				0				0			
悪性および詳細不明の女性生殖器系新生物	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
外陰部癌第０期	0				1	(0.1)	1	0.1	0				0			
子宮内膜腺癌	0				0				1	(0.1)	1	0.1	0			
子宮内膜肉腫	0				0				0				1	(0.1)	1	0.1
卵巣上皮癌	1	(0.1)	1	0.1	0				0				0			
卵巣莢膜細胞腫	1	(0.1)	1	0.1	0				0				0			
白血病	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
慢性リンパ性白血病	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
急性リンパ性白血病	0				0				0				1	(0.1)	1	0.1
急性骨髄性白血病	0				0				1	(0.1)	1	0.1	0			
転移	2	(0.2)	3	0.2	1	(0.1)	1	0.1	0				0			
リンパ節転移	1	(0.1)	1	0.1	0				0				0			
肝転移	1	(0.1)	1	0.1	0				0				0			
中枢神経系転移	0				1	(0.1)	1	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
乳癌第３期	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳房の上皮内癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼球新生物	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
眼の母斑	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
眼瞼乳頭腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脈絡膜黒色腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
涙管の良性新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
非ホジキンＢ細胞性リンパ腫	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
Ｂ細胞性リンパ腫	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
Ｂ細胞性小リンパ球性リンパ腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
節外周辺帯Ｂ細胞リンパ腫（ＭＡＬＴ型）	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
悪性および詳細不明の女性生殖器系新生物	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
外陰部癌第０期	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
子宮内膜腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮内膜肉腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
卵巣上皮癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
卵巣莢膜細胞腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
白血病	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
慢性リンパ性白血病	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
急性リンパ性白血病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性骨髄性白血病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
転移	3	(0.2)	4	0.1	0				3	(0.1)	4	0.1
リンパ節転移	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝転移	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
中枢神経系転移	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
肺転移	1	(0.1)	1	0.1	0				0				0			
形質細胞新生物	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
単クローン性免疫グロブリン血症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
形質細胞性骨髄腫	0				0				0				1	(0.1)	1	0.1
良性肝胆道系新生物	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
肝臓血管腫	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
肝腺腫	0				0				1	(0.1)	1	0.1	0			
良性男性生殖器新生物	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
前立腺腺腫	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
悪性および詳細不明のその他および部位不明新生物	0				2	(0.2)	2	0.1	0				0			
扁平上皮癌	0				2	(0.2)	2	0.1	0				0			
造血系新生物（白血病およびリンパ腫を除く）	2	(0.2)	2	0.1	0				0				0			
リンパ節の良性新生物	1	(0.1)	1	0.1	0				0				0			
本態性血小板血症	1	(0.1)	1	0.1	0				0				0			
良性骨格系新生物	0				0				2	(0.2)	2	0.1	0			
骨血管腫	0				0				2	(0.2)	2	0.1	0			
悪性および詳細不明の骨格系新生物	0				1	(0.1)	1	0.1	0				0			
遠隔転移を伴う骨癌	0				1	(0.1)	1	0.1	0				0			
悪性および詳細不明の神経系新生物ＮＥＣ	0				0				0				1	(0.1)	1	0.1
退形成星細胞腫	0				0				0				1	(0.1)	1	0.1
良性腎尿路系新生物	0				1	(0.1)	1	0.1	0				0			
膀胱乳頭腫	0				1	(0.1)	1	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肺転移	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
形質細胞新生物	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
単クローン性免疫グロブリン血症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
形質細胞性骨髄腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性肝胆道系新生物	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
肝臓血管腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肝腺腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性男性生殖器新生物	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
前立腺腺腫	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
悪性および詳細不明のその他および部位不明新生物	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
扁平上皮癌	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
造血系新生物（白血病およびリンパ腫を除く）	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
リンパ節の良性新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
本態性血小板血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性骨格系新生物	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
骨血管腫	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
悪性および詳細不明の骨格系新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う骨癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
悪性および詳細不明の神経系新生物ＮＥＣ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
退形成星細胞腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性腎尿路系新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱乳頭腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
良性乳房新生物（乳頭を含む）	0				1	(0.1)	1	0.1	0				0			
乳腺線維腺腫	0				1	(0.1)	1	0.1	0				0			
血液およびリンパ系障害	59	(7.2)	68	4.6	47	(5.7)	52	3.6	57	(7.0)	66	4.4	68	(8.2)	83	5.4
非溶血性貧血と骨髄抑制	46	(5.6)	49	3.3	39	(4.8)	41	2.8	41	(5.0)	43	2.9	51	(6.2)	57	3.7
貧血	34	(4.1)	37	2.5	29	(3.5)	30	2.1	38	(4.6)	40	2.7	44	(5.3)	49	3.2
鉄欠乏性貧血	5	(0.6)	5	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1
出血性貧血	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0				2	(0.2)	2	0.1
正色素性正球性貧血	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
小球性貧血	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
腎性貧血	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
悪性貧血	0				0				0				1	(0.1)	1	0.1
巨赤芽球性貧血	1	(0.1)	1	0.1	0				0				0			
大球性貧血	0				0				1	(0.1)	1	0.1	0			
汎血球減少症	1	(0.1)	1	0.1	0				0				0			
慢性疾患の貧血	0				1	(0.1)	1	0.1	0				0			
白血球障害	6	(0.7)	6	0.4	4	(0.5)	4	0.3	8	(1.0)	8	0.5	7	(0.8)	7	0.5
白血球増加症	5	(0.6)	5	0.3	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
白血球減少症	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
好酸球増加症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
リンパ球減少症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
好中球増加症	0				0				0				1	(0.1)	1	0.1
単クローン性Ｂ細胞リンパ球増加症	1	(0.1)	1	0.1	0				0				0			
単球増加症	0				0				0				1	(0.1)	1	0.1
血小板障害	5	(0.6)	5	0.3	2	(0.2)	2	0.1	7	(0.9)	7	0.5	7	(0.8)	8	0.5
血小板減少症	3	(0.4)	3	0.2	0				6	(0.7)	6	0.4	5	(0.6)	5	0.3
血小板増加症	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				1	(0.1)	2	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
良性乳房新生物（乳頭を含む）	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳腺線維腺腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血液およびリンパ系障害	106	(6.5)	120	4.1	125	(7.6)	149	4.9	231	(7.0)	269	4.5
非溶血性貧血と骨髄抑制	85	(5.2)	90	3.1	92	(5.6)	100	3.3	177	(5.4)	190	3.2
貧血	63	(3.8)	67	2.3	82	(5.0)	89	2.9	145	(4.4)	156	2.6
鉄欠乏性貧血	9	(0.5)	9	0.3	4	(0.2)	4	0.1	13	(0.4)	13	0.2
出血性貧血	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
正色素性正球性貧血	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
小球性貧血	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
腎性貧血	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
悪性貧血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
巨赤芽球性貧血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大球性貧血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
汎血球減少症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
慢性疾患の貧血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
白血球障害	10	(0.6)	10	0.3	15	(0.9)	15	0.5	25	(0.8)	25	0.4
白血球増加症	6	(0.4)	6	0.2	5	(0.3)	5	0.2	11	(0.3)	11	0.2
白血球減少症	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
好酸球増加症	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
リンパ球減少症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
好中球増加症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
単クローン性Ｂ細胞リンパ球増加症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
単球増加症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血小板障害	7	(0.4)	7	0.2	14	(0.9)	15	0.5	21	(0.6)	22	0.4
血小板減少症	3	(0.2)	3	0.1	11	(0.7)	11	0.4	14	(0.4)	14	0.2
血小板増加症	4	(0.2)	4	0.1	1	(0.1)	2	0.1	5	(0.2)	6	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
ヘパリン起因性血小板減少症	0				0				0				1	(0.1)	1	0.1
免疫性血小板減少性紫斑病	0				0				1	(0.1)	1	0.1	0			
脾臓、リンパ節および細網内皮系障害	4	(0.5)	6	0.4	3	(0.4)	3	0.2	5	(0.6)	5	0.3	6	(0.7)	8	0.5
リンパ節症	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	2	(0.2)	3	0.2
縦隔リンパ節腫脹	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
脾腫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
脾臓石灰化	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
リンパ節炎	0				0				0				1	(0.1)	1	0.1
肺門リンパ節腫脹	1	(0.1)	1	0.1	0				0				0			
脾静脈血栓症	0				0				0				1	(0.1)	1	0.1
脾臓障害	0				0				1	(0.1)	1	0.1	0			
脾肉芽腫	1	(0.1)	1	0.1	0				0				0			
赤血球障害	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
赤血球増加症	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
小赤血球症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
大赤血球症	0				0				0				1	(0.1)	1	0.1
凝固障害および出血性素因（血小板減少性を除く）	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
凝固因子異常	1	(0.1)	1	0.1	0				0				0			
播種性血管内凝固	0				0				0				1	(0.1)	1	0.1
精神障害	54	(6.6)	69	4.6	60	(7.3)	67	4.6	49	(6.0)	52	3.4	46	(5.6)	59	3.9
抑うつ性気分障害	27	(3.3)	29	1.9	21	(2.6)	21	1.5	17	(2.1)	17	1.1	16	(1.9)	18	1.2
うつ病	23	(2.8)	24	1.6	19	(2.3)	19	1.3	15	(1.8)	15	1.0	15	(1.8)	17	1.1
大うつ病	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ヘパリン起因性血小板減少症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
免疫性血小板減少性紫斑病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脾臓、リンパ節および細網内皮系障害	7	(0.4)	9	0.3	11	(0.7)	13	0.4	18	(0.5)	22	0.4
リンパ節症	2	(0.1)	2	0.1	4	(0.2)	5	0.2	6	(0.2)	7	0.1
縦隔リンパ節腫脹	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
脾腫	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
脾臓石灰化	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
リンパ節炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺門リンパ節腫脹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脾静脈血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脾臓障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脾肉芽腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
赤血球障害	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
赤血球増加症	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
小赤血球症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
大赤血球症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
凝固障害および出血性素因（血小板減少性を除く）	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
凝固因子異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
播種性血管内凝固	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精神障害	114	(6.9)	136	4.6	95	(5.8)	111	3.7	209	(6.4)	247	4.1
抑うつ性気分障害	48	(2.9)	50	1.7	33	(2.0)	35	1.2	81	(2.5)	85	1.4
うつ病	42	(2.6)	43	1.5	30	(1.8)	32	1.1	72	(2.2)	75	1.3
大うつ病	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
抑うつ気分	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
抑うつ症状	1	(0.1)	2	0.1	1	(0.1)	1	0.1	0				0			
気分変調性障害	1	(0.1)	1	0.1	0				0				0			
絶望感	0				0				1	(0.1)	1	0.1	0			
睡眠障害	16	(1.9)	18	1.2	23	(2.8)	25	1.7	17	(2.1)	17	1.1	10	(1.2)	10	0.7
不眠症	15	(1.8)	17	1.1	22	(2.7)	22	1.5	17	(2.1)	17	1.1	6	(0.7)	6	0.4
睡眠障害	0				1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
異常な夢	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
睡眠時驚愕	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
不安障害および不安症状	17	(2.1)	17	1.1	12	(1.5)	12	0.8	10	(1.2)	10	0.7	17	(2.1)	19	1.2
不安	13	(1.6)	13	0.9	8	(1.0)	8	0.6	8	(1.0)	8	0.5	13	(1.6)	13	0.9
ストレス	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1
激越	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
パニック発作	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
不安障害	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
心的外傷後ストレス障害	0				0				1	(0.1)	1	0.1	0			
神経過敏	0				1	(0.1)	1	0.1	0				0			
神経症	0				1	(0.1)	1	0.1	0				0			
譫妄（錯乱を含む）	1	(0.1)	2	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2	3	(0.4)	3	0.2
錯乱状態	1	(0.1)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
譫妄	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
気分障害ＮＥＣ	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
気分変化	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
易刺激性	1	(0.1)	1	0.1	0				0				0			
感情的苦悩	0				0				0				1	(0.1)	1	0.1
気力低下	1	(0.1)	1	0.1	0				0				0			
怒り	0				0				0				1	(0.1)	1	0.1
無感情	0				1	(0.1)	1	0.1	0				0			
精神医学的障害ＮＥＣ	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	4	(0.5)	4	0.3

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
抑うつ気分	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
抑うつ症状	2	(0.1)	3	0.1	0				2	(0.1)	3	0.1
気分変調性障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
絶望感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
睡眠障害	39	(2.4)	43	1.5	27	(1.6)	27	0.9	66	(2.0)	70	1.2
不眠症	37	(2.3)	39	1.3	23	(1.4)	23	0.8	60	(1.8)	62	1.0
睡眠障害	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
異常な夢	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
睡眠時驚愕	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
不安障害および不安症状	29	(1.8)	29	1.0	27	(1.6)	29	1.0	56	(1.7)	58	1.0
不安	21	(1.3)	21	0.7	21	(1.3)	21	0.7	42	(1.3)	42	0.7
ストレス	3	(0.2)	3	0.1	2	(0.1)	3	0.1	5	(0.2)	6	0.1
激越	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
パニック発作	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
不安障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心的外傷後ストレス障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経過敏	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
譫妄（錯乱を含む）	4	(0.2)	5	0.2	6	(0.4)	6	0.2	10	(0.3)	11	0.2
錯乱状態	2	(0.1)	3	0.1	4	(0.2)	4	0.1	6	(0.2)	7	0.1
譫妄	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
気分障害ＮＥＣ	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
気分変化	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
易刺激性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感情的苦悩	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
気力低下	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
怒り	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
無感情	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
精神医学的障害ＮＥＣ	1	(0.1)	1	<0.1	6	(0.4)	6	0.2	7	(0.2)	7	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
精神状態変化	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	4	(0.5)	4	0.3
身体の活動性の変化	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
落ち着きのなさ	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
性障害および性同一性障害	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
リビドー減退	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
摂食障害	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
食物嫌悪	0				0				1	(0.1)	1	0.1	0			
神経性過食症	0				0				0				1	(0.1)	1	0.1
思考障害および認知障害	0				1	(0.1)	1	0.1	0				0			
幻視	0				1	(0.1)	1	0.1	0				0			
身体表現性障害および虚偽性障害	0				0				0				1	(0.1)	1	0.1
身体表現性障害	0				0				0				1	(0.1)	1	0.1
統合失調症およびその他の精神障害	0				1	(0.1)	1	0.1	0				0			
統合失調感情障害	0				1	(0.1)	1	0.1	0				0			
肝胆道系障害	45	(5.5)	54	3.6	43	(5.3)	57	3.9	52	(6.3)	71	4.7	37	(4.5)	53	3.5
肝および肝胆道系障害	26	(3.2)	27	1.8	27	(3.3)	29	2.0	29	(3.5)	31	2.1	24	(2.9)	27	1.8
脂肪肝	15	(1.8)	15	1.0	19	(2.3)	20	1.4	21	(2.6)	21	1.4	19	(2.3)	19	1.2
肝嚢胞	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
肝腫大	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
肝硬変	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
肝障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
肝脾腫大	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
虚血性肝炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
胆汁うっ滞	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
黄疸	1	(0.1)	1	0.1	0				0				0			
肝機能異常	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
精神状態変化	1	(0.1)	1	<0.1	6	(0.4)	6	0.2	7	(0.2)	7	0.1
身体の活動性の変化	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
落ち着きのなさ	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
性障害および性同一性障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
リビドー減退	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
摂食障害	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
食物嫌悪	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経性過食症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
思考障害および認知障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
幻視	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
身体表現性障害および虚偽性障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
身体表現性障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
統合失調症およびその他の精神障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
統合失調感情障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝胆道系障害	88	(5.4)	111	3.8	89	(5.4)	124	4.1	177	(5.4)	235	3.9
肝および肝胆道系障害	53	(3.2)	56	1.9	53	(3.2)	58	1.9	106	(3.2)	114	1.9
脂肪肝	34	(2.1)	35	1.2	40	(2.4)	40	1.3	74	(2.3)	75	1.3
肝嚢胞	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
肝腫大	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
肝硬変	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
肝障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
肝脾腫大	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
虚血性肝炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胆汁うっ滞	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
黄疸	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝機能異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
肝腫瘤	0				0				1	(0.1)	1	0.1	0			
肝石灰化	0				0				1	(0.1)	1	0.1	0			
肝臓うっ血	0				0				0				1	(0.1)	1	0.1
肝臓痛	0				0				0				1	(0.1)	1	0.1
高ビリルビン血症	0				0				1	(0.1)	1	0.1	0			
自己免疫性肝炎	1	(0.1)	1	0.1	0				0				0			
心臓性肝硬変	1	(0.1)	1	0.1	0				0				0			
胆汁うっ滞性黄疸	0				1	(0.1)	1	0.1	0				0			
胆汁性肝硬変	0				1	(0.1)	1	0.1	0				0			
薬物性肝障害	0				0				0				1	(0.1)	1	0.1
胆嚢障害	23	(2.8)	25	1.7	20	(2.4)	21	1.5	31	(3.8)	36	2.4	18	(2.2)	21	1.4
胆石症	19	(2.3)	19	1.3	17	(2.1)	17	1.2	17	(2.1)	17	1.1	10	(1.2)	10	0.7
急性胆嚢炎	4	(0.5)	4	0.3	0				6	(0.7)	6	0.4	2	(0.2)	2	0.1
慢性胆嚢炎	0				1	(0.1)	1	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3
胆嚢ポリープ	0				1	(0.1)	1	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2
胆嚢炎	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
水腫性胆嚢炎	1	(0.1)	1	0.1	0				0				0			
胆嚢コレステリン沈着症	0				0				1	(0.1)	1	0.1	0			
胆嚢壊死	0				0				1	(0.1)	1	0.1	0			
胆嚢痛	0				1	(0.1)	1	0.1	0				0			
閉塞性胆石症	1	(0.1)	1	0.1	0				0				0			
胆管系障害	2	(0.2)	2	0.1	7	(0.9)	7	0.5	4	(0.5)	4	0.3	5	(0.6)	5	0.3
胆道仙痛	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1
胆管結石	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
胆管炎	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
胆道障害	0				2	(0.2)	2	0.1	0				0			
オッディ括約筋機能不全	0				0				0				1	(0.1)	1	0.1
胆管拡張	0				0				0				1	(0.1)	1	0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肝腫瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝石灰化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝臓うっ血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝臓痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高ビリルビン血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
自己免疫性肝炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心臓性肝硬変	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆汁うっ滞性黄疸	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆汁性肝硬変	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
薬物性肝障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆嚢障害	43	(2.6)	46	1.6	49	(3.0)	57	1.9	92	(2.8)	103	1.7
胆石症	36	(2.2)	36	1.2	27	(1.6)	27	0.9	63	(1.9)	63	1.1
急性胆嚢炎	4	(0.2)	4	0.1	8	(0.5)	8	0.3	12	(0.4)	12	0.2
慢性胆嚢炎	1	(0.1)	1	<0.1	8	(0.5)	8	0.3	9	(0.3)	9	0.2
胆嚢ポリープ	1	(0.1)	1	<0.1	7	(0.4)	7	0.2	8	(0.2)	8	0.1
胆嚢炎	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
水腫性胆嚢炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆嚢コレステリン沈着症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆嚢壊死	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆嚢痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
閉塞性胆石症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆管系障害	9	(0.5)	9	0.3	9	(0.5)	9	0.3	18	(0.5)	18	0.3
胆道仙痛	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
胆管結石	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
胆管炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胆道障害	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
オッディ括約筋機能不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆管拡張	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
生殖系および乳房障害	36	(4.4)	36	2.4	32	(3.9)	36	2.5	26	(3.2)	34	2.3	35	(4.2)	38	2.5
前立腺障害（感染および炎症を除く）	20	(2.4)	20	1.3	14	(1.7)	14	1.0	8	(1.0)	8	0.5	17	(2.1)	18	1.2
良性前立腺肥大症	16	(1.9)	16	1.1	9	(1.1)	9	0.6	3	(0.4)	3	0.2	12	(1.5)	12	0.8
前立腺腫大	4	(0.5)	4	0.3	5	(0.6)	5	0.3	4	(0.5)	4	0.3	3	(0.4)	3	0.2
前立腺石灰化	0				0				0				2	(0.2)	2	0.1
前立腺障害	0				0				0				1	(0.1)	1	0.1
前立腺閉塞	0				0				1	(0.1)	1	0.1	0			
子宮、骨盤および広間膜障害	2	(0.2)	2	0.1	5	(0.6)	5	0.3	6	(0.7)	8	0.5	2	(0.2)	2	0.1
子宮内膜増殖症	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
膀胱瘤	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
膣脱	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
子宮ポリープ	0				0				2	(0.2)	2	0.1	0			
子宮障害	1	(0.1)	1	0.1	0				0				0			
子宮脱	0				0				1	(0.1)	1	0.1	0			
子宮付属器嚢胞	0				0				0				1	(0.1)	1	0.1
子宮膣脱	0				1	(0.1)	1	0.1	0				0			
性器脱	0				0				1	(0.1)	1	0.1	0			
膣瘤	0				0				1	(0.1)	1	0.1	0			
乳房異常	5	(0.6)	5	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1	5	(0.6)	5	0.3
女性化乳房	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2
乳房痛	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				0			
乳房圧痛	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
乳汁漏出症	0				0				0				1	(0.1)	1	0.1
乳房過形成	0				1	(0.1)	1	0.1	0				0			
乳房腫瘤	0				1	(0.1)	1	0.1	0				0			
乳房石灰化	0				0				0				1	(0.1)	1	0.1
乳房線維化	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
生殖系および乳房障害	68	(4.1)	72	2.5	61	(3.7)	72	2.4	129	(3.9)	144	2.4
前立腺障害（感染および炎症を除く）	34	(2.1)	34	1.2	25	(1.5)	26	0.9	59	(1.8)	60	1.0
良性前立腺肥大症	25	(1.5)	25	0.9	15	(0.9)	15	0.5	40	(1.2)	40	0.7
前立腺腫大	9	(0.5)	9	0.3	7	(0.4)	7	0.2	16	(0.5)	16	0.3
前立腺石灰化	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
前立腺障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
前立腺閉塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮、骨盤および広間膜障害	7	(0.4)	7	0.2	8	(0.5)	10	0.3	15	(0.5)	17	0.3
子宮内膜増殖症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
膀胱瘤	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
膣脱	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
子宮ポリープ	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
子宮障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
子宮脱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮付属器嚢胞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮膣脱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
性器脱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膣瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳房異常	9	(0.5)	9	0.3	7	(0.4)	7	0.2	16	(0.5)	16	0.3
女性化乳房	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
乳房痛	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
乳房圧痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
乳汁漏出症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳房過形成	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳房腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳房石灰化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳房線維化	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
性機能および生殖能障害	2	(0.2)	2	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1	4	(0.5)	4	0.3
勃起不全	2	(0.2)	2	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1	3	(0.4)	3	0.2
血精液症	0				0				0				1	(0.1)	1	0.1
性機能不全	0				0				1	(0.1)	1	0.1	0			
男性生殖器系感染および炎症	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	5	0.3	1	(0.1)	2	0.1
前立腺炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1
亀頭包皮炎	0				1	(0.1)	1	0.1	2	(0.2)	4	0.3	0			
外陰膣障害（感染および炎症を除く）	2	(0.2)	2	0.1	0				3	(0.4)	4	0.3	2	(0.2)	2	0.1
外陰膣痛	0				0				2	(0.2)	2	0.1	0			
外陰部障害	1	(0.1)	1	0.1	0				0				0			
外陰膣そう痒症	0				0				0				1	(0.1)	1	0.1
外陰膣乾燥	1	(0.1)	1	0.1	0				0				0			
外陰膣腫脹	0				0				1	(0.1)	1	0.1	0			
膣出血	0				0				0				1	(0.1)	1	0.1
膣分泌物	0				0				1	(0.1)	1	0.1	0			
閉経関連症状	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
閉経後出血	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
萎縮性外陰膣炎	0				0				0				2	(0.2)	2	0.1
生殖器系障害ＮＥＣ	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	0			
骨盤痛	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
陰部そう痒症	0				0				1	(0.1)	1	0.1	0			
性器発疹	0				0				1	(0.1)	1	0.1	0			
精巣および精巣上体障害	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
精巣腫脹	0				1	(0.1)	1	0.1	0				0			
精巣腫瘤	0				1	(0.1)	1	0.1	0				0			
精巣上体圧痛	0				0				1	(0.1)	1	0.1	0			
精巣嚢胞	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
性機能および生殖能障害	6	(0.4)	6	0.2	6	(0.4)	6	0.2	12	(0.4)	12	0.2
勃起不全	6	(0.4)	6	0.2	4	(0.2)	4	0.1	10	(0.3)	10	0.2
血精液症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
性機能不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
男性生殖器系感染および炎症	3	(0.2)	3	0.1	4	(0.2)	7	0.2	7	(0.2)	10	0.2
前立腺炎	2	(0.1)	2	0.1	2	(0.1)	3	0.1	4	(0.1)	5	0.1
亀頭包皮炎	1	(0.1)	1	<0.1	2	(0.1)	4	0.1	3	(0.1)	5	0.1
外陰膣障害（感染および炎症を除く）	2	(0.1)	2	0.1	5	(0.3)	6	0.2	7	(0.2)	8	0.1
外陰膣痛	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
外陰部障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
外陰膣そう痒症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外陰膣乾燥	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
外陰膣腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膣出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膣分泌物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
閉経関連症状	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
閉経後出血	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
萎縮性外陰膣炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
生殖器系障害ＮＥＣ	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
骨盤痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
陰部そう痒症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
性器発疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精巣および精巣上体障害	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
精巣腫脹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
精巣腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
精巣上体圧痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精巣嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
卵巣および卵管障害	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
卵巣嚢胞	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
卵巣腫大	0				0				0				1	(0.1)	1	0.1
月経周期および子宮出血障害	0				2	(0.2)	2	0.1	0				0			
月経過多	0				1	(0.1)	1	0.1	0				0			
不正子宮出血	0				1	(0.1)	1	0.1	0				0			
子宮頚部障害（感染および炎症を除く）	0				1	(0.1)	2	0.1	0				0			
子宮頚管ポリープ	0				1	(0.1)	2	0.1	0				0			
陰嚢および陰茎障害（感染および炎症を除く）	0				0				0				1	(0.1)	1	0.1
陰茎腫脹	0				0				0				1	(0.1)	1	0.1
耳および迷路障害	34	(4.1)	39	2.6	29	(3.5)	30	2.1	28	(3.4)	29	1.9	23	(2.8)	29	1.9
内耳および第８脳神経障害	18	(2.2)	19	1.3	18	(2.2)	18	1.2	14	(1.7)	14	0.9	18	(2.2)	20	1.3
回転性めまい	13	(1.6)	14	0.9	12	(1.5)	12	0.8	10	(1.2)	10	0.7	13	(1.6)	14	0.9
耳鳴	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	3	(0.4)	4	0.3
頭位性回転性めまい	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
メニエール病	1	(0.1)	1	0.1	0				0				0			
前庭障害	0				1	(0.1)	1	0.1	0				0			
耳部障害ＮＥＣ	5	(0.6)	5	0.3	4	(0.5)	5	0.3	8	(1.0)	8	0.5	1	(0.1)	2	0.1
耳痛	3	(0.4)	3	0.2	2	(0.2)	2	0.1	4	(0.5)	4	0.3	1	(0.1)	2	0.1
耳不快感	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
耳閉	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
耳漏	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
耳の障害	0				0				1	(0.1)	1	0.1	0			
耳出血	0				1	(0.1)	1	0.1	0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
卵巣および卵管障害	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
卵巣嚢胞	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
卵巣腫大	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
月経周期および子宮出血障害	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
月経過多	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
不正子宮出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
子宮頚部障害（感染および炎症を除く）	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
子宮頚管ポリープ	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
陰嚢および陰茎障害（感染および炎症を除く）	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
陰茎腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
耳および迷路障害	63	(3.8)	69	2.4	51	(3.1)	58	1.9	114	(3.5)	127	2.1
内耳および第８脳神経障害	36	(2.2)	37	1.3	32	(1.9)	34	1.1	68	(2.1)	71	1.2
回転性めまい	25	(1.5)	26	0.9	23	(1.4)	24	0.8	48	(1.5)	50	0.8
耳鳴	5	(0.3)	5	0.2	5	(0.3)	6	0.2	10	(0.3)	11	0.2
頭位性回転性めまい	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
メニエール病	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
前庭障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
耳部障害ＮＥＣ	9	(0.5)	10	0.3	9	(0.5)	10	0.3	18	(0.5)	20	0.3
耳痛	5	(0.3)	5	0.2	5	(0.3)	6	0.2	10	(0.3)	11	0.2
耳不快感	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
耳閉	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
耳漏	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
耳の障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
耳出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
外耳障害（先天性障害を除く）	8	(1.0)	8	0.5	1	(0.1)	1	0.1	2	(0.2)	2	0.1	4	(0.5)	4	0.3
耳垢栓塞	8	(1.0)	8	0.5	1	(0.1)	1	0.1	2	(0.2)	2	0.1	4	(0.5)	4	0.3
聴覚障害	3	(0.4)	3	0.2	5	(0.6)	5	0.3	3	(0.4)	3	0.2	3	(0.4)	3	0.2
聴力低下	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
難聴	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
両耳難聴	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
感音性難聴	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
中耳障害（先天性障害を除く）	4	(0.5)	4	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
鼓膜穿孔	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
中耳の炎症	2	(0.2)	2	0.1	0				0				0			
耳管機能障害	1	(0.1)	1	0.1	0				0				0			
耳硬化症	0				0				1	(0.1)	1	0.1	0			
中耳滲出液	0				0				1	(0.1)	1	0.1	0			
内分泌障害	17	(2.1)	18	1.2	17	(2.1)	18	1.2	13	(1.6)	14	0.9	19	(2.3)	19	1.2
甲状腺障害	15	(1.8)	15	1.0	15	(1.8)	16	1.1	11	(1.3)	11	0.7	15	(1.8)	15	1.0
甲状腺機能低下症	9	(1.1)	9	0.6	6	(0.7)	6	0.4	5	(0.6)	5	0.3	8	(1.0)	8	0.5
甲状腺腫	4	(0.5)	4	0.3	4	(0.5)	4	0.3	5	(0.6)	5	0.3	5	(0.6)	5	0.3
甲状腺機能亢進症	1	(0.1)	1	0.1	2	(0.2)	3	0.2	0				1	(0.1)	1	0.1
甲状腺嚢腫	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
原発性甲状腺機能低下症	0				0				0				1	(0.1)	1	0.1
甲状腺炎	0				1	(0.1)	1	0.1	0				0			
甲状腺障害	0				1	(0.1)	1	0.1	0				0			
自己免疫性甲状腺炎	0				0				1	(0.1)	1	0.1	0			
性腺機能の内分泌性障害	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
性腺機能低下	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
男性性腺機能低下	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
外耳障害（先天性障害を除く）	9	(0.5)	9	0.3	6	(0.4)	6	0.2	15	(0.5)	15	0.3
耳垢栓塞	9	(0.5)	9	0.3	6	(0.4)	6	0.2	15	(0.5)	15	0.3
聴覚障害	8	(0.5)	8	0.3	6	(0.4)	6	0.2	14	(0.4)	14	0.2
聴力低下	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
難聴	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
両耳難聴	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
感音性難聴	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
中耳障害（先天性障害を除く）	5	(0.3)	5	0.2	2	(0.1)	2	0.1	7	(0.2)	7	0.1
鼓膜穿孔	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
中耳の炎症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
耳管機能障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
耳硬化症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
中耳滲出液	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
内分泌障害	34	(2.1)	36	1.2	32	(1.9)	33	1.1	66	(2.0)	69	1.2
甲状腺障害	30	(1.8)	31	1.1	26	(1.6)	26	0.9	56	(1.7)	57	1.0
甲状腺機能低下症	15	(0.9)	15	0.5	13	(0.8)	13	0.4	28	(0.9)	28	0.5
甲状腺腫	8	(0.5)	8	0.3	10	(0.6)	10	0.3	18	(0.5)	18	0.3
甲状腺機能亢進症	3	(0.2)	4	0.1	1	(0.1)	1	<0.1	4	(0.1)	5	0.1
甲状腺嚢腫	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
原発性甲状腺機能低下症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
甲状腺炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
甲状腺障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
自己免疫性甲状腺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
性腺機能の内分泌性障害	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
性腺機能低下	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
男性性腺機能低下	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
副甲状腺障害	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
続発性副甲状腺機能亢進症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
原発性副甲状腺機能亢進症	0				0				0				1	(0.1)	1	0.1
副甲状腺機能亢進症	0				0				0				1	(0.1)	1	0.1
副腎障害	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
副腎機能亢進症	0				0				0				1	(0.1)	1	0.1
副腎腫瘤	0				0				1	(0.1)	1	0.1	0			
副腎障害	0				1	(0.1)	1	0.1	0				0			
視床下部および下垂体障害	0				0				1	(0.1)	1	0.1	0			
抗利尿ホルモン不適合分泌	0				0				1	(0.1)	1	0.1	0			
免疫系障害	13	(1.6)	13	0.9	10	(1.2)	10	0.7	7	(0.9)	8	0.5	8	(1.0)	8	0.5
アレルギー性疾患	13	(1.6)	13	0.9	10	(1.2)	10	0.7	7	(0.9)	8	0.5	8	(1.0)	8	0.5
季節性アレルギー	6	(0.7)	6	0.4	5	(0.6)	5	0.3	3	(0.4)	3	0.2	2	(0.2)	2	0.1
薬物過敏症	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	3	0.2	3	(0.4)	3	0.2
過敏症	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0				0			
アナフィラキシーショック	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
食物アレルギー	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
節足動物咬傷アレルギー	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
アナフィラキシー反応	0				0				0				1	(0.1)	1	0.1
香料過敏症	0				1	(0.1)	1	0.1	0				0			
動物アレルギー	0				0				0				1	(0.1)	1	0.1
先天性、家族性および遺伝性障害	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	6	(0.7)	6	0.4

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
副甲状腺障害	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
続発性副甲状腺機能亢進症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
原発性副甲状腺機能亢進症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副甲状腺機能亢進症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副腎障害	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
副腎機能亢進症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副腎腫瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副腎障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
視床下部および下垂体障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
抗利尿ホルモン不適合分泌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
免疫系障害	23	(1.4)	23	0.8	15	(0.9)	16	0.5	38	(1.2)	39	0.7
アレルギー性疾患	23	(1.4)	23	0.8	15	(0.9)	16	0.5	38	(1.2)	39	0.7
季節性アレルギー	11	(0.7)	11	0.4	5	(0.3)	5	0.2	16	(0.5)	16	0.3
薬物過敏症	4	(0.2)	4	0.1	5	(0.3)	6	0.2	9	(0.3)	10	0.2
過敏症	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
アナフィラキシーショック	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
食物アレルギー	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
節足動物咬傷アレルギー	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
アナフィラキシー反応	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
香料過敏症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
動物アレルギー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
先天性、家族性および遺伝性障害	4	(0.2)	4	0.1	8	(0.5)	8	0.3	12	(0.4)	12	0.2

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
先天性心血管系障害	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
心室中隔欠損症	0				0				1	(0.1)	1	0.1	0			
心房中隔欠損症	0				0				1	(0.1)	1	0.1	0			
動静脈奇形	1	(0.1)	1	0.1	0				0				0			
先天性生殖器系および乳房障害	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
陰嚢水瘤	0				0				0				2	(0.2)	2	0.1
包茎	0				1	(0.1)	1	0.1	0				0			
先天性消化管障害	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
過長結腸	0				0				0				1	(0.1)	1	0.1
臍奇形	1	(0.1)	1	0.1	0				0				0			
先天性眼部障害	0				1	(0.1)	1	0.1	0				0			
色覚異常	0				1	(0.1)	1	0.1	0				0			
先天性腎尿路系障害	0				0				0				1	(0.1)	1	0.1
融合腎	0				0				0				1	(0.1)	1	0.1
先天性代謝および栄養障害	0				0				0				1	(0.1)	1	0.1
α１抗トリプシン欠損症	0				0				0				1	(0.1)	1	0.1
先天性皮膚および皮下組織異常	0				0				0				1	(0.1)	1	0.1
皮様嚢腫	0				0				0				1	(0.1)	1	0.1
社会環境	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
生活スタイル問題	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
運動不能	0				1	(0.1)	1	0.1	0				0			
歯科補てつ物使用者	0				0				0				1	(0.1)	1	0.1
食事療法非遵守	1	(0.1)	1	0.1	0				0				0			

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Adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
先天性心血管系障害	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
心室中隔欠損症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心房中隔欠損症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
動静脈奇形	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
先天性生殖器系および乳房障害	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
陰嚢水瘤	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
包茎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
先天性消化管障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
過長結腸	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
臍奇形	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
先天性眼部障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
色覚異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
先天性腎尿路系障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
融合腎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
先天性代謝および栄養障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
α１抗トリプシン欠損症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
先天性皮膚および皮下組織異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮様嚢腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
社会環境	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
生活スタイル問題	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
運動不能	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
歯科補てつ物使用者	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
食事療法非遵守	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.25.2- 2　重篤な有害事象（器官別大分類、高位グループ語及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
Number of subjects	823				819				819				825			
Exposure time (year)	1488.3				1443.9				1508.0				1526.8			
Events	264	(32.1)	599	40.2	240	(29.3)	481	33.3	297	(36.3)	647	42.9	277	(33.6)	609	39.9
心臓障害	97	(11.8)	137	9.2	72	(8.8)	121	8.4	109	(13.3)	150	9.9	96	(11.6)	146	9.6
冠動脈障害	54	(6.6)	62	4.2	43	(5.3)	53	3.7	66	(8.1)	76	5.0	59	(7.2)	75	4.9
急性心筋梗塞	13	(1.6)	14	0.9	9	(1.1)	9	0.6	15	(1.8)	15	1.0	23	(2.8)	24	1.6
不安定狭心症	10	(1.2)	11	0.7	11	(1.3)	14	1.0	19	(2.3)	21	1.4	20	(2.4)	21	1.4
狭心症	8	(1.0)	8	0.5	7	(0.9)	8	0.6	15	(1.8)	16	1.1	10	(1.2)	10	0.7
心筋梗塞	4	(0.5)	4	0.3	8	(1.0)	8	0.6	8	(1.0)	9	0.6	11	(1.3)	12	0.8
冠動脈疾患	11	(1.3)	11	0.7	9	(1.1)	9	0.6	5	(0.6)	6	0.4	0			
冠動脈狭窄	4	(0.5)	4	0.3	2	(0.2)	2	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1
心筋虚血	6	(0.7)	6	0.4	0				3	(0.4)	3	0.2	2	(0.2)	2	0.1
急性冠動脈症候群	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
冠動脈硬化症	0				0				0				3	(0.4)	3	0.2
冠動脈閉塞	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
無症候性心筋梗塞	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
冠動脈不全	1	(0.1)	1	0.1	0				0				0			
不整脈	25	(3.0)	29	1.9	28	(3.4)	39	2.7	31	(3.8)	39	2.6	33	(4.0)	39	2.6
心房細動	11	(1.3)	12	0.8	12	(1.5)	15	1.0	18	(2.2)	20	1.3	17	(2.1)	18	1.2
心室性頻脈	1	(0.1)	1	0.1	7	(0.9)	7	0.5	1	(0.1)	1	0.1	1	(0.1)	1	0.1
心停止	3	(0.4)	3	0.2	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
完全房室ブロック	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2
左脚ブロック	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
心房粗動	0				1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1
徐脈	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
心室細動	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	1642				1644				3286			
Exposure time (year)	2932.2				3034.8				5967.0			
Events	504	(30.7)	1080	36.8	574	(34.9)	1256	41.4	1078	(32.8)	2336	39.1
心臓障害	169	(10.3)	258	8.8	205	(12.5)	296	9.8	374	(11.4)	554	9.3
冠動脈障害	97	(5.9)	115	3.9	125	(7.6)	151	5.0	222	(6.8)	266	4.5
急性心筋梗塞	22	(1.3)	23	0.8	38	(2.3)	39	1.3	60	(1.8)	62	1.0
不安定狭心症	21	(1.3)	25	0.9	39	(2.4)	42	1.4	60	(1.8)	67	1.1
狭心症	15	(0.9)	16	0.5	25	(1.5)	26	0.9	40	(1.2)	42	0.7
心筋梗塞	12	(0.7)	12	0.4	19	(1.2)	21	0.7	31	(0.9)	33	0.6
冠動脈疾患	20	(1.2)	20	0.7	5	(0.3)	6	0.2	25	(0.8)	26	0.4
冠動脈狭窄	6	(0.4)	6	0.2	5	(0.3)	5	0.2	11	(0.3)	11	0.2
心筋虚血	6	(0.4)	6	0.2	5	(0.3)	5	0.2	11	(0.3)	11	0.2
急性冠動脈症候群	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
冠動脈硬化症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
冠動脈閉塞	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
無症候性心筋梗塞	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
冠動脈不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
不整脈	53	(3.2)	68	2.3	64	(3.9)	78	2.6	117	(3.6)	146	2.4
心房細動	23	(1.4)	27	0.9	35	(2.1)	38	1.3	58	(1.8)	65	1.1
心室性頻脈	8	(0.5)	8	0.3	2	(0.1)	2	0.1	10	(0.3)	10	0.2
心停止	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
完全房室ブロック	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
左脚ブロック	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
心房粗動	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
徐脈	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
心室細動	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
不整脈	1	(0.1)	2	0.1	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2
上室性頻脈	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
第二度房室ブロック	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
洞結節機能不全	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
心室性期外収縮	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
心肺停止	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
第一度房室ブロック	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
洞性徐脈	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
右脚ブロック	0				1	(0.1)	1	0.1	0				0			
結節性不整脈	1	(0.1)	1	0.1	0				0				0			
上室性期外収縮	0				1	(0.1)	1	0.1	0				0			
心室性頻脈性不整脈	1	(0.1)	1	0.1	0				0				0			
心室性不整脈	1	(0.1)	1	0.1	0				0				0			
心室無収縮	0				0				0				1	(0.1)	1	0.1
頻脈	0				1	(0.1)	1	0.1	0				0			
房室ブロック	0				0				1	(0.1)	1	0.1	0			
心不全	33	(4.0)	39	2.6	20	(2.4)	25	1.7	27	(3.3)	34	2.3	24	(2.9)	28	1.8
うっ血性心不全	14	(1.7)	17	1.1	10	(1.2)	13	0.9	13	(1.6)	17	1.1	16	(1.9)	18	1.2
心不全	10	(1.2)	11	0.7	8	(1.0)	8	0.6	5	(0.6)	5	0.3	2	(0.2)	2	0.1
慢性心不全	7	(0.9)	7	0.5	3	(0.4)	3	0.2	5	(0.6)	5	0.3	3	(0.4)	3	0.2
急性心不全	2	(0.2)	2	0.1	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
心原性ショック	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
左室不全	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
右室不全	0				0				0				1	(0.1)	1	0.1
急性左室不全	0				0				0				1	(0.1)	1	0.1
心臓性喘息	1	(0.1)	1	0.1	0				0				0			
心肺不全	0				0				1	(0.1)	1	0.1	0			
心筋障害	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	3	0.2
高血圧性心筋症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
不整脈	1	(0.1)	2	0.1	4	(0.2)	4	0.1	5	(0.2)	6	0.1
上室性頻脈	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
第二度房室ブロック	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
洞結節機能不全	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
心室性期外収縮	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
心肺停止	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
第一度房室ブロック	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
洞性徐脈	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
右脚ブロック	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
結節性不整脈	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
上室性期外収縮	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心室性頻脈性不整脈	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心室性不整脈	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心室無収縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頻脈	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
房室ブロック	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心不全	53	(3.2)	64	2.2	51	(3.1)	62	2.0	104	(3.2)	126	2.1
うっ血性心不全	24	(1.5)	30	1.0	29	(1.8)	35	1.2	53	(1.6)	65	1.1
心不全	18	(1.1)	19	0.6	7	(0.4)	7	0.2	25	(0.8)	26	0.4
慢性心不全	10	(0.6)	10	0.3	8	(0.5)	8	0.3	18	(0.5)	18	0.3
急性心不全	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
心原性ショック	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
左室不全	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
右室不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性左室不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心臓性喘息	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心肺不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心筋障害	4	(0.2)	4	0.1	3	(0.2)	4	0.1	7	(0.2)	8	0.1
高血圧性心筋症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
うっ血性心筋症	1	(0.1)	1	0.1	0				0				0			
虚血性心筋症	0				0				0				1	(0.1)	1	0.1
心筋炎	1	(0.1)	1	0.1	0				0				0			
心筋症	0				1	(0.1)	1	0.1	0				0			
心室壁運動低下	0				0				1	(0.1)	1	0.1	0			
糖尿病性心筋症	0				0				0				1	(0.1)	1	0.1
心臓弁膜障害	2	(0.2)	3	0.2	1	(0.1)	1	0.1	0				0			
三尖弁閉鎖不全症	1	(0.1)	1	0.1	0				0				0			
僧帽弁閉鎖不全症	1	(0.1)	1	0.1	0				0				0			
大動脈弁狭窄	0				1	(0.1)	1	0.1	0				0			
大動脈弁疾患	1	(0.1)	1	0.1	0				0				0			
心障害徴候および症状	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
心血管不全	0				1	(0.1)	1	0.1	0				0			
心室血栓症	0				0				0				1	(0.1)	1	0.1
心膜障害	1	(0.1)	2	0.1	0				0				0			
心タンポナーデ	1	(0.1)	1	0.1	0				0				0			
心嚢液貯留	1	(0.1)	1	0.1	0				0				0			
感染症および寄生虫症	59	(7.2)	77	5.2	42	(5.1)	50	3.5	70	(8.5)	87	5.8	58	(7.0)	72	4.7
詳細不明な感染体による感染症	47	(5.7)	56	3.8	34	(4.2)	38	2.6	58	(7.1)	69	4.6	47	(5.7)	54	3.5
肺炎	15	(1.8)	15	1.0	11	(1.3)	11	0.8	18	(2.2)	21	1.4	12	(1.5)	12	0.8
尿路感染	8	(1.0)	8	0.5	2	(0.2)	2	0.1	9	(1.1)	9	0.6	4	(0.5)	4	0.3
敗血症	5	(0.6)	5	0.3	4	(0.5)	4	0.3	3	(0.4)	3	0.2	5	(0.6)	5	0.3
骨髄炎	5	(0.6)	5	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
気管支炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
胃腸炎	0				2	(0.2)	2	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1
敗血症性ショック	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	3	(0.4)	3	0.2
限局性感染	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	2	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
うっ血性心筋症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
虚血性心筋症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心筋炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心筋症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心室壁運動低下	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糖尿病性心筋症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心臓弁膜障害	3	(0.2)	4	0.1	0				3	(0.1)	4	0.1
三尖弁閉鎖不全症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
僧帽弁閉鎖不全症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大動脈弁狭窄	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大動脈弁疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心障害徴候および症状	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心血管不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心室血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心膜障害	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
心タンポナーデ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心嚢液貯留	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染症および寄生虫症	101	(6.2)	127	4.3	128	(7.8)	159	5.2	229	(7.0)	286	4.8
詳細不明な感染体による感染症	81	(4.9)	94	3.2	105	(6.4)	123	4.1	186	(5.7)	217	3.6
肺炎	26	(1.6)	26	0.9	30	(1.8)	33	1.1	56	(1.7)	59	1.0
尿路感染	10	(0.6)	10	0.3	13	(0.8)	13	0.4	23	(0.7)	23	0.4
敗血症	9	(0.5)	9	0.3	8	(0.5)	8	0.3	17	(0.5)	17	0.3
骨髄炎	6	(0.4)	6	0.2	4	(0.2)	4	0.1	10	(0.3)	10	0.2
気管支炎	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
胃腸炎	2	(0.1)	2	0.1	5	(0.3)	5	0.2	7	(0.2)	7	0.1
敗血症性ショック	1	(0.1)	1	<0.1	6	(0.4)	6	0.2	7	(0.2)	7	0.1
限局性感染	3	(0.2)	3	0.1	3	(0.2)	4	0.1	6	(0.2)	7	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
術後創感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
憩室炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
尿路性敗血症	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
副鼻腔炎	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	2	0.1
咽頭炎	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
処置後感染	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
腎盂腎炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
切開部位感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
虫垂炎	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
慢性腎盂腎炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
膀胱炎	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
感染性大腸炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
気管支肺炎	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
急性腎盂腎炎	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
上気道感染	0				0				2	(0.2)	2	0.1	0			
大葉性肺炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
爪囲炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
糖尿病性足感染	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
腹膜炎	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
医療機器関連敗血症	0				0				1	(0.1)	1	0.1	0			
下気道感染	0				0				0				1	(0.1)	1	0.1
壊死性筋膜炎	0				0				1	(0.1)	1	0.1	0			
外耳炎	1	(0.1)	1	0.1	0				0				0			
感染による慢性閉塞性気道疾患の増悪	1	(0.1)	1	0.1	0				0				0			
感染性腸炎	0				0				1	(0.1)	1	0.1	0			
感染性皮膚潰瘍	0				1	(0.1)	1	0.1	0				0			
肝膿瘍	1	(0.1)	1	0.1	0				0				0			
菌血症	0				0				0				1	(0.1)	1	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
術後創感染	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
憩室炎	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
尿路性敗血症	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
副鼻腔炎	1	(0.1)	1	<0.1	3	(0.2)	4	0.1	4	(0.1)	5	0.1
咽頭炎	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
処置後感染	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
腎盂腎炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
切開部位感染	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
虫垂炎	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
慢性腎盂腎炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
膀胱炎	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
感染性大腸炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
気管支肺炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
急性腎盂腎炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
上気道感染	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
大葉性肺炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
爪囲炎	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
糖尿病性足感染	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
腹膜炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
医療機器関連敗血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
下気道感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
壊死性筋膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外耳炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染による慢性閉塞性気道疾患の増悪	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染性腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感染性皮膚潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
菌血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
四肢膿瘍	1	(0.1)	1	0.1	0				0				0			
歯膿瘍	1	(0.1)	1	0.1	0				0				0			
処置後肺炎	1	(0.1)	1	0.1	0				0				0			
心内膜炎	0				0				1	(0.1)	1	0.1	0			
精巣上体炎	0				0				0				1	(0.1)	1	0.1
直腸周囲膿瘍	0				1	(0.1)	1	0.1	0				0			
軟部組織感染	0				0				0				1	(0.1)	1	0.1
膿瘍	0				0				1	(0.1)	1	0.1	0			
肺敗血症	1	(0.1)	1	0.1	0				0				0			
皮下組織膿瘍	0				0				1	(0.1)	1	0.1	0			
埋込み部位感染	0				0				1	(0.1)	1	0.1	0			
迷路炎	1	(0.1)	1	0.1	0				0				0			
扁桃周囲膿瘍	0				0				0				1	(0.1)	1	0.1
脾臓膿瘍	0				0				0				1	(0.1)	1	0.1
臍帯周囲膿瘍	0				0				0				1	(0.1)	1	0.1
細菌感染症	12	(1.5)	13	0.9	9	(1.1)	10	0.7	11	(1.3)	12	0.8	11	(1.3)	14	0.9
蜂巣炎	6	(0.7)	6	0.4	3	(0.4)	3	0.2	5	(0.6)	5	0.3	8	(1.0)	9	0.6
壊疽	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	2	(0.2)	2	0.1
大腸菌性敗血症	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
クロストリジウム・ディフィシレ大腸炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
ブドウ球菌感染	2	(0.2)	2	0.1	0				0				0			
ブドウ球菌性敗血症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
カンピロバクター胃腸炎	0				1	(0.1)	1	0.1	0				0			
カンピロバクター感染	1	(0.1)	1	0.1	0				0				0			
サルモネラ菌性胃腸炎	0				1	(0.1)	1	0.1	0				0			
シュードモナス性尿路感染	0				1	(0.1)	1	0.1	0				0			
ブドウ球菌性骨髄炎	0				0				1	(0.1)	1	0.1	0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
四肢膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
歯膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
処置後肺炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心内膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精巣上体炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
直腸周囲膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
軟部組織感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺敗血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮下組織膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
埋込み部位感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
迷路炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
扁桃周囲膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脾臓膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
臍帯周囲膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌感染症	21	(1.3)	23	0.8	22	(1.3)	26	0.9	43	(1.3)	49	0.8
蜂巣炎	9	(0.5)	9	0.3	13	(0.8)	14	0.5	22	(0.7)	23	0.4
壊疽	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
大腸菌性敗血症	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
クロストリジウム・ディフィシレ大腸炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
ブドウ球菌感染	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
ブドウ球菌性敗血症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
カンピロバクター胃腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
カンピロバクター感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
サルモネラ菌性胃腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
シュードモナス性尿路感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ブドウ球菌性骨髄炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ブドウ球菌性尿路感染	0				0				0				1	(0.1)	1	0.1
偽膜性大腸炎	0				0				1	(0.1)	1	0.1	0			
細菌性髄膜炎	0				1	(0.1)	1	0.1	0				0			
大腸菌感染	0				0				0				1	(0.1)	1	0.1
腸球菌感染	1	(0.1)	1	0.1	0				0				0			
肺炎球菌性肺炎	0				0				1	(0.1)	1	0.1	0			
ウイルス感染症	8	(1.0)	8	0.5	1	(0.1)	1	0.1	3	(0.4)	4	0.3	3	(0.4)	3	0.2
インフルエンザ	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
ウイルス感染	2	(0.2)	2	0.1	0				0				0			
帯状疱疹	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
ウイルス性胃腸炎	0				0				1	(0.1)	1	0.1	0			
ウイルス性気道感染	1	(0.1)	1	0.1	0				0				0			
デング熱	1	(0.1)	1	0.1	0				0				0			
ロタウイルス胃腸炎	0				0				1	(0.1)	2	0.1	0			
急性Ｂ型肝炎	1	(0.1)	1	0.1	0				0				0			
前庭神経炎	1	(0.1)	1	0.1	0				0				0			
真菌感染症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
食道カンジダ症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
マイコバクテリア感染症	0				0				0				1	(0.1)	1	0.1
結核	0				0				0				1	(0.1)	1	0.1
リケッチア感染症	0				0				1	(0.1)	1	0.1	0			
ボタン熱	0				0				1	(0.1)	1	0.1	0			
外科および内科処置	41	(5.0)	48	3.2	31	(3.8)	33	2.3	60	(7.3)	64	4.2	55	(6.7)	65	4.3
血管治療手技	37	(4.5)	41	2.8	26	(3.2)	28	1.9	58	(7.1)	62	4.1	52	(6.3)	61	4.0
冠動脈ステント挿入	10	(1.2)	11	0.7	7	(0.9)	8	0.6	14	(1.7)	15	1.0	16	(1.9)	18	1.2
冠動脈血行再建	11	(1.3)	12	0.8	7	(0.9)	7	0.5	15	(1.8)	17	1.1	9	(1.1)	10	0.7
冠動脈バイパス	8	(1.0)	8	0.5	4	(0.5)	4	0.3	13	(1.6)	13	0.9	8	(1.0)	8	0.5
末梢血行再建	2	(0.2)	2	0.1	2	(0.2)	2	0.1	5	(0.6)	5	0.3	9	(1.1)	9	0.6

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ブドウ球菌性尿路感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
偽膜性大腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性髄膜炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大腸菌感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸球菌感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺炎球菌性肺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ウイルス感染症	9	(0.5)	9	0.3	6	(0.4)	7	0.2	15	(0.5)	16	0.3
インフルエンザ	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
ウイルス感染	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
帯状疱疹	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
ウイルス性胃腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ウイルス性気道感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
デング熱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ロタウイルス胃腸炎	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
急性Ｂ型肝炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
前庭神経炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
真菌感染症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
食道カンジダ症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
マイコバクテリア感染症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結核	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
リケッチア感染症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ボタン熱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外科および内科処置	72	(4.4)	81	2.8	115	(7.0)	129	4.3	187	(5.7)	210	3.5
血管治療手技	63	(3.8)	69	2.4	110	(6.7)	123	4.1	173	(5.3)	192	3.2
冠動脈ステント挿入	17	(1.0)	19	0.6	30	(1.8)	33	1.1	47	(1.4)	52	0.9
冠動脈血行再建	18	(1.1)	19	0.6	24	(1.5)	27	0.9	42	(1.3)	46	0.8
冠動脈バイパス	12	(0.7)	12	0.4	21	(1.3)	21	0.7	33	(1.0)	33	0.6
末梢血行再建	4	(0.2)	4	0.1	14	(0.9)	14	0.5	18	(0.5)	18	0.3

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
冠動脈形成	1	(0.1)	1	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3
経皮的冠インターベンション	2	(0.2)	2	0.1	0				3	(0.4)	4	0.3	4	(0.5)	5	0.3
末梢動脈形成	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
頚動脈内膜剥離術	0				0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
頚動脈血行再建	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
血管形成	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
末梢動脈ステント挿入	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
頚動脈ステント挿入	0				1	(0.1)	1	0.1	0				0			
頚動脈形成	0				0				0				1	(0.1)	1	0.1
末梢動脈バイパス	0				0				1	(0.1)	1	0.1	0			
末梢動脈内膜剥離術	0				1	(0.1)	1	0.1	0				0			
治療的手技および補助療法ＮＥＣ	3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
ステント装着	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
近距離照射療法	0				0				0				1	(0.1)	1	0.1
入院	1	(0.1)	1	0.1	0				0				0			
眼科治療手技	1	(0.1)	2	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
白内障手術	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
翼状片手術	1	(0.1)	1	0.1	0				0				0			
消化管治療手技	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
開腹	1	(0.1)	1	0.1	0				0				0			
腹部ヘルニア修復	0				1	(0.1)	1	0.1	0				0			
臍ヘルニア修復	0				1	(0.1)	1	0.1	0				0			
呼吸器系治療手技	1	(0.1)	1	0.1	0				0				0			
機械的換気	1	(0.1)	1	0.1	0				0				0			
骨および関節治療手技	0				0				1	(0.1)	1	0.1	0			
内固定除去	0				0				1	(0.1)	1	0.1	0			
頭頚部治療手技	0				0				0				1	(0.1)	1	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
冠動脈形成	2	(0.1)	2	0.1	8	(0.5)	8	0.3	10	(0.3)	10	0.2
経皮的冠インターベンション	2	(0.1)	2	0.1	7	(0.4)	9	0.3	9	(0.3)	11	0.2
末梢動脈形成	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
頚動脈内膜剥離術	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
頚動脈血行再建	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
血管形成	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
末梢動脈ステント挿入	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
頚動脈ステント挿入	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頚動脈形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈バイパス	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈内膜剥離術	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
治療的手技および補助療法ＮＥＣ	5	(0.3)	5	0.2	2	(0.1)	2	0.1	7	(0.2)	7	0.1
ステント装着	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
近距離照射療法	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
入院	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼科治療手技	2	(0.1)	3	0.1	2	(0.1)	2	0.1	4	(0.1)	5	0.1
白内障手術	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
翼状片手術	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管治療手技	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
開腹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹部ヘルニア修復	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
臍ヘルニア修復	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
呼吸器系治療手技	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
機械的換気	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨および関節治療手技	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
内固定除去	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頭頚部治療手技	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
鼻ポリープ切除	0				0				0				1	(0.1)	1	0.1
神経系障害	36	(4.4)	42	2.8	28	(3.4)	39	2.7	47	(5.7)	54	3.6	34	(4.1)	43	2.8
中枢神経系血管障害	22	(2.7)	24	1.6	16	(2.0)	20	1.4	34	(4.2)	36	2.4	21	(2.5)	23	1.5
虚血性脳卒中	8	(1.0)	8	0.5	6	(0.7)	7	0.5	14	(1.7)	14	0.9	4	(0.5)	4	0.3
一過性脳虚血発作	7	(0.9)	8	0.5	5	(0.6)	6	0.4	10	(1.2)	10	0.7	4	(0.5)	4	0.3
脳血管発作	1	(0.1)	1	0.1	2	(0.2)	2	0.1	6	(0.7)	6	0.4	5	(0.6)	5	0.3
頚動脈狭窄	0				0				3	(0.4)	3	0.2	2	(0.2)	2	0.1
出血性卒中	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
脳梗塞	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
頭蓋内動脈瘤	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
ラクナ梗塞	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
虚血性脳梗塞	0				0				0				1	(0.1)	1	0.1
塞栓性脳卒中	0				0				0				1	(0.1)	1	0.1
視床梗塞	0				1	(0.1)	1	0.1	0				0			
小脳出血	0				0				1	(0.1)	1	0.1	0			
頭蓋内出血	0				0				0				1	(0.1)	1	0.1
脳幹梗塞	1	(0.1)	1	0.1	0				0				0			
脳虚血	0				0				0				1	(0.1)	1	0.1
脳血管障害	1	(0.1)	1	0.1	0				0				0			
脳室内出血	0				0				0				1	(0.1)	1	0.1
脳出血	1	(0.1)	1	0.1	0				0				0			
神経学的障害ＮＥＣ	6	(0.7)	6	0.4	12	(1.5)	13	0.9	8	(1.0)	10	0.7	9	(1.1)	12	0.8
低血糖性意識消失	5	(0.6)	5	0.3	3	(0.4)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	6	0.4
失神	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	3	(0.4)	3	0.2
失神寸前の状態	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
浮動性めまい	0				0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
意識消失	0				1	(0.1)	1	0.1	0				0			
感覚鈍麻	0				1	(0.1)	1	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
鼻ポリープ切除	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経系障害	64	(3.9)	81	2.8	81	(4.9)	97	3.2	145	(4.4)	178	3.0
中枢神経系血管障害	38	(2.3)	44	1.5	55	(3.3)	59	1.9	93	(2.8)	103	1.7
虚血性脳卒中	14	(0.9)	15	0.5	18	(1.1)	18	0.6	32	(1.0)	33	0.6
一過性脳虚血発作	12	(0.7)	14	0.5	14	(0.9)	14	0.5	26	(0.8)	28	0.5
脳血管発作	3	(0.2)	3	0.1	11	(0.7)	11	0.4	14	(0.4)	14	0.2
頚動脈狭窄	0				5	(0.3)	5	0.2	5	(0.2)	5	0.1
出血性卒中	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
脳梗塞	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
頭蓋内動脈瘤	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
ラクナ梗塞	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
虚血性脳梗塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
塞栓性脳卒中	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
視床梗塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
小脳出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頭蓋内出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳幹梗塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳虚血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳血管障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳室内出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経学的障害ＮＥＣ	18	(1.1)	19	0.6	17	(1.0)	22	0.7	35	(1.1)	41	0.7
低血糖性意識消失	8	(0.5)	8	0.3	4	(0.2)	7	0.2	12	(0.4)	15	0.3
失神	4	(0.2)	4	0.1	5	(0.3)	5	0.2	9	(0.3)	9	0.2
失神寸前の状態	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
浮動性めまい	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
意識消失	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感覚鈍麻	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
協調運動異常	0				0				0				1	(0.1)	1	0.1
昏睡	0				1	(0.1)	2	0.1	0				0			
小脳症候群	0				0				1	(0.1)	1	0.1	0			
神経痛	0				1	(0.1)	1	0.1	0				0			
脳圧低下	0				0				1	(0.1)	1	0.1	0			
脳脊髄液漏	0				0				1	(0.1)	1	0.1	0			
脳症	3	(0.4)	3	0.2	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
代謝性脳症	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
肝性脳症	1	(0.1)	1	0.1	0				0				0			
高血圧性脳症	0				0				0				1	(0.1)	1	0.1
低酸素性虚血性脳症	0				0				1	(0.1)	1	0.1	0			
脊髄および神経根障害	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
神経根障害	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
頚髄症	0				0				0				1	(0.1)	1	0.1
頚髄神経根障害	0				1	(0.1)	1	0.1	0				0			
腰仙部神経根炎	1	(0.1)	1	0.1	0				0				0			
脳神経障害（新生物を除く）	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
第７脳神経麻痺	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
第６脳神経障害	1	(0.1)	1	0.1	0				0				0			
発作（亜型を含む）	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
痙攣発作	0				0				0				3	(0.4)	3	0.2
てんかん	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
運動障害（パーキンソニズムを含む）	1	(0.1)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
パーキンソニズム	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
運動障害	0				0				1	(0.1)	1	0.1	0			
血管性パーキンソニズム	1	(0.1)	1	0.1	0				0				0			
頭痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
協調運動異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
昏睡	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
小脳症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳圧低下	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳脊髄液漏	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳症	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
代謝性脳症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
肝性脳症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高血圧性脳症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
低酸素性虚血性脳症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脊髄および神経根障害	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
神経根障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
頚髄症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頚髄神経根障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腰仙部神経根炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳神経障害（新生物を除く）	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
第７脳神経麻痺	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
第６脳神経障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
発作（亜型を含む）	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
痙攣発作	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
てんかん	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
運動障害（パーキンソニズムを含む）	2	(0.1)	3	0.1	1	(0.1)	1	<0.1	3	(0.1)	4	0.1
パーキンソニズム	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
運動障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管性パーキンソニズム	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頭痛	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
頭痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
片頭痛	0				0				1	(0.1)	1	0.1	0			
頭蓋内圧亢進および水頭症	0				0				0				2	(0.2)	2	0.1
水頭症	0				0				0				1	(0.1)	1	0.1
脳浮腫	0				0				0				1	(0.1)	1	0.1
末梢性ニューロパチー	2	(0.2)	2	0.1	0				0				0			
糖尿病性単ニューロパチー	1	(0.1)	1	0.1	0				0				0			
慢性炎症性脱髄性多発根ニューロパチー	1	(0.1)	1	0.1	0				0				0			
眼部神経学的障害	0				1	(0.1)	1	0.1	0				0			
視野欠損	0				1	(0.1)	1	0.1	0				0			
脱髄疾患	0				0				1	(0.1)	1	0.1	0			
多発性硬化症	0				0				1	(0.1)	1	0.1	0			
腎および尿路障害	32	(3.9)	36	2.4	20	(2.4)	24	1.7	33	(4.0)	37	2.5	29	(3.5)	35	2.3
腎障害（腎症を除く）	23	(2.8)	25	1.7	14	(1.7)	16	1.1	28	(3.4)	30	2.0	21	(2.5)	25	1.6
急性腎不全	12	(1.5)	14	0.9	5	(0.6)	6	0.4	13	(1.6)	13	0.9	16	(1.9)	17	1.1
慢性腎臓病	6	(0.7)	6	0.4	4	(0.5)	4	0.3	12	(1.5)	14	0.9	5	(0.6)	5	0.3
腎機能障害	3	(0.4)	3	0.2	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
腎不全	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
水腎症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
急性腎前性腎不全	1	(0.1)	1	0.1	0				0				0			
高窒素血症	1	(0.1)	1	0.1	0				0				0			
腎動脈の動脈硬化症	0				1	(0.1)	1	0.1	0				0			
腎嚢胞	0				1	(0.1)	1	0.1	0				0			
尿石症	5	(0.6)	5	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1	5	(0.6)	5	0.3
腎結石症	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
尿管結石	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
頭痛	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
片頭痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頭蓋内圧亢進および水頭症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
水頭症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢性ニューロパチー	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
糖尿病性単ニューロパチー	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
慢性炎症性脱髄性多発根ニューロパチー	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼部神経学的障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
視野欠損	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脱髄疾患	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
多発性硬化症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎および尿路障害	52	(3.2)	60	2.0	62	(3.8)	72	2.4	114	(3.5)	132	2.2
腎障害（腎症を除く）	37	(2.3)	41	1.4	49	(3.0)	55	1.8	86	(2.6)	96	1.6
急性腎不全	17	(1.0)	20	0.7	29	(1.8)	30	1.0	46	(1.4)	50	0.8
慢性腎臓病	10	(0.6)	10	0.3	17	(1.0)	19	0.6	27	(0.8)	29	0.5
腎機能障害	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
腎不全	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
水腎症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
急性腎前性腎不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高窒素血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎動脈の動脈硬化症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿石症	9	(0.5)	9	0.3	7	(0.4)	7	0.2	16	(0.5)	16	0.3
腎結石症	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
尿管結石	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
尿路結石	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
鹿角状結石	0				1	(0.1)	1	0.1	0				0			
尿路系徴候および症状	3	(0.4)	4	0.3	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1
血尿	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
尿閉	2	(0.2)	3	0.2	1	(0.1)	1	0.1	0				0			
腎仙痛	0				0				0				1	(0.1)	1	0.1
蛋白尿	0				1	(0.1)	1	0.1	0				0			
尿失禁	0				0				1	(0.1)	1	0.1	0			
排尿困難	0				0				1	(0.1)	1	0.1	0			
腎症	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1	1	(0.1)	1	0.1
ネフローゼ症候群	1	(0.1)	1	0.1	0				1	(0.1)	2	0.1	0			
腎症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
慢性糸球体腎炎	1	(0.1)	1	0.1	0				0				0			
膀胱および膀胱頚部障害（結石を除く）	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
膀胱ポリープ	0				0				0				1	(0.1)	1	0.1
膀胱肉柱形成	0				0				1	(0.1)	1	0.1	0			
尿道障害（結石を除く）	0				0				0				1	(0.1)	1	0.1
尿道狭窄	0				0				0				1	(0.1)	1	0.1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	22	(2.7)	27	1.8	33	(4.0)	38	2.6	29	(3.5)	31	2.1	29	(3.5)	30	2.0
悪性および詳細不明の消化管新生物	6	(0.7)	6	0.4	3	(0.4)	3	0.2	6	(0.7)	6	0.4	4	(0.5)	4	0.3
結腸腺癌	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
胃腺癌	2	(0.2)	2	0.1	0				0				0			
結腸癌	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
直腸癌	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
尿路結石	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
鹿角状結石	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿路系徴候および症状	6	(0.4)	7	0.2	4	(0.2)	4	0.1	10	(0.3)	11	0.2
血尿	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
尿閉	3	(0.2)	4	0.1	0				3	(0.1)	4	0.1
腎仙痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
蛋白尿	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿失禁	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
排尿困難	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎症	3	(0.2)	3	0.1	2	(0.1)	3	0.1	5	(0.2)	6	0.1
ネフローゼ症候群	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
腎症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
慢性糸球体腎炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱および膀胱頚部障害（結石を除く）	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
膀胱ポリープ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膀胱肉柱形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿道障害（結石を除く）	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿道狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	55	(3.3)	65	2.2	58	(3.5)	61	2.0	113	(3.4)	126	2.1
悪性および詳細不明の消化管新生物	9	(0.5)	9	0.3	10	(0.6)	10	0.3	19	(0.6)	19	0.3
結腸腺癌	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
胃腺癌	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
結腸癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
直腸癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胃癌	1	(0.1)	1	0.1	0				0				0			
遠隔転移を伴う胃癌	1	(0.1)	1	0.1	0				0				0			
遠隔転移を伴う結腸癌	0				0				0				1	(0.1)	1	0.1
遠隔転移を伴う膵癌	0				0				1	(0.1)	1	0.1	0			
結腸新生物	0				0				1	(0.1)	1	0.1	0			
結腸直腸癌	0				0				1	(0.1)	1	0.1	0			
口唇の悪性新生物、病期不明	1	(0.1)	1	0.1	0				0				0			
虫垂新生物	0				1	(0.1)	1	0.1	0				0			
膵癌	0				0				0				1	(0.1)	1	0.1
膵腺癌	0				0				0				1	(0.1)	1	0.1
悪性および詳細不明の呼吸器系および縦隔新生物	2	(0.2)	2	0.1	6	(0.7)	6	0.4	5	(0.6)	5	0.3	4	(0.5)	4	0.3
小細胞肺癌	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
気管支癌	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
喉頭扁平上皮癌	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
肺の悪性新生物	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
肺腺癌	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
肺癌第４期、細胞タイプ不明	0				1	(0.1)	1	0.1	0				0			
肺新生物	0				1	(0.1)	1	0.1	0				0			
肺腺癌第４期	0				1	(0.1)	1	0.1	0				0			
肺扁平上皮癌	0				0				0				1	(0.1)	1	0.1
非小細胞肺癌	0				0				0				1	(0.1)	1	0.1
悪性および詳細不明の男性生殖器系新生物	3	(0.4)	3	0.2	3	(0.4)	3	0.2	4	(0.5)	4	0.3	4	(0.5)	4	0.3
前立腺癌	3	(0.4)	3	0.2	2	(0.2)	2	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1
遠隔転移を伴う前立腺癌	0				1	(0.1)	1	0.1	0				0			
再発前立腺癌	0				0				0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胃癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う胃癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う結腸癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
遠隔転移を伴う膵癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結腸新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結腸直腸癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口唇の悪性新生物、病期不明	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
虫垂新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膵腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
悪性および詳細不明の呼吸器系および縦隔新生物	8	(0.5)	8	0.3	9	(0.5)	9	0.3	17	(0.5)	17	0.3
小細胞肺癌	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
気管支癌	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
喉頭扁平上皮癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肺の悪性新生物	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肺腺癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肺癌第４期、細胞タイプ不明	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺腺癌第４期	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺扁平上皮癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
非小細胞肺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
悪性および詳細不明の男性生殖器系新生物	6	(0.4)	6	0.2	8	(0.5)	8	0.3	14	(0.4)	14	0.2
前立腺癌	5	(0.3)	5	0.2	5	(0.3)	5	0.2	10	(0.3)	10	0.2
遠隔転移を伴う前立腺癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
再発前立腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
前立腺癌第１期	0				0				0				1	(0.1)	1	0.1
前立腺癌第３期	0				0				0				1	(0.1)	1	0.1
悪性および詳細不明の腎尿路系新生物	2	(0.2)	2	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1	4	(0.5)	5	0.3
膀胱移行上皮癌	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
移行上皮癌	1	(0.1)	1	0.1	0				0				0			
遠隔転移を伴う腎癌	1	(0.1)	1	0.1	0				0				0			
再発膀胱移行上皮癌	0				0				0				1	(0.1)	1	0.1
腎癌第１期	0				0				0				1	(0.1)	1	0.1
腎細胞癌	0				1	(0.1)	1	0.1	0				0			
腎明細胞癌	0				0				0				1	(0.1)	1	0.1
尿管癌	0				1	(0.1)	1	0.1	0				0			
膀胱移行上皮癌第２期	0				1	(0.1)	1	0.1	0				0			
膀胱新生物	0				0				0				1	(0.1)	1	0.1
悪性および詳細不明の内分泌新生物	1	(0.1)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
甲状腺新生物	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
成長ホルモン産生性下垂体腫瘍	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
褐色細胞腫	1	(0.1)	1	0.1	0				0				0			
乳頭様甲状腺癌	0				0				1	(0.1)	1	0.1	0			
傍神経節新生物	1	(0.1)	1	0.1	0				0				0			
悪性および詳細不明の乳房新生物（乳頭を含む）	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
浸潤性乳管癌	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
乳癌	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
乳癌第３期	0				0				0				1	(0.1)	1	0.1
乳房の上皮内癌	0				1	(0.1)	1	0.1	0				0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
前立腺癌第１期	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
前立腺癌第３期	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
悪性および詳細不明の腎尿路系新生物	6	(0.4)	6	0.2	6	(0.4)	7	0.2	12	(0.4)	13	0.2
膀胱移行上皮癌	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
移行上皮癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う腎癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
再発膀胱移行上皮癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎癌第１期	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎細胞癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎明細胞癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿管癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱移行上皮癌第２期	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
悪性および詳細不明の内分泌新生物	3	(0.2)	4	0.1	3	(0.2)	3	0.1	6	(0.2)	7	0.1
甲状腺新生物	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
成長ホルモン産生性下垂体腫瘍	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
褐色細胞腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳頭様甲状腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
傍神経節新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
悪性および詳細不明の乳房新生物（乳頭を含む）	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
浸潤性乳管癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
乳癌	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
乳癌第３期	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳房の上皮内癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
非ホジキンＢ細胞性リンパ腫	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
Ｂ細胞性リンパ腫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
Ｂ細胞性小リンパ球性リンパ腫	0				0				1	(0.1)	1	0.1	0			
節外周辺帯Ｂ細胞リンパ腫（ＭＡＬＴ型）	1	(0.1)	1	0.1	0				0				0			
良性内分泌新生物	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
良性副甲状腺腫瘍	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
甲状腺の良性新生物	0				0				0				1	(0.1)	1	0.1
悪性および詳細不明の肝胆道系新生物	1	(0.1)	1	0.1	0				2	(0.2)	3	0.2	0			
肝癌	1	(0.1)	1	0.1	0				0				0			
肝内胆管癌	0				0				1	(0.1)	2	0.1	0			
胆嚢腺癌	0				0				1	(0.1)	1	0.1	0			
悪性および詳細不明の皮膚新生物	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				0			
基底細胞癌	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
悪性黒色腫	1	(0.1)	1	0.1	0				0				0			
皮膚有棘細胞癌	0				1	(0.1)	1	0.1	0				0			
消化器の良性新生物	0				4	(0.5)	4	0.3	0				0			
大腸腺腫	0				4	(0.5)	4	0.3	0				0			
転移	2	(0.2)	3	0.2	1	(0.1)	1	0.1	0				0			
リンパ節転移	1	(0.1)	1	0.1	0				0				0			
肝転移	1	(0.1)	1	0.1	0				0				0			
中枢神経系転移	0				1	(0.1)	1	0.1	0				0			
肺転移	1	(0.1)	1	0.1	0				0				0			
白血病	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
慢性リンパ性白血病	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
非ホジキンＢ細胞性リンパ腫	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
Ｂ細胞性リンパ腫	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
Ｂ細胞性小リンパ球性リンパ腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
節外周辺帯Ｂ細胞リンパ腫（ＭＡＬＴ型）	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性内分泌新生物	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
良性副甲状腺腫瘍	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
甲状腺の良性新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
悪性および詳細不明の肝胆道系新生物	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
肝癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝内胆管癌	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
胆嚢腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
悪性および詳細不明の皮膚新生物	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
基底細胞癌	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
悪性黒色腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮膚有棘細胞癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化器の良性新生物	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
大腸腺腫	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
転移	3	(0.2)	4	0.1	0				3	(0.1)	4	0.1
リンパ節転移	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝転移	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
中枢神経系転移	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺転移	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
白血病	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
慢性リンパ性白血病	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
急性リンパ性白血病	0				0				0				1	(0.1)	1	0.1
急性骨髄性白血病	0				0				1	(0.1)	1	0.1	0			
良性女性生殖器系新生物	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
子宮平滑筋腫	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
卵巣胚細胞良性奇形腫	1	(0.1)	1	0.1	0				0				0			
その他および部位不明の良性新生物	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
真珠腫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
悪性および詳細不明の女性生殖器系新生物	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
子宮内膜腺癌	0				0				1	(0.1)	1	0.1	0			
子宮内膜肉腫	0				0				0				1	(0.1)	1	0.1
卵巣上皮癌	1	(0.1)	1	0.1	0				0				0			
悪性および詳細不明のその他および部位不明新生物	0				1	(0.1)	1	0.1	0				0			
扁平上皮癌	0				1	(0.1)	1	0.1	0				0			
悪性および詳細不明の骨格系新生物	0				1	(0.1)	1	0.1	0				0			
遠隔転移を伴う骨癌	0				1	(0.1)	1	0.1	0				0			
悪性および詳細不明の神経系新生物ＮＥＣ	0				0				0				1	(0.1)	1	0.1
退形成星細胞腫	0				0				0				1	(0.1)	1	0.1
眼球新生物	1	(0.1)	1	0.1	0				0				0			
脈絡膜黒色腫	1	(0.1)	1	0.1	0				0				0			
形質細胞新生物	0				0				0				1	(0.1)	1	0.1
形質細胞性骨髄腫	0				0				0				1	(0.1)	1	0.1
造血系新生物（白血病およびリンパ腫を除く）	1	(0.1)	1	0.1	0				0				0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
急性リンパ性白血病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性骨髄性白血病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性女性生殖器系新生物	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
子宮平滑筋腫	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
卵巣胚細胞良性奇形腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
その他および部位不明の良性新生物	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
真珠腫	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
悪性および詳細不明の女性生殖器系新生物	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
子宮内膜腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮内膜肉腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
卵巣上皮癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
悪性および詳細不明のその他および部位不明新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
扁平上皮癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
悪性および詳細不明の骨格系新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う骨癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
悪性および詳細不明の神経系新生物ＮＥＣ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
退形成星細胞腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼球新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脈絡膜黒色腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
形質細胞新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
形質細胞性骨髄腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
造血系新生物（白血病およびリンパ腫を除く）	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
リンパ節の良性新生物	1	(0.1)	1	0.1	0				0				0			
良性肝胆道系新生物	0				0				1	(0.1)	1	0.1	0			
肝腺腫	0				0				1	(0.1)	1	0.1	0			
良性腎尿路系新生物	0				1	(0.1)	1	0.1	0				0			
膀胱乳頭腫	0				1	(0.1)	1	0.1	0				0			
良性軟部組織新生物	0				1	(0.1)	1	0.1	0				0			
グロームス腫瘍	0				1	(0.1)	1	0.1	0				0			
胃腸障害	36	(4.4)	38	2.6	29	(3.5)	35	2.4	16	(2.0)	17	1.1	24	(2.9)	32	2.1
消化管徴候および症状	2	(0.2)	2	0.1	7	(0.9)	10	0.7	4	(0.5)	4	0.3	5	(0.6)	6	0.4
腹痛	1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1
嘔吐	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
悪心	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
下腹部痛	1	(0.1)	1	0.1	0				0				0			
上腹部痛	0				0				1	(0.1)	1	0.1	0			
心窩部不快感	0				1	(0.1)	1	0.1	0				0			
腹部腫瘤	0				1	(0.1)	1	0.1	0				0			
変色便	0				0				0				1	(0.1)	1	0.1
消化管運動および排泄障害	7	(0.9)	7	0.5	9	(1.1)	9	0.6	3	(0.4)	3	0.2	2	(0.2)	2	0.1
下痢	2	(0.2)	2	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1	1	(0.1)	1	0.1
胃食道逆流性疾患	3	(0.4)	3	0.2	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1
便秘	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
胃排出不全	1	(0.1)	1	0.1	0				0				0			
便習慣変化	0				1	(0.1)	1	0.1	0				0			
消化管出血ＮＥＣ	6	(0.7)	6	0.4	2	(0.2)	2	0.1	2	(0.2)	2	0.1	5	(0.6)	5	0.3
胃腸出血	3	(0.4)	3	0.2	0				0				3	(0.4)	3	0.2
上部消化管出血	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
メレナ	0				1	(0.1)	1	0.1	0				0			
下部消化管出血	1	(0.1)	1	0.1	0				0				0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
リンパ節の良性新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性肝胆道系新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝腺腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性腎尿路系新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱乳頭腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性軟部組織新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
グロームス腫瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃腸障害	65	(4.0)	73	2.5	40	(2.4)	49	1.6	105	(3.2)	122	2.0
消化管徴候および症状	9	(0.5)	12	0.4	9	(0.5)	10	0.3	18	(0.5)	22	0.4
腹痛	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
嘔吐	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
悪心	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
下腹部痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
上腹部痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心窩部不快感	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹部腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
変色便	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
消化管運動および排泄障害	16	(1.0)	16	0.5	5	(0.3)	5	0.2	21	(0.6)	21	0.4
下痢	6	(0.4)	6	0.2	3	(0.2)	3	0.1	9	(0.3)	9	0.2
胃食道逆流性疾患	6	(0.4)	6	0.2	1	(0.1)	1	<0.1	7	(0.2)	7	0.1
便秘	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
胃排出不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
便習慣変化	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管出血ＮＥＣ	8	(0.5)	8	0.3	7	(0.4)	7	0.2	15	(0.5)	15	0.3
胃腸出血	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
上部消化管出血	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
メレナ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
下部消化管出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
大腸出血	0				1	(0.1)	1	0.1	0				0			
腸出血	0				0				0				1	(0.1)	1	0.1
消化管炎症性疾患	4	(0.5)	4	0.3	2	(0.2)	2	0.1	3	(0.4)	3	0.2	3	(0.4)	5	0.3
胃炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
十二指腸炎	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
出血性胃炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
胃十二指腸炎	0				0				0				1	(0.1)	1	0.1
虚血性大腸炎	0				0				0				1	(0.1)	1	0.1
出血性腸炎	0				0				0				1	(0.1)	1	0.1
出血性直腸炎	0				0				1	(0.1)	1	0.1	0			
大腸炎	1	(0.1)	1	0.1	0				0				0			
潰瘍性大腸炎	0				1	(0.1)	1	0.1	0				0			
慢性胃炎	1	(0.1)	1	0.1	0				0				0			
消化管潰瘍および穿孔	4	(0.5)	4	0.3	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1
十二指腸潰瘍	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
消化性潰瘍	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
胃潰瘍	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
出血性胃潰瘍	2	(0.2)	2	0.1	0				0				0			
出血性十二指腸潰瘍	0				1	(0.1)	1	0.1	0				0			
膵外分泌障害	4	(0.5)	4	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1	5	(0.6)	5	0.3
膵炎	2	(0.2)	2	0.1	0				0				4	(0.5)	4	0.3
急性膵炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
膵嚢胞	1	(0.1)	1	0.1	0				0				0			
腹部ヘルニアおよびその他の腹壁状態	5	(0.6)	5	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
鼠径ヘルニア	3	(0.4)	3	0.2	0				0				1	(0.1)	1	0.1
臍ヘルニア	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
裂孔ヘルニア	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
消化管狭窄および閉塞	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
大腸出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腸出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
消化管炎症性疾患	6	(0.4)	6	0.2	6	(0.4)	8	0.3	12	(0.4)	14	0.2
胃炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
十二指腸炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
出血性胃炎	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
胃十二指腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
虚血性大腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性直腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
潰瘍性大腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
慢性胃炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管潰瘍および穿孔	7	(0.4)	7	0.2	4	(0.2)	4	0.1	11	(0.3)	11	0.2
十二指腸潰瘍	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
消化性潰瘍	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
胃潰瘍	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
出血性胃潰瘍	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
出血性十二指腸潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵外分泌障害	5	(0.3)	5	0.2	6	(0.4)	6	0.2	11	(0.3)	11	0.2
膵炎	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
急性膵炎	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
膵嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹部ヘルニアおよびその他の腹壁状態	6	(0.4)	6	0.2	3	(0.2)	3	0.1	9	(0.3)	9	0.2
鼠径ヘルニア	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
臍ヘルニア	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
裂孔ヘルニア	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
消化管狭窄および閉塞	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
胃イレウス	0				0				0				1	(0.1)	1	0.1
小腸捻転	0				1	(0.1)	1	0.1	0				0			
小腸閉塞	0				0				0				1	(0.1)	1	0.1
腸閉塞	1	(0.1)	1	0.1	0				0				0			
腹膜および後腹膜疾患	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
腹水	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
腹膜出血	1	(0.1)	1	0.1	0				0				0			
良性消化管新生物	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
大腸ポリープ	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
胃ポリープ	0				0				0				1	(0.1)	1	0.1
憩室疾患	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
憩室	0				1	(0.1)	1	0.1	0				0			
腸憩室	1	(0.1)	1	0.1	0				0				0			
消化管血行障害	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
胃腸虚血	0				0				0				1	(0.1)	1	0.1
腸管虚血	0				1	(0.1)	1	0.1	0				0			
口腔内軟部組織疾患	1	(0.1)	1	0.1	0				0				0			
口腔内潰瘍形成	1	(0.1)	1	0.1	0				0				0			
消化管の状態ＮＥＣ	0				1	(0.1)	1	0.1	0				0			
胃障害	0				1	(0.1)	1	0.1	0				0			
肛門および直腸の状態ＮＥＣ	1	(0.1)	1	0.1	0				0				0			
直腸脱	1	(0.1)	1	0.1	0				0				0			
呼吸器、胸郭および縦隔障害	17	(2.1)	18	1.2	19	(2.3)	27	1.9	20	(2.4)	24	1.6	24	(2.9)	28	1.8
呼吸器系障害ＮＥＣ	7	(0.9)	7	0.5	8	(1.0)	11	0.8	10	(1.2)	11	0.7	8	(1.0)	8	0.5
呼吸困難	3	(0.4)	3	0.2	4	(0.5)	4	0.3	3	(0.4)	3	0.2	4	(0.5)	4	0.3
呼吸不全	2	(0.2)	2	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2	3	(0.4)	3	0.2
急性呼吸不全	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胃イレウス	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
小腸捻転	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
小腸閉塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸閉塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹膜および後腹膜疾患	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
腹水	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
腹膜出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性消化管新生物	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
大腸ポリープ	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
胃ポリープ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
憩室疾患	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
憩室	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腸憩室	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管血行障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胃腸虚血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸管虚血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔内軟部組織疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔内潰瘍形成	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管の状態ＮＥＣ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肛門および直腸の状態ＮＥＣ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
直腸脱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
呼吸器、胸郭および縦隔障害	36	(2.2)	45	1.5	44	(2.7)	52	1.7	80	(2.4)	97	1.6
呼吸器系障害ＮＥＣ	15	(0.9)	18	0.6	18	(1.1)	19	0.6	33	(1.0)	37	0.6
呼吸困難	7	(0.4)	7	0.2	7	(0.4)	7	0.2	14	(0.4)	14	0.2
呼吸不全	5	(0.3)	5	0.2	6	(0.4)	6	0.2	11	(0.3)	11	0.2
急性呼吸不全	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
安静時呼吸困難	0				0				1	(0.1)	1	0.1	0			
呼吸窮迫	0				0				1	(0.1)	1	0.1	0			
呼吸停止	0				0				1	(0.1)	1	0.1	0			
低酸素症	1	(0.1)	1	0.1	0				0				0			
肺腫瘤	0				1	(0.1)	1	0.1	0				0			
喀血	0				1	(0.1)	3	0.2	0				0			
下気道障害（閉塞および感染を除く）	5	(0.6)	5	0.3	5	(0.6)	6	0.4	1	(0.1)	1	0.1	6	(0.7)	7	0.5
肺水腫	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3
急性肺水腫	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
誤嚥性肺炎	0				2	(0.2)	3	0.2	0				0			
肺うっ血	0				0				0				1	(0.1)	1	0.1
無気肺	1	(0.1)	1	0.1	0				0				0			
気管支障害（新生物を除く）	1	(0.1)	1	0.1	3	(0.4)	3	0.2	6	(0.7)	6	0.4	6	(0.7)	7	0.5
慢性閉塞性肺疾患	1	(0.1)	1	0.1	3	(0.4)	3	0.2	6	(0.7)	6	0.4	5	(0.6)	6	0.4
喘息	0				0				0				1	(0.1)	1	0.1
肺血管障害	2	(0.2)	2	0.1	5	(0.6)	5	0.3	1	(0.1)	1	0.1	4	(0.5)	4	0.3
肺塞栓症	2	(0.2)	2	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1	3	(0.4)	3	0.2
肺高血圧症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
胸膜障害	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	4	0.3	2	(0.2)	2	0.1
気胸	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
胸水	0				1	(0.1)	1	0.1	2	(0.2)	3	0.2	0			
胸水症	1	(0.1)	1	0.1	0				0				0			
胸膜炎	0				0				0				1	(0.1)	1	0.1
上気道障害（感染を除く）	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
喉頭狭窄	0				0				1	(0.1)	1	0.1	0			
鼻出血	0				1	(0.1)	1	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
安静時呼吸困難	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼吸窮迫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼吸停止	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
低酸素症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
喀血	1	(0.1)	3	0.1	0				1	(<0.1)	3	0.1
下気道障害（閉塞および感染を除く）	10	(0.6)	11	0.4	7	(0.4)	8	0.3	17	(0.5)	19	0.3
肺水腫	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
急性肺水腫	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
誤嚥性肺炎	2	(0.1)	3	0.1	0				2	(0.1)	3	0.1
肺うっ血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
無気肺	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
気管支障害（新生物を除く）	4	(0.2)	4	0.1	12	(0.7)	13	0.4	16	(0.5)	17	0.3
慢性閉塞性肺疾患	4	(0.2)	4	0.1	11	(0.7)	12	0.4	15	(0.5)	16	0.3
喘息	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺血管障害	7	(0.4)	7	0.2	5	(0.3)	5	0.2	12	(0.4)	12	0.2
肺塞栓症	6	(0.4)	6	0.2	4	(0.2)	4	0.1	10	(0.3)	10	0.2
肺高血圧症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胸膜障害	3	(0.2)	3	0.1	5	(0.3)	6	0.2	8	(0.2)	9	0.2
気胸	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
胸水	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
胸水症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胸膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
上気道障害（感染を除く）	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
喉頭狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鼻出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
胸郭障害（肺および胸膜を除く）	1	(0.1)	1	0.1	0				0				0			
後天性横隔膜性内臓転位	1	(0.1)	1	0.1	0				0				0			
傷害、中毒および処置合併症	23	(2.8)	26	1.7	18	(2.2)	20	1.4	18	(2.2)	22	1.5	23	(2.8)	27	1.8
損傷ＮＥＣ	15	(1.8)	16	1.1	12	(1.5)	12	0.8	13	(1.6)	14	0.9	13	(1.6)	15	1.0
転倒	9	(1.1)	9	0.6	4	(0.5)	4	0.3	7	(0.9)	7	0.5	7	(0.8)	7	0.5
交通事故	0				4	(0.5)	4	0.3	3	(0.4)	3	0.2	3	(0.4)	4	0.3
硬膜下血腫	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
頭部損傷	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
労働災害	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
外傷性血胸	0				0				1	(0.1)	1	0.1	0			
外傷性潰瘍	0				1	(0.1)	1	0.1	0				0			
挫傷	0				0				1	(0.1)	1	0.1	0			
四肢損傷	1	(0.1)	1	0.1	0				0				0			
創壊死	0				0				1	(0.1)	1	0.1	0			
創傷	1	(0.1)	1	0.1	0				0				0			
損傷	0				1	(0.1)	1	0.1	0				0			
動物咬傷	1	(0.1)	1	0.1	0				0				0			
肉離れ	0				0				0				1	(0.1)	1	0.1
皮膚擦過傷	0				0				0				1	(0.1)	1	0.1
裂傷	1	(0.1)	1	0.1	0				0				0			
腱断裂	0				0				0				1	(0.1)	1	0.1
骨および関節損傷	4	(0.5)	4	0.3	4	(0.5)	6	0.4	2	(0.2)	2	0.1	5	(0.6)	7	0.5
上腕骨骨折	0				2	(0.2)	3	0.2	0				1	(0.1)	1	0.1
足関節部骨折	2	(0.2)	2	0.1	0				0				0			
大腿骨骨折	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
半月板損傷	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
肋骨骨折	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胸郭障害（肺および胸膜を除く）	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
後天性横隔膜性内臓転位	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
傷害、中毒および処置合併症	41	(2.5)	46	1.6	41	(2.5)	49	1.6	82	(2.5)	95	1.6
損傷ＮＥＣ	27	(1.6)	28	1.0	26	(1.6)	29	1.0	53	(1.6)	57	1.0
転倒	13	(0.8)	13	0.4	14	(0.9)	14	0.5	27	(0.8)	27	0.5
交通事故	4	(0.2)	4	0.1	6	(0.4)	7	0.2	10	(0.3)	11	0.2
硬膜下血腫	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
頭部損傷	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
労働災害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
外傷性血胸	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外傷性潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
挫傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
四肢損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
創壊死	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
創傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
動物咬傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肉離れ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚擦過傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
裂傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腱断裂	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
骨および関節損傷	8	(0.5)	10	0.3	7	(0.4)	9	0.3	15	(0.5)	19	0.3
上腕骨骨折	2	(0.1)	3	0.1	1	(0.1)	1	<0.1	3	(0.1)	4	0.1
足関節部骨折	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
大腿骨骨折	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
半月板損傷	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肋骨骨折	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
外傷性骨折	1	(0.1)	1	0.1	0				0				0			
肩甲骨骨折	0				0				0				1	(0.1)	1	0.1
手骨折	0				0				0				1	(0.1)	1	0.1
脊椎圧迫骨折	0				0				1	(0.1)	1	0.1	0			
足骨折	0				0				0				1	(0.1)	1	0.1
頭蓋骨骨折	0				0				0				1	(0.1)	1	0.1
橈骨骨折	0				1	(0.1)	1	0.1	0				0			
処置による損傷および合併症ＮＥＣ	3	(0.4)	3	0.2	1	(0.1)	1	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1
移植血管合併症	0				0				1	(0.1)	1	0.1	0			
移植血管閉塞	0				0				1	(0.1)	1	0.1	0			
血管偽動脈瘤	1	(0.1)	1	0.1	0				0				0			
硬膜裂傷	0				0				1	(0.1)	1	0.1	0			
術後イレウス	0				1	(0.1)	1	0.1	0				0			
術後呼吸不全	1	(0.1)	1	0.1	0				0				0			
術後貧血	1	(0.1)	1	0.1	0				0				0			
処置後血腫	0				0				0				1	(0.1)	1	0.1
吻合不全	0				0				0				1	(0.1)	1	0.1
漿液腫	0				0				1	(0.1)	1	0.1	0			
投薬過誤	2	(0.2)	3	0.2	0				0				0			
誤薬投与	1	(0.1)	1	0.1	0				0				0			
誤用量投与	1	(0.1)	2	0.1	0				0				0			
曝露、化学的損傷および中毒	0				0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
各種物質毒性	0				0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
製品使用に関する問題	0				0				0				2	(0.2)	2	0.1
過量投与	0				0				0				1	(0.1)	1	0.1
企図的過量投与	0				0				0				1	(0.1)	1	0.1
物理的要因による損傷	0				1	(0.1)	1	0.1	0				0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
外傷性骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肩甲骨骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
手骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脊椎圧迫骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
足骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頭蓋骨骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
橈骨骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
処置による損傷および合併症ＮＥＣ	4	(0.2)	4	0.1	6	(0.4)	6	0.2	10	(0.3)	10	0.2
移植血管合併症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
移植血管閉塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管偽動脈瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
硬膜裂傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
術後イレウス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
術後呼吸不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
術後貧血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
処置後血腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
吻合不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
漿液腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
投薬過誤	2	(0.1)	3	0.1	0				2	(0.1)	3	0.1
誤薬投与	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
誤用量投与	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
曝露、化学的損傷および中毒	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
各種物質毒性	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
製品使用に関する問題	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
過量投与	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
企図的過量投与	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
物理的要因による損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
熱傷	0				1	(0.1)	1	0.1	0				0			
代謝および栄養障害	21	(2.6)	26	1.7	10	(1.2)	11	0.8	23	(2.8)	32	2.1	17	(2.1)	19	1.2
糖代謝障害（糖尿病を含む）	13	(1.6)	14	0.9	4	(0.5)	4	0.3	12	(1.5)	16	1.1	11	(1.3)	13	0.9
低血糖症	7	(0.9)	8	0.5	1	(0.1)	1	0.1	3	(0.4)	5	0.3	5	(0.6)	5	0.3
コントロール不良の糖尿病	2	(0.2)	2	0.1	0				5	(0.6)	7	0.5	4	(0.5)	5	0.3
高血糖	3	(0.4)	3	0.2	2	(0.2)	2	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
糖尿病	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
電解質および水分バランス異常	6	(0.7)	6	0.4	4	(0.5)	4	0.3	9	(1.1)	13	0.9	2	(0.2)	2	0.1
高カリウム血症	0				1	(0.1)	1	0.1	3	(0.4)	4	0.3	1	(0.1)	1	0.1
脱水	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
低ナトリウム血症	1	(0.1)	1	0.1	0				4	(0.5)	4	0.3	0			
水分過負荷	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1	0			
低カリウム血症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
血液量減少症	1	(0.1)	1	0.1	0				0				0			
電解質失調	0				0				1	(0.1)	1	0.1	0			
糖尿病合併症	1	(0.1)	2	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
糖尿病性ケトアシドーシス	1	(0.1)	2	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
プリンおよびピリミジン代謝障害	1	(0.1)	2	0.1	0				0				1	(0.1)	1	0.1
痛風	1	(0.1)	2	0.1	0				0				1	(0.1)	1	0.1
骨、カルシウム、マグネシウムおよびリン代謝障害	1	(0.1)	1	0.1	1	(0.1)	2	0.1	0				0			
低マグネシウム血症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
熱傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
代謝および栄養障害	31	(1.9)	37	1.3	40	(2.4)	51	1.7	71	(2.2)	88	1.5
糖代謝障害（糖尿病を含む）	17	(1.0)	18	0.6	23	(1.4)	29	1.0	40	(1.2)	47	0.8
低血糖症	8	(0.5)	9	0.3	8	(0.5)	10	0.3	16	(0.5)	19	0.3
コントロール不良の糖尿病	2	(0.1)	2	0.1	9	(0.5)	12	0.4	11	(0.3)	14	0.2
高血糖	5	(0.3)	5	0.2	6	(0.4)	6	0.2	11	(0.3)	11	0.2
糖尿病	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
電解質および水分バランス異常	10	(0.6)	10	0.3	11	(0.7)	15	0.5	21	(0.6)	25	0.4
高カリウム血症	1	(0.1)	1	<0.1	4	(0.2)	5	0.2	5	(0.2)	6	0.1
脱水	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
低ナトリウム血症	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
水分過負荷	3	(0.2)	3	0.1	1	(0.1)	2	0.1	4	(0.1)	5	0.1
低カリウム血症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血液量減少症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
電解質失調	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糖尿病合併症	1	(0.1)	2	0.1	3	(0.2)	3	0.1	4	(0.1)	5	0.1
糖尿病性ケトアシドーシス	1	(0.1)	2	0.1	3	(0.2)	3	0.1	4	(0.1)	5	0.1
プリンおよびピリミジン代謝障害	1	(0.1)	2	0.1	1	(0.1)	1	<0.1	2	(0.1)	3	0.1
痛風	1	(0.1)	2	0.1	1	(0.1)	1	<0.1	2	(0.1)	3	0.1
骨、カルシウム、マグネシウムおよびリン代謝障害	2	(0.1)	3	0.1	0				2	(0.1)	3	0.1
低マグネシウム血症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
低カルシウム血症	0				1	(0.1)	1	0.1	0				0			
酸・アルカリ障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
乳酸アシドーシス	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
アシドーシス	1	(0.1)	1	0.1	0				0				0			
食欲および総合的栄養摂取障害	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
成長障害	0				0				0				1	(0.1)	1	0.1
肥満	0				0				1	(0.1)	1	0.1	0			
筋骨格系および結合組織障害	12	(1.5)	14	0.9	15	(1.8)	16	1.1	21	(2.6)	29	1.9	19	(2.3)	22	1.4
関節障害	5	(0.6)	6	0.4	9	(1.1)	9	0.6	13	(1.6)	13	0.9	12	(1.5)	13	0.9
変形性関節症	5	(0.6)	6	0.4	6	(0.7)	6	0.4	8	(1.0)	8	0.5	10	(1.2)	10	0.7
関節炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
関節痛	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
変形性脊椎症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
関節リウマチ	0				1	(0.1)	1	0.1	0				0			
糖尿病性関節障害	0				0				1	(0.1)	1	0.1	0			
筋骨格系および結合組織障害ＮＥＣ	2	(0.2)	3	0.2	4	(0.5)	5	0.3	4	(0.5)	5	0.3	8	(1.0)	8	0.5
背部痛	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				5	(0.6)	5	0.3
筋骨格系胸痛	0				1	(0.1)	1	0.1	4	(0.5)	5	0.3	2	(0.2)	2	0.1
筋骨格痛	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
頚部痛	0				1	(0.1)	1	0.1	0				0			
四肢痛	1	(0.1)	2	0.1	0				0				0			
筋骨格系および結合組織変形（椎間板障害を含む）	4	(0.5)	4	0.3	1	(0.1)	1	0.1	4	(0.5)	7	0.5	1	(0.1)	1	0.1
腰部脊柱管狭窄症	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
椎間板突出	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
低カルシウム血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
酸・アルカリ障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
乳酸アシドーシス	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
アシドーシス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
食欲および総合的栄養摂取障害	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
成長障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肥満	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋骨格系および結合組織障害	27	(1.6)	30	1.0	40	(2.4)	51	1.7	67	(2.0)	81	1.4
関節障害	14	(0.9)	15	0.5	25	(1.5)	26	0.9	39	(1.2)	41	0.7
変形性関節症	11	(0.7)	12	0.4	18	(1.1)	18	0.6	29	(0.9)	30	0.5
関節炎	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
関節痛	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
変形性脊椎症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
関節リウマチ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病性関節障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋骨格系および結合組織障害ＮＥＣ	6	(0.4)	8	0.3	12	(0.7)	13	0.4	18	(0.5)	21	0.4
背部痛	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
筋骨格系胸痛	1	(0.1)	1	<0.1	6	(0.4)	7	0.2	7	(0.2)	8	0.1
筋骨格痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
頚部痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
四肢痛	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
筋骨格系および結合組織変形（椎間板障害を含む）	5	(0.3)	5	0.2	5	(0.3)	8	0.3	10	(0.3)	13	0.2
腰部脊柱管狭窄症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
椎間板突出	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
脊柱管狭窄症	0				1	(0.1)	1	0.1	1	(0.1)	4	0.3	0			
足変形	1	(0.1)	1	0.1	0				0				0			
椎間板障害	1	(0.1)	1	0.1	0				0				0			
筋障害	0				0				2	(0.2)	2	0.1	0			
筋痙縮	0				0				1	(0.1)	1	0.1	0			
線維筋痛	0				0				1	(0.1)	1	0.1	0			
腱、靱帯および軟骨障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
軟骨溶解	1	(0.1)	1	0.1	0				0				0			
肋軟骨炎	0				1	(0.1)	1	0.1	0				0			
滑膜および滑液包障害	0				0				1	(0.1)	1	0.1	0			
滑液嚢腫	0				0				1	(0.1)	1	0.1	0			
骨障害（先天性障害および骨折を除く）	0				0				1	(0.1)	1	0.1	0			
骨壊死	0				0				1	(0.1)	1	0.1	0			
一般・全身障害および投与部位の状態	17	(2.1)	17	1.1	9	(1.1)	11	0.8	21	(2.6)	23	1.5	14	(1.7)	15	1.0
全身障害ＮＥＣ	9	(1.1)	9	0.6	6	(0.7)	7	0.5	16	(2.0)	18	1.2	13	(1.6)	14	0.9
非心臓性胸痛	7	(0.9)	7	0.5	2	(0.2)	2	0.1	7	(0.9)	7	0.5	4	(0.5)	5	0.3
胸痛	1	(0.1)	1	0.1	3	(0.4)	3	0.2	5	(0.6)	6	0.4	2	(0.2)	2	0.1
胸部不快感	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
末梢性浮腫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
無力症	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
多臓器不全	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
歩行障害	0				0				0				2	(0.2)	2	0.1
全身性浮腫	1	(0.1)	1	0.1	0				0				0			
微石症	0				0				1	(0.1)	1	0.1	0			
致命的転帰	4	(0.5)	4	0.3	2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
死亡	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脊柱管狭窄症	1	(0.1)	1	<0.1	1	(0.1)	4	0.1	2	(0.1)	5	0.1
足変形	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
椎間板障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
筋障害	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
筋痙縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
線維筋痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腱、靱帯および軟骨障害	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
軟骨溶解	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肋軟骨炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
滑膜および滑液包障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
滑液嚢腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
骨障害（先天性障害および骨折を除く）	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
骨壊死	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
一般・全身障害および投与部位の状態	26	(1.6)	28	1.0	35	(2.1)	38	1.3	61	(1.9)	66	1.1
全身障害ＮＥＣ	15	(0.9)	16	0.5	29	(1.8)	32	1.1	44	(1.3)	48	0.8
非心臓性胸痛	9	(0.5)	9	0.3	11	(0.7)	12	0.4	20	(0.6)	21	0.4
胸痛	4	(0.2)	4	0.1	7	(0.4)	8	0.3	11	(0.3)	12	0.2
胸部不快感	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
末梢性浮腫	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
無力症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
多臓器不全	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
歩行障害	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
全身性浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
微石症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
致命的転帰	6	(0.4)	6	0.2	4	(0.2)	4	0.1	10	(0.3)	10	0.2
死亡	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
突然死	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
心突然死	1	(0.1)	1	0.1	0				0				0			
組織障害ＮＥＣ	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
化生	1	(0.1)	1	0.1	0				0				0			
壊死	1	(0.1)	1	0.1	0				0				0			
治癒不良	0				0				1	(0.1)	1	0.1	0			
体温異常	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
発熱	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
悪性高熱	0				1	(0.1)	1	0.1	0				0			
医療機器に関する問題	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
医療機器機能不良	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
血管障害	19	(2.3)	22	1.5	8	(1.0)	8	0.6	16	(2.0)	16	1.1	17	(2.1)	18	1.2
動脈硬化、狭窄、血流障害および壊死	6	(0.7)	6	0.4	2	(0.2)	2	0.1	4	(0.5)	4	0.3	5	(0.6)	5	0.3
末梢動脈閉塞性疾患	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
四肢壊死	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
大腿動脈閉塞	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
大動脈狭窄	2	(0.2)	2	0.1	0				0				0			
末梢動脈狭窄	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
動脈不全	0				0				1	(0.1)	1	0.1	0			
末梢性虚血	0				0				1	(0.1)	1	0.1	0			
高血圧性血管障害	5	(0.6)	5	0.3	2	(0.2)	2	0.1	3	(0.4)	3	0.2	5	(0.6)	5	0.3
高血圧	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
高血圧クリーゼ	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
高血圧緊急症	3	(0.4)	3	0.2	0				0				0			
血圧低下、非特異的血圧障害およびショック	4	(0.5)	4	0.3	0				4	(0.5)	4	0.3	4	(0.5)	4	0.3
低血圧	2	(0.2)	2	0.1	0				3	(0.4)	3	0.2	3	(0.4)	3	0.2

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
突然死	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心突然死	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
組織障害ＮＥＣ	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
化生	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
壊死	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
治癒不良	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
体温異常	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
発熱	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
悪性高熱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
医療機器に関する問題	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
医療機器機能不良	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
血管障害	27	(1.6)	30	1.0	33	(2.0)	34	1.1	60	(1.8)	64	1.1
動脈硬化、狭窄、血流障害および壊死	8	(0.5)	8	0.3	9	(0.5)	9	0.3	17	(0.5)	17	0.3
末梢動脈閉塞性疾患	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
四肢壊死	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
大腿動脈閉塞	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
大動脈狭窄	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
末梢動脈狭窄	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
動脈不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢性虚血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高血圧性血管障害	7	(0.4)	7	0.2	8	(0.5)	8	0.3	15	(0.5)	15	0.3
高血圧	2	(0.1)	2	0.1	6	(0.4)	6	0.2	8	(0.2)	8	0.1
高血圧クリーゼ	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
高血圧緊急症	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
血圧低下、非特異的血圧障害およびショック	4	(0.2)	4	0.1	8	(0.5)	8	0.3	12	(0.4)	12	0.2
低血圧	2	(0.1)	2	0.1	6	(0.4)	6	0.2	8	(0.2)	8	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
起立性低血圧	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
出血性ショック	0				0				1	(0.1)	1	0.1	0			
循環虚脱	1	(0.1)	1	0.1	0				0				0			
血管障害ＮＥＣ	0				0				2	(0.2)	2	0.1	3	(0.4)	3	0.2
末梢血管障害	0				0				2	(0.2)	2	0.1	3	(0.4)	3	0.2
塞栓症および血栓症	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
末梢動脈血栓症	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
深部静脈血栓症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
瘤および動脈解離	2	(0.2)	3	0.2	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
大動脈瘤	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
大動脈解離	0				0				0				1	(0.1)	1	0.1
末梢動脈瘤	1	(0.1)	1	0.1	0				0				0			
血管の炎症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
血管炎	0				0				1	(0.1)	1	0.1	0			
側頭動脈炎	1	(0.1)	1	0.1	0				0				0			
血管性出血障害	1	(0.1)	2	0.1	0				0				0			
血腫	1	(0.1)	1	0.1	0				0				0			
腹腔内血腫	1	(0.1)	1	0.1	0				0				0			
静脈瘤	0				1	(0.1)	1	0.1	0				0			
静脈瘤	0				1	(0.1)	1	0.1	0				0			
眼障害	12	(1.5)	15	1.0	10	(1.2)	11	0.8	7	(0.9)	7	0.5	13	(1.6)	16	1.0
網膜、脈絡膜および硝子体の出血および血管障害	7	(0.9)	7	0.5	5	(0.6)	6	0.4	2	(0.2)	2	0.1	4	(0.5)	4	0.3
糖尿病網膜症	4	(0.5)	4	0.3	2	(0.2)	3	0.2	2	(0.2)	2	0.1	4	(0.5)	4	0.3
硝子体出血	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				0			
出血性網膜症	1	(0.1)	1	0.1	0				0				0			
網膜動脈閉塞	0				1	(0.1)	1	0.1	0				0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
起立性低血圧	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
出血性ショック	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
循環虚脱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管障害ＮＥＣ	0				5	(0.3)	5	0.2	5	(0.2)	5	0.1
末梢血管障害	0				5	(0.3)	5	0.2	5	(0.2)	5	0.1
塞栓症および血栓症	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
末梢動脈血栓症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
深部静脈血栓症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
瘤および動脈解離	3	(0.2)	4	0.1	1	(0.1)	1	<0.1	4	(0.1)	5	0.1
大動脈瘤	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
大動脈解離	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管の炎症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血管炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
側頭動脈炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管性出血障害	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
血腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹腔内血腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
静脈瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
静脈瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼障害	22	(1.3)	26	0.9	20	(1.2)	23	0.8	42	(1.3)	49	0.8
網膜、脈絡膜および硝子体の出血および血管障害	12	(0.7)	13	0.4	6	(0.4)	6	0.2	18	(0.5)	19	0.3
糖尿病網膜症	6	(0.4)	7	0.2	6	(0.4)	6	0.2	12	(0.4)	13	0.2
硝子体出血	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
出血性網膜症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
網膜動脈閉塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
眼前方部構造変化、沈着および変性	3	(0.4)	4	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1	6	(0.7)	7	0.5
白内障	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	5	(0.6)	6	0.4
核性白内障	1	(0.1)	2	0.1	0				0				0			
眼瞼皮膚のたるみ	1	(0.1)	1	0.1	0				0				0			
皮質白内障	0				0				0				1	(0.1)	1	0.1
眼部構造変化、沈着および変性ＮＥＣ	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
黄斑線維症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
網膜剥離	0				0				0				2	(0.2)	2	0.1
網膜変性	1	(0.1)	1	0.1	0				0				0			
眼部感染、刺激症状および炎症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
黄斑浮腫	0				1	(0.1)	1	0.1	0				0			
虹彩毛様体炎	0				0				0				1	(0.1)	1	0.1
嚢胞様黄斑浮腫	1	(0.1)	1	0.1	0				0				0			
視覚障害	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
失明	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
複視	1	(0.1)	1	0.1	0				0				0			
緑内障および高眼圧症	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
緑内障	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
開放隅角緑内障	0				0				0				1	(0.1)	1	0.1
眼部出血および血管障害ＮＥＣ	0				2	(0.2)	2	0.1	0				0			
虚血性視神経症	0				2	(0.2)	2	0.1	0				0			
眼神経筋障害	0				0				1	(0.1)	1	0.1	0			
眼瞼下垂	0				0				1	(0.1)	1	0.1	0			
肝胆道系障害	11	(1.3)	12	0.8	6	(0.7)	7	0.5	14	(1.7)	19	1.3	8	(1.0)	9	0.6

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
眼前方部構造変化、沈着および変性	4	(0.2)	5	0.2	7	(0.4)	8	0.3	11	(0.3)	13	0.2
白内障	2	(0.1)	2	0.1	6	(0.4)	7	0.2	8	(0.2)	9	0.2
核性白内障	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
眼瞼皮膚のたるみ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮質白内障	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼部構造変化、沈着および変性ＮＥＣ	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
黄斑線維症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
網膜剥離	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
網膜変性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼部感染、刺激症状および炎症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
黄斑浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
虹彩毛様体炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
嚢胞様黄斑浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
視覚障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
失明	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
複視	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
緑内障および高眼圧症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
緑内障	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
開放隅角緑内障	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼部出血および血管障害ＮＥＣ	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
虚血性視神経症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
眼神経筋障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼瞼下垂	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝胆道系障害	17	(1.0)	19	0.6	22	(1.3)	28	0.9	39	(1.2)	47	0.8

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
胆嚢障害	8	(1.0)	9	0.6	2	(0.2)	3	0.2	12	(1.5)	14	0.9	5	(0.6)	6	0.4
急性胆嚢炎	3	(0.4)	3	0.2	0				6	(0.7)	6	0.4	2	(0.2)	2	0.1
胆石症	4	(0.5)	4	0.3	2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
胆嚢炎	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
水腫性胆嚢炎	1	(0.1)	1	0.1	0				0				0			
胆嚢ポリープ	0				0				1	(0.1)	1	0.1	0			
胆嚢壊死	0				0				1	(0.1)	1	0.1	0			
閉塞性胆石症	1	(0.1)	1	0.1	0				0				0			
慢性胆嚢炎	0				0				0				1	(0.1)	1	0.1
胆管系障害	2	(0.2)	2	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
胆管結石	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
胆道仙痛	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
胆管炎	1	(0.1)	1	0.1	0				0				0			
肝および肝胆道系障害	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
肝硬変	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
虚血性肝炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
黄疸	1	(0.1)	1	0.1	0				0				0			
肝臓うっ血	0				0				0				1	(0.1)	1	0.1
胆汁うっ滞	0				0				1	(0.1)	1	0.1	0			
皮膚および皮下組織障害	13	(1.6)	16	1.1	3	(0.4)	4	0.3	7	(0.9)	7	0.5	6	(0.7)	10	0.7
皮膚および皮下組織障害ＮＥＣ	8	(1.0)	10	0.7	1	(0.1)	1	0.1	4	(0.5)	4	0.3	6	(0.7)	10	0.7
糖尿病性足病変	6	(0.7)	7	0.5	1	(0.1)	1	0.1	3	(0.4)	3	0.2	5	(0.6)	8	0.5
皮膚潰瘍	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1	1	(0.1)	2	0.1
表皮および皮膚異常	4	(0.5)	5	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
乾癬	1	(0.1)	2	0.1	0				1	(0.1)	1	0.1	0			
皮膚壊死	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
そう痒症	0				1	(0.1)	1	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胆嚢障害	10	(0.6)	12	0.4	17	(1.0)	20	0.7	27	(0.8)	32	0.5
急性胆嚢炎	3	(0.2)	3	0.1	8	(0.5)	8	0.3	11	(0.3)	11	0.2
胆石症	6	(0.4)	6	0.2	4	(0.2)	4	0.1	10	(0.3)	10	0.2
胆嚢炎	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
水腫性胆嚢炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆嚢ポリープ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆嚢壊死	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
閉塞性胆石症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
慢性胆嚢炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆管系障害	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
胆管結石	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
胆道仙痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胆管炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝および肝胆道系障害	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
肝硬変	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
虚血性肝炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
黄疸	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝臓うっ血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆汁うっ滞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚および皮下組織障害	16	(1.0)	20	0.7	13	(0.8)	17	0.6	29	(0.9)	37	0.6
皮膚および皮下組織障害NEC	9	(0.5)	11	0.4	10	(0.6)	14	0.5	19	(0.6)	25	0.4
糖尿病性足病変	7	(0.4)	8	0.3	8	(0.5)	11	0.4	15	(0.5)	19	0.3
皮膚潰瘍	3	(0.2)	3	0.1	2	(0.1)	3	0.1	5	(0.2)	6	0.1
表皮および皮膚異常	6	(0.4)	7	0.2	2	(0.1)	2	0.1	8	(0.2)	9	0.2
乾癬	1	(0.1)	2	0.1	1	(0.1)	1	<0.1	2	(0.1)	3	0.1
皮膚壊死	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
そう痒症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
スティーブンス・ジョンソン症候群	1	(0.1)	1	0.1	0				0				0			
丘疹性皮疹	0				0				1	(0.1)	1	0.1	0			
褥瘡性潰瘍	1	(0.1)	1	0.1	0				0				0			
角化および皮膚異栄養性障害	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
過角化	0				0				1	(0.1)	1	0.1	0			
日光角化症	1	(0.1)	1	0.1	0				0				0			
血管浮腫および蕁麻疹	0				1	(0.1)	1	0.1	0				0			
血管浮腫	0				1	(0.1)	1	0.1	0				0			
臨床検査	4	(0.5)	9	0.6	5	(0.6)	6	0.4	5	(0.6)	8	0.5	7	(0.8)	7	0.5
心血管系検査（酵素検査を除く）	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
冠血管造影	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
駆出率減少	1	(0.1)	1	0.1	0				0				0			
心カテーテル検査	0				0				1	(0.1)	1	0.1	0			
心電図ＱＴ延長	0				1	(0.1)	1	0.1	0				0			
心電図ＳＴ部分異常	0				0				1	(0.1)	1	0.1	0			
心電図Ｔ波逆転	0				0				1	(0.1)	1	0.1	0			
心電図変化	0				0				0				1	(0.1)	1	0.1
代謝、栄養学的および血液ガス検査	1	(0.1)	6	0.4	0				0				2	(0.2)	2	0.1
血中ブドウ糖増加	1	(0.1)	6	0.4	0				0				1	(0.1)	1	0.1
血中ブドウ糖変動	0				0				0				1	(0.1)	1	0.1
酵素検査ＮＥＣ	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
トロポニン増加	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
血中アルカリホスファターゼ増加	0				0				1	(0.1)	1	0.1	0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
スティーブンス・ジョンソン症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
丘疹性皮疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
褥瘡性潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
角化および皮膚異栄養性障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
過角化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
日光角化症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管浮腫および蕁麻疹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
臨床検査	9	(0.5)	15	0.5	12	(0.7)	15	0.5	21	(0.6)	30	0.5
心血管系検査（酵素検査を除く）	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
冠血管造影	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
駆出率減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心カテーテル検査	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図ＱＴ延長	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心電図ＳＴ部分異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図Ｔ波逆転	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図変化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
代謝、栄養学的および血液ガス検査	1	(0.1)	6	0.2	2	(0.1)	2	0.1	3	(0.1)	8	0.1
血中ブドウ糖増加	1	(0.1)	6	0.2	1	(0.1)	1	<0.1	2	(0.1)	7	0.1
血中ブドウ糖変動	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
酵素検査ＮＥＣ	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
トロポニン増加	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
血中アルカリホスファターゼ増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肝胆道系検査	0				1	(0.1)	1	0.1	1	(0.1)	2	0.1	0			
トランスアミナーゼ上昇	0				0				1	(0.1)	1	0.1	0			
肝機能検査異常	0				1	(0.1)	1	0.1	0				0			
血中ビリルビン増加	0				0				1	(0.1)	1	0.1	0			
消化管検査	1	(0.1)	1	0.1	1	(0.1)	2	0.1	0				0			
アミラーゼ増加	0				1	(0.1)	1	0.1	0				0			
リパーゼ増加	0				1	(0.1)	1	0.1	0				0			
膵酵素増加	1	(0.1)	1	0.1	0				0				0			
腎尿路系検査および尿検査	0				0				1	(0.1)	2	0.1	0			
血中クレアチニン増加	0				0				1	(0.1)	1	0.1	0			
血中尿素増加	0				0				1	(0.1)	1	0.1	0			
身体的診察および器官系の状態に関する事項	0				1	(0.1)	1	0.1	0				0			
体重減少	0				1	(0.1)	1	0.1	0				0			
微生物学的および血清学的検査	0				0				0				1	(0.1)	1	0.1
細菌検査陽性	0				0				0				1	(0.1)	1	0.1
血液およびリンパ系障害	7	(0.9)	7	0.5	7	(0.9)	7	0.5	3	(0.4)	3	0.2	5	(0.6)	6	0.4
非溶血性貧血と骨髄抑制	5	(0.6)	5	0.3	6	(0.7)	6	0.4	2	(0.2)	2	0.1	3	(0.4)	3	0.2
貧血	3	(0.4)	3	0.2	4	(0.5)	4	0.3	2	(0.2)	2	0.1	1	(0.1)	1	0.1
出血性貧血	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
小球性貧血	0				0				0				1	(0.1)	1	0.1
鉄欠乏性貧血	1	(0.1)	1	0.1	0				0				0			
脾臓、リンパ節および細網内皮系障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
縦隔リンパ節腫脹	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
リンパ節症	1	(0.1)	1	0.1	0				0				0			
脾腫	0				0				0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肝胆道系検査	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
トランスアミナーゼ上昇	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝機能検査異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中ビリルビン増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
消化管検査	2	(0.1)	3	0.1	0				2	(0.1)	3	0.1
アミラーゼ増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
リパーゼ増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵酵素増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎尿路系検査および尿検査	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
血中クレアチニン増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中尿素増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
身体的診察および器官系の状態に関する事項	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
体重減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
微生物学的および血清学的検査	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌検査陽性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血液およびリンパ系障害	14	(0.9)	14	0.5	8	(0.5)	9	0.3	22	(0.7)	23	0.4
非溶血性貧血と骨髄抑制	11	(0.7)	11	0.4	5	(0.3)	5	0.2	16	(0.5)	16	0.3
貧血	7	(0.4)	7	0.2	3	(0.2)	3	0.1	10	(0.3)	10	0.2
出血性貧血	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
小球性貧血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鉄欠乏性貧血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脾臓、リンパ節および細網内皮系障害	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
縦隔リンパ節腫脹	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
リンパ節症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脾腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
脾静脈血栓症	0				0				0				1	(0.1)	1	0.1
血小板障害	0				0				0				1	(0.1)	1	0.1
血小板減少症	0				0				0				1	(0.1)	1	0.1
白血球障害	1	(0.1)	1	0.1	0				0				0			
白血球増加症	1	(0.1)	1	0.1	0				0				0			
生殖系および乳房障害	5	(0.6)	5	0.3	5	(0.6)	5	0.3	4	(0.5)	5	0.3	3	(0.4)	3	0.2
前立腺障害（感染および炎症を除く）	4	(0.5)	4	0.3	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
良性前立腺肥大症	3	(0.4)	3	0.2	2	(0.2)	2	0.1	0				0			
前立腺腫大	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
前立腺閉塞	0				0				1	(0.1)	1	0.1	0			
子宮、骨盤および広間膜障害	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
膣脱	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
子宮ポリープ	0				0				1	(0.1)	1	0.1	0			
子宮内膜増殖症	0				0				1	(0.1)	1	0.1	0			
膀胱瘤	0				0				0				1	(0.1)	1	0.1
精巣および精巣上体障害	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
精巣上体圧痛	0				0				1	(0.1)	1	0.1	0			
精巣嚢胞	1	(0.1)	1	0.1	0				0				0			
月経周期および子宮出血障害	0				1	(0.1)	1	0.1	0				0			
月経過多	0				1	(0.1)	1	0.1	0				0			
性機能および生殖能障害	0				1	(0.1)	1	0.1	0				0			
勃起不全	0				1	(0.1)	1	0.1	0				0			
卵巣および卵管障害	0				0				0				1	(0.1)	1	0.1
卵巣嚢胞	0				0				0				1	(0.1)	1	0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脾静脈血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血小板障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血小板減少症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
白血球障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
白血球増加症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
生殖系および乳房障害	10	(0.6)	10	0.3	7	(0.4)	8	0.3	17	(0.5)	18	0.3
前立腺障害（感染および炎症を除く）	6	(0.4)	6	0.2	2	(0.1)	2	0.1	8	(0.2)	8	0.1
良性前立腺肥大症	5	(0.3)	5	0.2	0				5	(0.2)	5	0.1
前立腺腫大	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
前立腺閉塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮、骨盤および広間膜障害	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
膣脱	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
子宮ポリープ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮内膜増殖症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膀胱瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精巣および精巣上体障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
精巣上体圧痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精巣嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
月経周期および子宮出血障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
月経過多	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
性機能および生殖能障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
勃起不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
卵巣および卵管障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
卵巣嚢胞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
精神障害	3	(0.4)	3	0.2	6	(0.7)	6	0.4	5	(0.6)	6	0.4	3	(0.4)	3	0.2
精神医学的障害ＮＥＣ	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
精神状態変化	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
抑うつ性気分障害	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
うつ病	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
譫妄（錯乱を含む）	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
譫妄	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
錯乱状態	0				1	(0.1)	1	0.1	0				0			
不安障害および不安症状	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
心的外傷後ストレス障害	0				0				1	(0.1)	1	0.1	0			
不安	0				1	(0.1)	1	0.1	0				0			
睡眠障害	1	(0.1)	1	0.1	0				0				0			
睡眠時驚愕	1	(0.1)	1	0.1	0				0				0			
統合失調症およびその他の精神障害	0				1	(0.1)	1	0.1	0				0			
統合失調感情障害	0				1	(0.1)	1	0.1	0				0			
内分泌障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
甲状腺障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
甲状腺腫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
甲状腺機能亢進症	1	(0.1)	1	0.1	0				0				0			
視床下部および下垂体障害	0				0				1	(0.1)	1	0.1	0			
抗利尿ホルモン不適合分泌	0				0				1	(0.1)	1	0.1	0			
耳および迷路障害	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	0			
中耳障害（先天性障害を除く）	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
鼓膜穿孔	1	(0.1)	1	0.1	0				0				0			

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
精神障害	9	(0.5)	9	0.3	8	(0.5)	9	0.3	17	(0.5)	18	0.3
精神医学的障害ＮＥＣ	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
精神状態変化	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
抑うつ性気分障害	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
うつ病	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
譫妄（錯乱を含む）	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
譫妄	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
錯乱状態	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
不安障害および不安症状	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心的外傷後ストレス障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
不安	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
睡眠障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
睡眠時驚愕	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
統合失調症およびその他の精神障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
統合失調感情障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
内分泌障害	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
甲状腺障害	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
甲状腺腫	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
甲状腺機能亢進症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
視床下部および下垂体障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
抗利尿ホルモン不適合分泌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
耳および迷路障害	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
中耳障害（先天性障害を除く）	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
鼓膜穿孔	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
耳硬化症	0				0				1	(0.1)	1	0.1	0			
聴覚障害	0				0				1	(0.1)	1	0.1	0			
感音性難聴	0				0				1	(0.1)	1	0.1	0			
内耳および第８脳神経障害	0				0				1	(0.1)	1	0.1	0			
回転性めまい	0				0				1	(0.1)	1	0.1	0			
免疫系障害	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
アレルギー性疾患	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
アナフィラキシーショック	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
過敏症	1	(0.1)	1	0.1	0				0				0			
薬物過敏症	0				0				0				1	(0.1)	1	0.1
先天性、家族性および遺伝性障害	0				1	(0.1)	1	0.1	0				0			
先天性生殖器系および乳房障害	0				1	(0.1)	1	0.1	0				0			
包茎	0				1	(0.1)	1	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Serious adverse events by system organ class, high level group term and preferred term - summary - on-treatment - safety analysis set

System organ class High level group term Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
耳硬化症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
聴覚障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感音性難聴	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
内耳および第８脳神経障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
回転性めまい	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
免疫系障害	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
アレルギー性疾患	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
アナフィラキシーショック	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
過敏症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
薬物過敏症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
先天性、家族性および遺伝性障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
先天性生殖器系および乳房障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
包茎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.25.2- 3　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（器官別大分類及び基本語別） - on-treatment 期間 - 安全性解析対象集団

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	823				819				819				825			
Exposure time (year)	1488.3				1443.9				1508.0				1526.8			
Events	380	(46.2)	1252	84.1	432	(52.7)	1563	108.3	292	(35.7)	718	47.6	259	(31.4)	606	39.7
胃腸障害	254	(30.9)	713	47.9	307	(37.5)	930	64.4	137	(16.7)	284	18.8	123	(14.9)	219	14.3
悪心	111	(13.5)	179	12.0	156	(19.0)	237	16.4	46	(5.6)	58	3.8	50	(6.1)	69	4.5
下痢	91	(11.1)	169	11.4	106	(12.9)	166	11.5	54	(6.6)	93	6.2	44	(5.3)	54	3.5
嘔吐	56	(6.8)	78	5.2	91	(11.1)	130	9.0	23	(2.8)	28	1.9	16	(1.9)	20	1.3
消化不良	34	(4.1)	46	3.1	44	(5.4)	64	4.4	6	(0.7)	7	0.5	4	(0.5)	4	0.3
腹部不快感	27	(3.3)	59	4.0	33	(4.0)	83	5.7	18	(2.2)	25	1.7	6	(0.7)	10	0.7
便秘	19	(2.3)	23	1.5	42	(5.1)	53	3.7	9	(1.1)	9	0.6	11	(1.3)	11	0.7
腹痛	30	(3.6)	32	2.2	21	(2.6)	25	1.7	15	(1.8)	17	1.1	14	(1.7)	16	1.0
上腹部痛	18	(2.2)	20	1.3	27	(3.3)	33	2.3	11	(1.3)	12	0.8	7	(0.8)	7	0.5
腹部膨満	14	(1.7)	20	1.3	18	(2.2)	22	1.5	7	(0.9)	10	0.7	5	(0.6)	5	0.3
放屁	11	(1.3)	19	1.3	22	(2.7)	26	1.8	4	(0.5)	5	0.3	4	(0.5)	5	0.3
胃食道逆流性疾患	11	(1.3)	17	1.1	13	(1.6)	15	1.0	3	(0.4)	3	0.2	1	(0.1)	1	0.1
おくび	10	(1.2)	12	0.8	16	(2.0)	18	1.2	0				0			
胃炎	5	(0.6)	5	0.3	9	(1.1)	10	0.7	1	(0.1)	1	0.1	1	(0.1)	1	0.1
胃腸障害	3	(0.4)	3	0.2	7	(0.9)	7	0.5	0				0			
膵炎	5	(0.6)	5	0.3	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2
胃排出不全	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0				2	(0.2)	2	0.1
下腹部痛	0				1	(0.1)	1	0.1	0				4	(0.5)	4	0.3
過敏性腸症候群	3	(0.4)	3	0.2	2	(0.2)	2	0.1	0				0			
急性膵炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
口内乾燥	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
レッチング	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
心窩部不快感	1	(0.1)	2	0.1	2	(0.2)	3	0.2	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	1642				1644				3286			
Exposure time (year)	2932.2				3034.8				5967.0			
Events	812	(49.5)	2815	96.0	551	(33.5)	1324	43.6	1363	(41.5)	4139	69.4
胃腸障害	561	(34.2)	1643	56.0	260	(15.8)	503	16.6	821	(25.0)	2146	36.0
悪心	267	(16.3)	416	14.2	96	(5.8)	127	4.2	363	(11.0)	543	9.1
下痢	197	(12.0)	335	11.4	98	(6.0)	147	4.8	295	(9.0)	482	8.1
嘔吐	147	(9.0)	208	7.1	39	(2.4)	48	1.6	186	(5.7)	256	4.3
消化不良	78	(4.8)	110	3.8	10	(0.6)	11	0.4	88	(2.7)	121	2.0
腹部不快感	60	(3.7)	142	4.8	24	(1.5)	35	1.2	84	(2.6)	177	3.0
便秘	61	(3.7)	76	2.6	20	(1.2)	20	0.7	81	(2.5)	96	1.6
腹痛	51	(3.1)	57	1.9	29	(1.8)	33	1.1	80	(2.4)	90	1.5
上腹部痛	45	(2.7)	53	1.8	18	(1.1)	19	0.6	63	(1.9)	72	1.2
腹部膨満	32	(1.9)	42	1.4	12	(0.7)	15	0.5	44	(1.3)	57	1.0
放屁	33	(2.0)	45	1.5	8	(0.5)	10	0.3	41	(1.2)	55	0.9
胃食道逆流性疾患	24	(1.5)	32	1.1	4	(0.2)	4	0.1	28	(0.9)	36	0.6
おくび	26	(1.6)	30	1.0	0				26	(0.8)	30	0.5
胃炎	14	(0.9)	15	0.5	2	(0.1)	2	0.1	16	(0.5)	17	0.3
胃腸障害	10	(0.6)	10	0.3	0				10	(0.3)	10	0.2
膵炎	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
胃排出不全	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
下腹部痛	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
過敏性腸症候群	5	(0.3)	5	0.2	0				5	(0.2)	5	0.1
急性膵炎	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
口内乾燥	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
レッチング	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
心窩部不快感	3	(0.2)	5	0.2	0				3	(0.1)	5	0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
軟便	3	(0.4)	3	0.2	0				0				0			
排便回数増加	0				0				3	(0.4)	3	0.2	0			
嚥下障害	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
びらん性胃炎	0				2	(0.2)	2	0.1	0				0			
胃腸音異常	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
呼気臭	0				2	(0.2)	2	0.1	0				0			
硬便	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
十二指腸炎	0				2	(0.2)	2	0.1	0				0			
大腸炎	2	(0.2)	2	0.1	0				0				0			
排便回数減少	0				2	(0.2)	2	0.1	0				0			
慢性胃炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
裂孔ヘルニア	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
キライディティ症候群	1	(0.1)	1	0.1	0				0				0			
胃ポリープ	0				1	(0.1)	1	0.1	0				0			
胃十二指腸炎	0				1	(0.1)	1	0.1	0				0			
胃障害	0				1	(0.1)	1	0.1	0				0			
胃食道括約筋機能不全	0				0				1	(0.1)	1	0.1	0			
逆流性胃炎	1	(0.1)	1	0.1	0				0				0			
空気嚥下	0				1	(0.1)	1	0.1	0				0			
口腔内潰瘍形成	0				0				1	(0.1)	1	0.1	0			
口唇腫脹	0				0				1	(0.1)	1	0.1	0			
口唇浮腫	1	(0.1)	3	0.2	0				0				0			
十二指腸潰瘍	0				1	(0.1)	1	0.1	0				0			
小腸炎	0				1	(0.1)	2	0.1	0				0			
消化管運動過剰	1	(0.1)	1	0.1	0				0				0			
消化器痛	0				1	(0.1)	1	0.1	0				0			
食中毒	0				1	(0.1)	1	0.1	0				0			
食道憩室	0				0				1	(0.1)	1	0.1	0			
舌腫脹	0				0				1	(0.1)	1	0.1	0			

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
軟便	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
排便回数増加	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
嚥下障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
びらん性胃炎	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
胃腸音異常	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
呼気臭	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
硬便	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
十二指腸炎	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
大腸炎	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
排便回数減少	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
慢性胃炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
裂孔ヘルニア	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
キライディティ症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃ポリープ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃十二指腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃食道括約筋機能不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
逆流性胃炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
空気嚥下	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔内潰瘍形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口唇腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口唇浮腫	1	(0.1)	3	0.1	0				1	(<0.1)	3	0.1
十二指腸潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
小腸炎	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
消化管運動過剰	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化器痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
食中毒	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
食道憩室	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
舌腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
大腸ポリープ	0				1	(0.1)	1	0.1	0				0			
腸管虚血	0				1	(0.1)	1	0.1	0				0			
腸閉塞	1	(0.1)	1	0.1	0				0				0			
吐き戻し	0				1	(0.1)	2	0.1	0				0			
糖尿病性胃不全麻痺	0				1	(0.1)	1	0.1	0				0			
腹水	1	(0.1)	1	0.1	0				0				0			
噴出性嘔吐	0				1	(0.1)	1	0.1	0				0			
慢性膵炎	0				1	(0.1)	1	0.1	0				0			
肛門周囲痛	1	(0.1)	1	0.1	0				0				0			
膵萎縮	0				1	(0.1)	1	0.1	0				0			
膵臓障害	0				0				0				1	(0.1)	1	0.1
膵嚢胞	1	(0.1)	1	0.1	0				0				0			
齲歯	0				0				1	(0.1)	1	0.1	0			
臨床検査	108	(13.1)	190	12.8	105	(12.8)	205	14.2	85	(10.4)	149	9.9	76	(9.2)	131	8.6
リパーゼ増加	67	(8.1)	84	5.6	66	(8.1)	93	6.4	47	(5.7)	51	3.4	45	(5.5)	55	3.6
アミラーゼ増加	24	(2.9)	29	1.9	38	(4.6)	46	3.2	20	(2.4)	21	1.4	20	(2.4)	24	1.6
血中クレアチニン増加	7	(0.9)	7	0.5	4	(0.5)	4	0.3	6	(0.7)	6	0.4	9	(1.1)	9	0.6
体重減少	9	(1.1)	10	0.7	11	(1.3)	11	0.8	4	(0.5)	4	0.3	1	(0.1)	1	0.1
膵酵素増加	12	(1.5)	13	0.9	4	(0.5)	5	0.3	3	(0.4)	3	0.2	3	(0.4)	4	0.3
アスパラギン酸アミノトランスフェラーゼ増加	8	(1.0)	9	0.6	1	(0.1)	1	0.1	5	(0.6)	5	0.3	4	(0.5)	4	0.3
アラニンアミノトランスフェラーゼ増加	8	(1.0)	10	0.7	3	(0.4)	4	0.3	4	(0.5)	5	0.3	3	(0.4)	3	0.2
血中カルシトニン増加	3	(0.4)	3	0.2	5	(0.6)	5	0.3	8	(1.0)	8	0.5	2	(0.2)	2	0.1
血圧上昇	1	(0.1)	5	0.3	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	4	0.3
血中カルシウム増加	4	(0.5)	5	0.3	1	(0.1)	1	0.1	1	(0.1)	2	0.1	1	(0.1)	1	0.1
血中カリウム増加	2	(0.2)	2	0.1	1	(0.1)	2	0.1	2	(0.2)	3	0.2	1	(0.1)	1	0.1
赤血球分布幅増加	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	3	0.2	1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
大腸ポリープ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腸管虚血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腸閉塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
吐き戻し	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
糖尿病性胃不全麻痺	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹水	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
噴出性嘔吐	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
慢性膵炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肛門周囲痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵萎縮	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵臓障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膵嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
齲歯	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
臨床検査	213	(13.0)	395	13.5	161	(9.8)	280	9.2	374	(11.4)	675	11.3
リパーゼ増加	133	(8.1)	177	6.0	92	(5.6)	106	3.5	225	(6.8)	283	4.7
アミラーゼ増加	62	(3.8)	75	2.6	40	(2.4)	45	1.5	102	(3.1)	120	2.0
血中クレアチニン増加	11	(0.7)	11	0.4	15	(0.9)	15	0.5	26	(0.8)	26	0.4
体重減少	20	(1.2)	21	0.7	5	(0.3)	5	0.2	25	(0.8)	26	0.4
膵酵素増加	16	(1.0)	18	0.6	6	(0.4)	7	0.2	22	(0.7)	25	0.4
アスパラギン酸アミノトランスフェラーゼ増加	9	(0.5)	10	0.3	9	(0.5)	9	0.3	18	(0.5)	19	0.3
アラニンアミノトランスフェラーゼ増加	11	(0.7)	14	0.5	7	(0.4)	8	0.3	18	(0.5)	22	0.4
血中カルシトニン増加	8	(0.5)	8	0.3	10	(0.6)	10	0.3	18	(0.5)	18	0.3
血圧上昇	3	(0.2)	7	0.2	4	(0.2)	5	0.2	7	(0.2)	12	0.2
血中カルシウム増加	5	(0.3)	6	0.2	2	(0.1)	3	0.1	7	(0.2)	9	0.2
血中カリウム増加	3	(0.2)	4	0.1	3	(0.2)	4	0.1	6	(0.2)	8	0.1
赤血球分布幅増加	3	(0.2)	3	0.1	3	(0.2)	4	0.1	6	(0.2)	7	0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
血中アルカリホスファターゼ増加	0				0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
血中ビリルビン増加	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
血中プロインスリン増加	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
血中尿素増加	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
好中球数増加	0				3	(0.4)	4	0.3	1	(0.1)	1	0.1	0			
遊離脂肪酸増加	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
グリコヘモグロビン増加	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
ヘモグロビン減少	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
肝機能検査異常	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
血中ブドウ糖増加	1	(0.1)	2	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
低比重リポ蛋白増加	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
リパーゼ異常	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
肝酵素上昇	0				0				0				2	(0.2)	2	0.1
血中インスリン増加	0				0				0				2	(0.2)	2	0.1
血中トリグリセリド増加	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
血中ブドウ糖減少	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
糸球体濾過率減少	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
心拍数増加	0				0				2	(0.2)	2	0.1	0			
体重増加	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
単球数増加	0				2	(0.2)	3	0.2	0				0			
尿中アルブミン	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
尿中ブドウ糖陽性	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
白血球数増加	0				2	(0.2)	2	0.1	0				0			
トランスアミナーゼ上昇	0				0				1	(0.1)	1	0.1	0			
トロポニンＩ増加	0				0				1	(0.1)	1	0.1	0			
肝酵素異常	0				0				0				1	(0.1)	1	0.1
駆出率減少	1	(0.1)	1	0.1	0				0				0			
血液検査異常	0				0				1	(0.1)	1	0.1	0			

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
血中アルカリホスファターゼ増加	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
血中ビリルビン増加	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
血中プロインスリン増加	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
血中尿素増加	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
好中球数増加	3	(0.2)	4	0.1	1	(0.1)	1	<0.1	4	(0.1)	5	0.1
遊離脂肪酸増加	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
グリコヘモグロビン増加	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
ヘモグロビン減少	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
肝機能検査異常	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
血中ブドウ糖増加	1	(0.1)	2	0.1	2	(0.1)	2	0.1	3	(0.1)	4	0.1
低比重リポ蛋白増加	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
リパーゼ異常	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肝酵素上昇	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
血中インスリン増加	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
血中トリグリセリド増加	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血中ブドウ糖減少	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
糸球体濾過率減少	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心拍数増加	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
体重増加	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
単球数増加	2	(0.1)	3	0.1	0				2	(0.1)	3	0.1
尿中アルブミン	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
尿中ブドウ糖陽性	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
白血球数増加	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
トランスアミナーゼ上昇	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
トロポニンＩ増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝酵素異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
駆出率減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血液検査異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
血小板数減少	0				0				1	(0.1)	2	0.1	0			
血小板数増加	0				1	(0.1)	1	0.1	0				0			
血中アルカリホスファターゼ異常	1	(0.1)	1	0.1	0				0				0			
血中カリウム減少	0				0				1	(0.1)	1	0.1	0			
血中コレステロール増加	0				0				1	(0.1)	1	0.1	0			
好塩基球数増加	0				0				0				1	(0.1)	1	0.1
好中球数減少	0				1	(0.1)	1	0.1	0				0			
高比重リポ蛋白減少	0				0				1	(0.1)	1	0.1	0			
国際標準比増加	0				0				1	(0.1)	1	0.1	0			
心電図ＱＴ延長	0				0				1	(0.1)	1	0.1	0			
心電図Ｔ波振幅減少	0				0				0				1	(0.1)	1	0.1
心電図異常ＱＲＳ群	0				0				0				1	(0.1)	1	0.1
心拍数異常	1	(0.1)	1	0.1	0				0				0			
糖鎖抗原１２５増加	0				1	(0.1)	1	0.1	0				0			
尿蛋白	0				1	(0.1)	1	0.1	0				0			
尿中アルブミン／クレアチニン比増加	0				0				1	(0.1)	1	0.1	0			
尿中アルブミン陽性	0				1	(0.1)	1	0.1	0				0			
尿中ビリルビン	0				1	(0.1)	1	0.1	0				0			
尿中ヘモグロビン	0				0				1	(0.1)	1	0.1	0			
尿中ヘモグロビン陽性	0				0				1	(0.1)	1	0.1	0			
尿中亜硝酸塩陽性	0				1	(0.1)	1	0.1	0				0			
尿中蛋白陽性	1	(0.1)	1	0.1	0				0				0			
尿中白血球陽性	0				0				1	(0.1)	1	0.1	0			
白血球数減少	0				1	(0.1)	1	0.1	0				0			
平均血小板容積増加	0				1	(0.1)	1	0.1	0				0			
平均赤血球ヘモグロビン減少	0				0				1	(0.1)	2	0.1	0			

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
血小板数減少	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
血小板数増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中アルカリホスファターゼ異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中カリウム減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中コレステロール増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
好塩基球数増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
好中球数減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高比重リポ蛋白減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
国際標準比増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図ＱＴ延長	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図Ｔ波振幅減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図異常ＱＲＳ群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心拍数異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖鎖抗原１２５増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿蛋白	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中アルブミン／クレアチニン比増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿中アルブミン陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中ビリルビン	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中ヘモグロビン	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿中ヘモグロビン陽性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿中亜硝酸塩陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中蛋白陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中白血球陽性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
白血球数減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
平均血小板容積増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
平均赤血球ヘモグロビン減少	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
平均赤血球容積減少	0				0				1	(0.1)	1	0.1	0			
代謝および栄養障害	96	(11.7)	112	7.5	93	(11.4)	109	7.5	42	(5.1)	50	3.3	33	(4.0)	38	2.5
食欲減退	78	(9.5)	86	5.8	71	(8.7)	82	5.7	15	(1.8)	17	1.1	7	(0.8)	8	0.5
低血糖症	5	(0.6)	6	0.4	5	(0.6)	9	0.6	8	(1.0)	11	0.7	11	(1.3)	12	0.8
コントロール不良の糖尿病	0				1	(0.1)	1	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3
高カルシウム血症	5	(0.6)	5	0.3	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
高カリウム血症	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	4	0.3
食欲亢進	2	(0.2)	2	0.1	4	(0.5)	4	0.3	0				1	(0.1)	1	0.1
高リパーゼ血症	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
高アミラーゼ血症	2	(0.2)	3	0.2	0				2	(0.2)	2	0.1	0			
痛風	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
高トリグリセリド血症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
高血糖	0				0				2	(0.2)	3	0.2	1	(0.1)	1	0.1
脱水	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
低カリウム血症	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
低ナトリウム血症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
２型糖尿病	0				0				1	(0.1)	1	0.1	0			
アルコール不耐性	1	(0.1)	1	0.1	0				0				0			
ビタミンＢ１２欠乏	0				1	(0.1)	1	0.1	0				0			
マグネシウム欠乏	0				1	(0.1)	1	0.1	0				0			
悪液質	0				1	(0.1)	1	0.1	0				0			
拒食	0				1	(0.1)	1	0.1	0				0			
血液量減少症	1	(0.1)	1	0.1	0				0				0			
高カルシトニン血症	0				0				1	(0.1)	1	0.1	0			
高コレステロール血症	0				0				0				1	(0.1)	1	0.1
高ナトリウム血症	0				0				1	(0.1)	1	0.1	0			
高脂血症	0				0				0				1	(0.1)	1	0.1
脂質異常症	0				1	(0.1)	1	0.1	0				0			

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
平均赤血球容積減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
代謝および栄養障害	189	(11.5)	221	7.5	75	(4.6)	88	2.9	264	(8.0)	309	5.2
食欲減退	149	(9.1)	168	5.7	22	(1.3)	25	0.8	171	(5.2)	193	3.2
低血糖症	10	(0.6)	15	0.5	19	(1.2)	23	0.8	29	(0.9)	38	0.6
コントロール不良の糖尿病	1	(0.1)	1	<0.1	8	(0.5)	8	0.3	9	(0.3)	9	0.2
高カルシウム血症	7	(0.4)	7	0.2	2	(0.1)	2	0.1	9	(0.3)	9	0.2
高カリウム血症	3	(0.2)	3	0.1	4	(0.2)	5	0.2	7	(0.2)	8	0.1
食欲亢進	6	(0.4)	6	0.2	1	(0.1)	1	<0.1	7	(0.2)	7	0.1
高リパーゼ血症	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
高アミラーゼ血症	2	(0.1)	3	0.1	2	(0.1)	2	0.1	4	(0.1)	5	0.1
痛風	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
高トリグリセリド血症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
高血糖	0				3	(0.2)	4	0.1	3	(0.1)	4	0.1
脱水	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
低カリウム血症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
低ナトリウム血症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
２型糖尿病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
アルコール不耐性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ビタミンＢ１２欠乏	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
マグネシウム欠乏	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
悪液質	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
拒食	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血液量減少症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高カルシトニン血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高コレステロール血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高ナトリウム血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高脂血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脂質異常症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
電解質失調	0				0				0				1	(0.1)	1	0.1
糖尿病	0				0				0				1	(0.1)	1	0.1
乳酸アシドーシス	0				0				0				1	(0.1)	1	0.1
葉酸欠乏	0				0				1	(0.1)	1	0.1	0			
神経系障害	38	(4.6)	46	3.1	57	(7.0)	78	5.4	28	(3.4)	50	3.3	33	(4.0)	44	2.9
頭痛	13	(1.6)	15	1.0	20	(2.4)	28	1.9	11	(1.3)	23	1.5	23	(2.8)	25	1.6
浮動性めまい	11	(1.3)	11	0.7	17	(2.1)	19	1.3	9	(1.1)	16	1.1	7	(0.8)	7	0.5
味覚異常	2	(0.2)	2	0.1	8	(1.0)	8	0.6	1	(0.1)	1	0.1	2	(0.2)	2	0.1
低血糖性意識消失	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	4	0.3
嗜眠	3	(0.4)	4	0.3	3	(0.4)	3	0.2	0				0			
虚血性脳卒中	2	(0.2)	2	0.1	3	(0.4)	3	0.2	0				0			
傾眠	1	(0.1)	1	0.1	2	(0.2)	3	0.2	1	(0.1)	1	0.1	0			
失神	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
脳梗塞	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
下肢静止不能症候群	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
坐骨神経痛	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
錯感覚	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
末梢性ニューロパチー	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
味覚減退	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
パーキンソニズム	0				1	(0.1)	1	0.1	0				0			
一過性脳虚血発作	0				0				1	(0.1)	1	0.1	0			
運動失調	0				0				0				1	(0.1)	1	0.1
感覚消失	0				1	(0.1)	1	0.1	0				0			
頚動脈狭窄	0				0				1	(0.1)	1	0.1	0			
健忘	1	(0.1)	1	0.1	0				0				0			
高血圧性脳症	0				0				0				1	(0.1)	1	0.1
腰髄神経根障害	0				0				1	(0.1)	1	0.1	0			
失語症	0				1	(0.1)	1	0.1	0				0			

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
電解質失調	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糖尿病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳酸アシドーシス	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
葉酸欠乏	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経系障害	95	(5.8)	124	4.2	61	(3.7)	94	3.1	156	(4.7)	218	3.7
頭痛	33	(2.0)	43	1.5	34	(2.1)	48	1.6	67	(2.0)	91	1.5
浮動性めまい	28	(1.7)	30	1.0	16	(1.0)	23	0.8	44	(1.3)	53	0.9
味覚異常	10	(0.6)	10	0.3	3	(0.2)	3	0.1	13	(0.4)	13	0.2
低血糖性意識消失	3	(0.2)	3	0.1	4	(0.2)	6	0.2	7	(0.2)	9	0.2
嗜眠	6	(0.4)	7	0.2	0				6	(0.2)	7	0.1
虚血性脳卒中	5	(0.3)	5	0.2	0				5	(0.2)	5	0.1
傾眠	3	(0.2)	4	0.1	1	(0.1)	1	<0.1	4	(0.1)	5	0.1
失神	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
脳梗塞	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
下肢静止不能症候群	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
坐骨神経痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
錯感覚	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
末梢性ニューロパチー	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
味覚減退	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
パーキンソニズム	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
一過性脳虚血発作	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
運動失調	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感覚消失	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頚動脈狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
健忘	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高血圧性脳症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腰髄神経根障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
失語症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
振戦	0				1	(0.1)	1	0.1	0				0			
神経痛	0				1	(0.1)	1	0.1	0				0			
糖尿病性ニューロパチー	0				0				1	(0.1)	1	0.1	0			
脳幹梗塞	1	(0.1)	1	0.1	0				0				0			
脳血管発作	0				0				0				1	(0.1)	1	0.1
平衡障害	1	(0.1)	1	0.1	0				0				0			
片頭痛	0				1	(0.1)	1	0.1	0				0			
慢性炎症性脱髄性多発根ニューロパチー	1	(0.1)	1	0.1	0				0				0			
肋間神経痛	0				0				0				1	(0.1)	1	0.1
一般・全身障害および投与部位の状態	20	(2.4)	23	1.5	46	(5.6)	61	4.2	26	(3.2)	27	1.8	22	(2.7)	23	1.5
疲労	6	(0.7)	8	0.5	18	(2.2)	19	1.3	2	(0.2)	2	0.1	5	(0.6)	5	0.3
無力症	2	(0.2)	2	0.1	13	(1.6)	14	1.0	3	(0.4)	3	0.2	4	(0.5)	4	0.3
注射部位内出血	1	(0.1)	1	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3
末梢性浮腫	0				0				4	(0.5)	4	0.3	2	(0.2)	2	0.1
早期満腹	2	(0.2)	2	0.1	3	(0.4)	3	0.2	0				0			
発熱	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
倦怠感	1	(0.1)	1	0.1	2	(0.2)	3	0.2	0				1	(0.1)	1	0.1
注射部位疼痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
非心臓性胸痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
悪寒	0				1	(0.1)	2	0.1	0				1	(0.1)	1	0.1
空腹	0				0				2	(0.2)	2	0.1	0			
口渇	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
先行疾患の改善	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
注射部位反応	1	(0.1)	1	0.1	0				1	(0.1)	2	0.1	0			
熱感	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
不快感	0				2	(0.2)	2	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
振戦	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病性ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳幹梗塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳血管発作	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
平衡障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
片頭痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
慢性炎症性脱髄性多発根ニューロパチー	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肋間神経痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
一般・全身障害および投与部位の状態	66	(4.0)	84	2.9	48	(2.9)	50	1.6	114	(3.5)	134	2.2
疲労	24	(1.5)	27	0.9	7	(0.4)	7	0.2	31	(0.9)	34	0.6
無力症	15	(0.9)	16	0.5	7	(0.4)	7	0.2	22	(0.7)	23	0.4
注射部位内出血	2	(0.1)	2	0.1	8	(0.5)	8	0.3	10	(0.3)	10	0.2
末梢性浮腫	0				6	(0.4)	6	0.2	6	(0.2)	6	0.1
早期満腹	5	(0.3)	5	0.2	0				5	(0.2)	5	0.1
発熱	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
倦怠感	3	(0.2)	4	0.1	1	(0.1)	1	<0.1	4	(0.1)	5	0.1
注射部位疼痛	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
非心臓性胸痛	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
悪寒	1	(0.1)	2	0.1	1	(0.1)	1	<0.1	2	(0.1)	3	0.1
空腹	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
口渇	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
先行疾患の改善	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
注射部位反応	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
熱感	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
不快感	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
インフルエンザ様疾患	0				1	(0.1)	1	0.1	0				0			
ポリープ	1	(0.1)	1	0.1	0				0				0			
胸痛	0				0				1	(0.1)	1	0.1	0			
胸部不快感	0				0				0				1	(0.1)	1	0.1
局所腫脹	0				0				1	(0.1)	1	0.1	0			
全身性浮腫	1	(0.1)	1	0.1	0				0				0			
多臓器不全	0				0				1	(0.1)	1	0.1	0			
注射部位結節	0				0				0				1	(0.1)	1	0.1
注射部位血腫	0				1	(0.1)	1	0.1	0				0			
注射部位硬結	1	(0.1)	1	0.1	0				0				0			
注射部位腫瘤	0				1	(0.1)	1	0.1	0				0			
注射部位出血	0				1	(0.1)	1	0.1	0				0			
注射部位熱感	0				0				1	(0.1)	1	0.1	0			
注射部位不快感	0				1	(0.1)	2	0.1	0				0			
突然死	1	(0.1)	1	0.1	0				0				0			
微石症	0				0				1	(0.1)	1	0.1	0			
歩行障害	0				1	(0.1)	1	0.1	0				0			
末梢腫脹	0				1	(0.1)	1	0.1	0				0			
薬剤離脱症候群	0				1	(0.1)	1	0.1	0				0			
薬物特異体質反応	0				1	(0.1)	1	0.1	0				0			
疼痛	0				0				1	(0.1)	1	0.1	0			
感染症および寄生虫症	23	(2.8)	29	1.9	26	(3.2)	33	2.3	13	(1.6)	18	1.2	15	(1.8)	20	1.3
胃腸炎	5	(0.6)	5	0.3	5	(0.6)	5	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1
尿路感染	3	(0.4)	4	0.3	3	(0.4)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	5	0.3
インフルエンザ	1	(0.1)	1	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2	0			
上気道感染	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
気管支炎	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
鼻咽頭炎	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
インフルエンザ様疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ポリープ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胸痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胸部不快感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
局所腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
全身性浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
多臓器不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
注射部位結節	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
注射部位血腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
注射部位硬結	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
注射部位腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
注射部位出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
注射部位熱感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
注射部位不快感	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
突然死	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
微石症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歩行障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
末梢腫脹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
薬剤離脱症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
薬物特異体質反応	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
疼痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感染症および寄生虫症	49	(3.0)	62	2.1	28	(1.7)	38	1.3	77	(2.3)	100	1.7
胃腸炎	10	(0.6)	10	0.3	4	(0.2)	4	0.1	14	(0.4)	14	0.2
尿路感染	6	(0.4)	7	0.2	4	(0.2)	6	0.2	10	(0.3)	13	0.2
インフルエンザ	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
上気道感染	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
気管支炎	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
鼻咽頭炎	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
憩室炎	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
肺炎	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
赤痢	1	(0.1)	1	0.1	1	(0.1)	4	0.3	1	(0.1)	1	0.1	0			
ウイルス感染	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
外陰部腟カンジダ症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
敗血症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
副鼻腔炎	1	(0.1)	1	0.1	1	(0.1)	3	0.2	0				0			
蜂巣炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
膀胱炎	1	(0.1)	2	0.1	1	(0.1)	1	0.1	0				0			
せつ	1	(0.1)	1	0.1	0				0				0			
ウイルス性胃腸炎	1	(0.1)	1	0.1	0				0				0			
ウイルス性消化管感染	0				1	(0.1)	1	0.1	0				0			
ウイルス性上気道感染	0				0				0				1	(0.1)	1	0.1
カンピロバクター感染	1	(0.1)	1	0.1	0				0				0			
シュードモナス性尿路感染	0				1	(0.1)	1	0.1	0				0			
咽頭炎	0				1	(0.1)	1	0.1	0				0			
下気道感染	0				0				1	(0.1)	1	0.1	0			
感染	1	(0.1)	1	0.1	0				0				0			
寄生虫性胃腸炎	0				1	(0.1)	1	0.1	0				0			
気管支肺炎	0				0				0				1	(0.1)	1	0.1
骨髄炎	0				0				1	(0.1)	1	0.1	0			
歯周炎	0				0				0				1	(0.1)	1	0.1
歯膿瘍	1	(0.1)	1	0.1	0				0				0			
真菌性口腔咽頭炎	0				0				0				1	(0.1)	1	0.1
腎盂腎炎	0				1	(0.1)	1	0.1	0				0			
単純ヘルペス	1	(0.1)	1	0.1	0				0				0			
軟骨膜炎	0				0				1	(0.1)	1	0.1	0			
慢性腎盂腎炎	0				1	(0.1)	1	0.1	0				0			

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
憩室炎	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
肺炎	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
赤痢	2	(0.1)	5	0.2	1	(0.1)	1	<0.1	3	(0.1)	6	0.1
ウイルス感染	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
外陰部腟カンジダ症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
敗血症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
副鼻腔炎	2	(0.1)	4	0.1	0				2	(0.1)	4	0.1
蜂巣炎	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
膀胱炎	2	(0.1)	3	0.1	0				2	(0.1)	3	0.1
せつ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ウイルス性胃腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ウイルス性消化管感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ウイルス性上気道感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
カンピロバクター感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
シュードモナス性尿路感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
咽頭炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
下気道感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
寄生虫性胃腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
気管支肺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
骨髄炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯周炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
真菌性口腔咽頭炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎盂腎炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
単純ヘルペス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
軟骨膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
慢性腎盂腎炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
心臓障害	15	(1.8)	24	1.6	22	(2.7)	27	1.9	17	(2.1)	24	1.6	20	(2.4)	25	1.6
心房細動	1	(0.1)	1	0.1	4	(0.5)	4	0.3	5	(0.6)	5	0.3	4	(0.5)	5	0.3
狭心症	3	(0.4)	3	0.2	3	(0.4)	3	0.2	3	(0.4)	3	0.2	4	(0.5)	5	0.3
急性心筋梗塞	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
心筋梗塞	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				3	(0.4)	4	0.3
動悸	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	3	0.2	0			
心不全	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
慢性心不全	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	0			
うっ血性心不全	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
冠動脈疾患	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
僧帽弁閉鎖不全症	3	(0.4)	3	0.2	0				0				0			
頻脈	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
左脚ブロック	0				1	(0.1)	1	0.1	0				1	(0.1)	2	0.1
三尖弁閉鎖不全症	2	(0.2)	2	0.1	0				0				0			
心室性期外収縮	0				2	(0.2)	2	0.1	0				0			
心房粗動	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
第一度房室ブロック	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
不整脈	1	(0.1)	2	0.1	0				0				1	(0.1)	1	0.1
冠動脈狭窄	0				0				0				1	(0.1)	1	0.1
冠動脈入口部狭窄	0				0				1	(0.1)	1	0.1	0			
急性冠動脈症候群	1	(0.1)	1	0.1	0				0				0			
左室機能不全	1	(0.1)	1	0.1	0				0				0			
左室不全	0				0				0				1	(0.1)	1	0.1
徐脈	0				0				1	(0.1)	1	0.1	0			
上室性期外収縮	0				1	(0.1)	1	0.1	0				0			
上室性頻脈	0				0				1	(0.1)	2	0.1	0			
心筋虚血	1	(0.1)	1	0.1	0				0				0			
心筋線維症	0				1	(0.1)	1	0.1	0				0			
心原性ショック	0				0				1	(0.1)	1	0.1	0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心臓障害	37	(2.3)	51	1.7	37	(2.3)	49	1.6	74	(2.3)	100	1.7
心房細動	5	(0.3)	5	0.2	9	(0.5)	10	0.3	14	(0.4)	15	0.3
狭心症	6	(0.4)	6	0.2	7	(0.4)	8	0.3	13	(0.4)	14	0.2
急性心筋梗塞	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
心筋梗塞	3	(0.2)	3	0.1	3	(0.2)	4	0.1	6	(0.2)	7	0.1
動悸	4	(0.2)	4	0.1	2	(0.1)	3	0.1	6	(0.2)	7	0.1
心不全	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
慢性心不全	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
うっ血性心不全	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
冠動脈疾患	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
僧帽弁閉鎖不全症	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
頻脈	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
左脚ブロック	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
三尖弁閉鎖不全症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
心室性期外収縮	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
心房粗動	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
第一度房室ブロック	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
不整脈	1	(0.1)	2	0.1	1	(0.1)	1	<0.1	2	(0.1)	3	0.1
冠動脈狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
冠動脈入口部狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性冠動脈症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
左室機能不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
左室不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
徐脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
上室性期外収縮	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
上室性頻脈	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
心筋虚血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心筋線維症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心原性ショック	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
心室性不整脈	0				0				0				1	(0.1)	1	0.1
心室内伝導障害	0				1	(0.1)	1	0.1	0				0			
心粗動	0				1	(0.1)	1	0.1	0				0			
心臓性喘息	1	(0.1)	1	0.1	0				0				0			
心停止	0				0				0				1	(0.1)	1	0.1
腎および尿路障害	8	(1.0)	8	0.5	20	(2.4)	24	1.7	15	(1.8)	18	1.2	21	(2.5)	21	1.4
急性腎不全	3	(0.4)	3	0.2	3	(0.4)	4	0.3	2	(0.2)	2	0.1	6	(0.7)	6	0.4
蛋白尿	3	(0.4)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3
ミクロアルブミン尿	0				4	(0.5)	4	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1
腎嚢胞	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
腎症	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	0			
慢性腎臓病	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
腎結石症	0				3	(0.4)	3	0.2	0				0			
腎不全	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
腎腫瘤	0				0				0				2	(0.2)	2	0.1
腎臓痛	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
尿異常	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
頻尿	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
夜間頻尿	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
下部尿路症状	0				0				1	(0.1)	1	0.1	0			
急性腎前性腎不全	0				0				0				1	(0.1)	1	0.1
緊張性膀胱	0				1	(0.1)	1	0.1	0				0			
腎機能障害	0				0				0				1	(0.1)	1	0.1
腎仙痛	0				1	(0.1)	1	0.1	0				0			
糖尿	0				0				1	(0.1)	1	0.1	0			
糖尿病性腎症	0				0				1	(0.1)	1	0.1	0			
尿閉	0				1	(0.1)	1	0.1	0				0			
膀胱肉柱形成	0				0				1	(0.1)	1	0.1	0			

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心室性不整脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心室内伝導障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心粗動	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心臓性喘息	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心停止	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎および尿路障害	28	(1.7)	32	1.1	36	(2.2)	39	1.3	64	(1.9)	71	1.2
急性腎不全	6	(0.4)	7	0.2	8	(0.5)	8	0.3	14	(0.4)	15	0.3
蛋白尿	4	(0.2)	4	0.1	7	(0.4)	7	0.2	11	(0.3)	11	0.2
ミクロアルブミン尿	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
腎嚢胞	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
腎症	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
慢性腎臓病	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
腎結石症	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
腎不全	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
腎腫瘤	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
腎臓痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
尿異常	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
頻尿	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
夜間頻尿	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
下部尿路症状	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性腎前性腎不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
緊張性膀胱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎機能障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎仙痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糖尿病性腎症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿閉	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱肉柱形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
筋骨格系および結合組織障害	9	(1.1)	14	0.9	8	(1.0)	9	0.6	15	(1.8)	20	1.3	8	(1.0)	10	0.7
関節痛	2	(0.2)	2	0.1	2	(0.2)	3	0.2	0				2	(0.2)	2	0.1
四肢痛	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
背部痛	3	(0.4)	3	0.2	0				1	(0.1)	2	0.1	2	(0.2)	2	0.1
筋肉痛	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
筋痙縮	1	(0.1)	5	0.3	0				2	(0.2)	3	0.2	1	(0.1)	1	0.1
変形性関節症	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
筋骨格系胸痛	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
筋力低下	0				0				2	(0.2)	2	0.1	0			
外骨腫	0				0				1	(0.1)	1	0.1	0			
関節リウマチ	0				0				1	(0.1)	1	0.1	0			
筋骨格痛	1	(0.1)	1	0.1	0				0				0			
頚部痛	0				0				0				1	(0.1)	1	0.1
骨障害	0				1	(0.1)	1	0.1	0				0			
四肢不快感	0				0				1	(0.1)	1	0.1	0			
斜頚	0				0				1	(0.1)	1	0.1	0			
足底腱膜線維腫症	0				0				0				1	(0.1)	1	0.1
椎間板障害	0				0				1	(0.1)	1	0.1	0			
椎間板変性症	0				0				1	(0.1)	1	0.1	0			
変形性脊椎症	0				0				1	(0.1)	1	0.1	0			
腱炎	0				1	(0.1)	1	0.1	0				0			
皮膚および皮下組織障害	15	(1.8)	16	1.1	10	(1.2)	12	0.8	10	(1.2)	12	0.8	12	(1.5)	13	0.9
そう痒症	2	(0.2)	2	0.1	3	(0.4)	4	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1
蕁麻疹	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
多汗症	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1	0			
発疹	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
乾癬	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
筋骨格系および結合組織障害	17	(1.0)	23	0.8	23	(1.4)	30	1.0	40	(1.2)	53	0.9
関節痛	4	(0.2)	5	0.2	2	(0.1)	2	0.1	6	(0.2)	7	0.1
四肢痛	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
背部痛	3	(0.2)	3	0.1	3	(0.2)	4	0.1	6	(0.2)	7	0.1
筋肉痛	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
筋痙縮	1	(0.1)	5	0.2	3	(0.2)	4	0.1	4	(0.1)	9	0.2
変形性関節症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
筋骨格系胸痛	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
筋力低下	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
外骨腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
関節リウマチ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋骨格痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頚部痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
骨障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
四肢不快感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
斜頚	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
足底腱膜線維腫症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎間板障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎間板変性症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
変形性脊椎症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腱炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮膚および皮下組織障害	25	(1.5)	28	1.0	22	(1.3)	25	0.8	47	(1.4)	53	0.9
そう痒症	5	(0.3)	6	0.2	4	(0.2)	4	0.1	9	(0.3)	10	0.2
蕁麻疹	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
多汗症	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
発疹	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
乾癬	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
顔面腫脹	1	(0.1)	2	0.1	1	(0.1)	1	0.1	0				0			
脱毛症	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
糖尿病性足病変	0				0				2	(0.2)	2	0.1	0			
斑状出血	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
そう痒性皮疹	0				0				0				1	(0.1)	1	0.1
アレルギー性皮膚炎	0				0				0				1	(0.1)	1	0.1
過角化	0				0				1	(0.1)	1	0.1	0			
紅斑	0				1	(0.1)	1	0.1	0				0			
湿疹	1	(0.1)	1	0.1	0				0				0			
寝汗	1	(0.1)	1	0.1	0				0				0			
神経皮膚炎	0				0				0				1	(0.1)	1	0.1
接触性皮膚炎	0				0				0				1	(0.1)	1	0.1
中毒性皮疹	1	(0.1)	1	0.1	0				0				0			
斑状丘疹状皮疹	0				0				0				1	(0.1)	1	0.1
斑状皮疹	0				0				1	(0.1)	1	0.1	0			
皮膚炎	1	(0.1)	1	0.1	0				0				0			
皮膚乾燥	0				1	(0.1)	1	0.1	0				0			
皮膚潰瘍	0				0				1	(0.1)	1	0.1	0			
皮膚病変	0				0				1	(0.1)	1	0.1	0			
冷汗	0				1	(0.1)	1	0.1	0				0			
痒疹	0				0				0				1	(0.1)	1	0.1
眼障害	13	(1.6)	17	1.1	12	(1.5)	12	0.8	10	(1.2)	10	0.7	7	(0.8)	10	0.7
糖尿病網膜症	6	(0.7)	6	0.4	4	(0.5)	4	0.3	3	(0.4)	3	0.2	1	(0.1)	1	0.1
白内障	4	(0.5)	5	0.3	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
視力障害	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
視力低下	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
出血性網膜症	2	(0.2)	2	0.1	0				0				0			
硝子体出血	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
顔面腫脹	2	(0.1)	3	0.1	0				2	(0.1)	3	0.1
脱毛症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
糖尿病性足病変	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
斑状出血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
そう痒性皮疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
アレルギー性皮膚炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
過角化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
紅斑	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
湿疹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
寝汗	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経皮膚炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
接触性皮膚炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
中毒性皮疹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
斑状丘疹状皮疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
斑状皮疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮膚乾燥	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮膚潰瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚病変	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
冷汗	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
痒疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼障害	25	(1.5)	29	1.0	17	(1.0)	20	0.7	42	(1.3)	49	0.8
糖尿病網膜症	10	(0.6)	10	0.3	4	(0.2)	4	0.1	14	(0.4)	14	0.2
白内障	6	(0.4)	7	0.2	2	(0.1)	2	0.1	8	(0.2)	9	0.2
視力障害	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
視力低下	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
出血性網膜症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
硝子体出血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
緑内障	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
黄斑線維症	0				1	(0.1)	1	0.1	0				0			
核性白内障	0				0				1	(0.1)	1	0.1	0			
眼球浮腫	0				1	(0.1)	1	0.1	0				0			
眼瞼浮腫	1	(0.1)	1	0.1	0				0				0			
近視	0				0				0				1	(0.1)	1	0.1
結膜充血	1	(0.1)	1	0.1	0				0				0			
光視症	0				0				0				1	(0.1)	1	0.1
硝子体障害	0				0				0				1	(0.1)	1	0.1
新生血管加齢黄斑変性	1	(0.1)	1	0.1	0				0				0			
糖尿病性白内障	0				1	(0.1)	1	0.1	0				0			
糖尿病性網膜浮腫	0				0				1	(0.1)	1	0.1	0			
動脈硬化性網膜症	0				0				0				1	(0.1)	1	0.1
複視	0				0				1	(0.1)	1	0.1	0			
霧視	0				1	(0.1)	1	0.1	0				0			
網膜血管障害	1	(0.1)	1	0.1	0				0				0			
網膜血管瘤	0				0				1	(0.1)	1	0.1	0			
呼吸器、胸郭および縦隔障害	5	(0.6)	9	0.6	16	(2.0)	18	1.2	7	(0.9)	8	0.5	10	(1.2)	11	0.7
咳嗽	1	(0.1)	1	0.1	3	(0.4)	4	0.3	2	(0.2)	2	0.1	4	(0.5)	4	0.3
しゃっくり	3	(0.4)	6	0.4	6	(0.7)	6	0.4	0				0			
呼吸困難	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
アレルギー性鼻炎	0				0				1	(0.1)	1	0.1	2	(0.2)	3	0.2
睡眠時無呼吸症候群	0				0				2	(0.2)	2	0.1	0			
肺腫瘤	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
逆流性喉頭炎	0				1	(0.1)	1	0.1	0				0			
胸水症	1	(0.1)	1	0.1	0				0				0			
口腔咽頭痛	0				0				0				1	(0.1)	1	0.1
肺気腫	0				1	(0.1)	1	0.1	0				0			

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
緑内障	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
黄斑線維症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
核性白内障	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼球浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼瞼浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
近視	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結膜充血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
光視症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
硝子体障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
新生血管加齢黄斑変性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病性白内障	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病性網膜浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
動脈硬化性網膜症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
複視	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
霧視	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
網膜血管障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
網膜血管瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼吸器、胸郭および縦隔障害	21	(1.3)	27	0.9	17	(1.0)	19	0.6	38	(1.2)	46	0.8
咳嗽	4	(0.2)	5	0.2	6	(0.4)	6	0.2	10	(0.3)	11	0.2
しゃっくり	9	(0.5)	12	0.4	0				9	(0.3)	12	0.2
呼吸困難	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
アレルギー性鼻炎	0				3	(0.2)	4	0.1	3	(0.1)	4	0.1
睡眠時無呼吸症候群	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
肺腫瘤	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
逆流性喉頭炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胸水症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔咽頭痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺気腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
肺高血圧症	1	(0.1)	1	0.1	0				0				0			
肺水腫	0				0				1	(0.1)	1	0.1	0			
発声障害	0				1	(0.1)	1	0.1	0				0			
鼻出血	0				1	(0.1)	1	0.1	0				0			
副鼻腔うっ血	0				1	(0.1)	1	0.1	0				0			
慢性気管支炎	0				1	(0.1)	1	0.1	0				0			
傷害、中毒および処置合併症	9	(1.1)	11	0.7	9	(1.1)	9	0.6	7	(0.9)	7	0.5	7	(0.8)	8	0.5
偶発的過量投与	3	(0.4)	3	0.2	1	(0.1)	1	0.1	2	(0.2)	2	0.1	4	(0.5)	5	0.3
過量投与	0				4	(0.5)	4	0.3	0				2	(0.2)	2	0.1
不適切な投与計画での薬剤の投与	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
誤薬投与	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
挫傷	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
転倒	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
熱傷	2	(0.2)	2	0.1	0				0				0			
各種物質毒性	0				0				1	(0.1)	1	0.1	0			
誤用量投与	1	(0.1)	2	0.1	0				0				0			
処置による疼痛	0				0				1	(0.1)	1	0.1	0			
投薬過誤	0				1	(0.1)	1	0.1	0				0			
肉離れ	1	(0.1)	1	0.1	0				0				0			
血管障害	8	(1.0)	9	0.6	4	(0.5)	4	0.3	8	(1.0)	9	0.6	7	(0.8)	7	0.5
高血圧	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	4	(0.5)	4	0.3
低血圧	2	(0.2)	2	0.1	0				3	(0.4)	4	0.3	1	(0.1)	1	0.1
ほてり	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
起立性低血圧	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
血腫	2	(0.2)	2	0.1	0				0				0			
血管炎	0				0				1	(0.1)	1	0.1	0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肺高血圧症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺水腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
発声障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
副鼻腔うっ血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
慢性気管支炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
傷害、中毒および処置合併症	18	(1.1)	20	0.7	14	(0.9)	15	0.5	32	(1.0)	35	0.6
偶発的過量投与	4	(0.2)	4	0.1	6	(0.4)	7	0.2	10	(0.3)	11	0.2
過量投与	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
不適切な投与計画での薬剤の投与	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
誤薬投与	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
挫傷	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
転倒	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
熱傷	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
各種物質毒性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
誤用量投与	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
処置による疼痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
投薬過誤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肉離れ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管障害	12	(0.7)	13	0.4	15	(0.9)	16	0.5	27	(0.8)	29	0.5
高血圧	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
低血圧	2	(0.1)	2	0.1	4	(0.2)	5	0.2	6	(0.2)	7	0.1
ほてり	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
起立性低血圧	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
血腫	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
血管炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
高血圧クリーゼ	1	(0.1)	1	0.1	0				0				0			
高血圧緊急症	1	(0.1)	1	0.1	0				0				0			
高血圧性血管障害	1	(0.1)	1	0.1	0				0				0			
大動脈狭窄	0				0				1	(0.1)	1	0.1	0			
大動脈硬化症	0				1	(0.1)	1	0.1	0				0			
潮紅	0				1	(0.1)	1	0.1	0				0			
末梢静脈疾患	0				0				0				1	(0.1)	1	0.1
末梢動脈閉塞性疾患	0				0				1	(0.1)	1	0.1	0			
肝胆道系障害	10	(1.2)	10	0.7	6	(0.7)	6	0.4	4	(0.5)	5	0.3	3	(0.4)	3	0.2
胆石症	4	(0.5)	4	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
急性胆嚢炎	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
肝嚢胞	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
胆道障害	0				2	(0.2)	2	0.1	0				0			
肝障害	0				1	(0.1)	1	0.1	0				0			
肝石灰化	0				0				1	(0.1)	1	0.1	0			
脂肪肝	1	(0.1)	1	0.1	0				0				0			
心臓性肝硬変	1	(0.1)	1	0.1	0				0				0			
水腫性胆嚢炎	1	(0.1)	1	0.1	0				0				0			
胆汁うっ滞	0				0				1	(0.1)	1	0.1	0			
胆汁うっ滞性黄疸	0				1	(0.1)	1	0.1	0				0			
胆嚢ポリープ	0				0				0				1	(0.1)	1	0.1
胆嚢炎	0				0				0				1	(0.1)	1	0.1
慢性胆嚢炎	0				1	(0.1)	1	0.1	0				0			
血液およびリンパ系障害	3	(0.4)	5	0.3	3	(0.4)	3	0.2	7	(0.9)	7	0.5	4	(0.5)	4	0.3
貧血	1	(0.1)	3	0.2	2	(0.2)	2	0.1	5	(0.6)	5	0.3	4	(0.5)	4	0.3
凝固因子異常	1	(0.1)	1	0.1	0				0				0			
血小板減少症	0				0				1	(0.1)	1	0.1	0			

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
高血圧クリーゼ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高血圧緊急症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高血圧性血管障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大動脈狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大動脈硬化症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
潮紅	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
末梢静脈疾患	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈閉塞性疾患	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝胆道系障害	16	(1.0)	16	0.5	7	(0.4)	8	0.3	23	(0.7)	24	0.4
胆石症	5	(0.3)	5	0.2	2	(0.1)	2	0.1	7	(0.2)	7	0.1
急性胆嚢炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
肝嚢胞	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胆道障害	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
肝障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝石灰化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脂肪肝	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心臓性肝硬変	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
水腫性胆嚢炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆汁うっ滞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆汁うっ滞性黄疸	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆嚢ポリープ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆嚢炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
慢性胆嚢炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血液およびリンパ系障害	6	(0.4)	8	0.3	11	(0.7)	11	0.4	17	(0.5)	19	0.3
貧血	3	(0.2)	5	0.2	9	(0.5)	9	0.3	12	(0.4)	14	0.2
凝固因子異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血小板減少症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
出血性貧血	1	(0.1)	1	0.1	0				0				0			
正色素性正球性貧血	0				1	(0.1)	1	0.1	0				0			
免疫性血小板減少性紫斑病	0				0				1	(0.1)	1	0.1	0			
精神障害	6	(0.7)	6	0.4	9	(1.1)	9	0.6	2	(0.2)	2	0.1	2	(0.2)	2	0.1
不眠症	3	(0.4)	3	0.2	5	(0.6)	5	0.3	1	(0.1)	1	0.1	0			
うつ病	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
リビドー減退	0				1	(0.1)	1	0.1	0				0			
異常な夢	0				1	(0.1)	1	0.1	0				0			
気分変化	0				1	(0.1)	1	0.1	0				0			
食物嫌悪	0				0				1	(0.1)	1	0.1	0			
無感情	0				1	(0.1)	1	0.1	0				0			
抑うつ気分	1	(0.1)	1	0.1	0				0				0			
抑うつ症状	1	(0.1)	1	0.1	0				0				0			
落ち着きのなさ	0				0				0				1	(0.1)	1	0.1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2	(0.2)	3	0.2	4	(0.5)	5	0.3	6	(0.7)	6	0.4	4	(0.5)	4	0.3
甲状腺新生物	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
甲状腺の良性新生物	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
遠隔転移を伴う腎癌	1	(0.1)	1	0.1	0				0				0			
遠隔転移を伴う膵癌	0				0				1	(0.1)	1	0.1	0			
褐色細胞腫	1	(0.1)	1	0.1	0				0				0			
肝新生物	0				1	(0.1)	1	0.1	0				0			
肝腺腫	0				0				1	(0.1)	1	0.1	0			
小細胞肺癌	0				0				1	(0.1)	1	0.1	0			
乳頭様甲状腺癌	0				0				1	(0.1)	1	0.1	0			
肺新生物	0				1	(0.1)	1	0.1	0				0			

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
出血性貧血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
正色素性正球性貧血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
免疫性血小板減少性紫斑病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精神障害	15	(0.9)	15	0.5	4	(0.2)	4	0.1	19	(0.6)	19	0.3
不眠症	8	(0.5)	8	0.3	1	(0.1)	1	<0.1	9	(0.3)	9	0.2
うつ病	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
リビドー減退	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
異常な夢	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
気分変化	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
食物嫌悪	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
無感情	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
抑うつ気分	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
抑うつ症状	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
落ち着きのなさ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	6	(0.4)	8	0.3	10	(0.6)	10	0.3	16	(0.5)	18	0.3
甲状腺新生物	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
甲状腺の良性新生物	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
遠隔転移を伴う腎癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う膵癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
褐色細胞腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝腺腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
小細胞肺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳頭様甲状腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
皮膚乳頭腫	0				0				0				1	(0.1)	1	0.1
傍神経節新生物	1	(0.1)	1	0.1	0				0				0			
膀胱移行上皮癌	0				1	(0.1)	1	0.1	0				0			
膵癌	0				0				0				1	(0.1)	1	0.1
外科および内科処置	2	(0.2)	2	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	5	(0.6)	5	0.3
冠動脈ステント挿入	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
冠動脈バイパス	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
冠動脈形成	0				0				0				2	(0.2)	2	0.1
冠動脈血行再建	0				0				1	(0.1)	1	0.1	0			
経皮的冠インターベンション	1	(0.1)	1	0.1	0				0				0			
消化管拡張術	0				0				1	(0.1)	1	0.1	0			
抜歯	0				1	(0.1)	1	0.1	0				0			
耳および迷路障害	2	(0.2)	2	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1	4	(0.5)	4	0.3
回転性めまい	1	(0.1)	1	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1	4	(0.5)	4	0.3
耳鳴	1	(0.1)	1	0.1	0				0				0			
生殖系および乳房障害	1	(0.1)	1	0.1	0				3	(0.4)	4	0.3	3	(0.4)	3	0.2
良性前立腺肥大症	0				0				0				2	(0.2)	2	0.1
陰茎腫脹	0				0				0				1	(0.1)	1	0.1
亀頭包皮炎	0				0				1	(0.1)	2	0.1	0			
子宮障害	1	(0.1)	1	0.1	0				0				0			
女性化乳房	0				0				1	(0.1)	1	0.1	0			
性器発疹	0				0				1	(0.1)	1	0.1	0			
内分泌障害	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1
甲状腺腫	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1

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Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
皮膚乳頭腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
傍神経節新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱移行上皮癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外科および内科処置	4	(0.2)	4	0.1	8	(0.5)	8	0.3	12	(0.4)	12	0.2
冠動脈ステント挿入	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
冠動脈バイパス	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
冠動脈形成	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
冠動脈血行再建	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
経皮的冠インターベンション	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管拡張術	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
抜歯	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
耳および迷路障害	6	(0.4)	6	0.2	6	(0.4)	6	0.2	12	(0.4)	12	0.2
回転性めまい	5	(0.3)	5	0.2	6	(0.4)	6	0.2	11	(0.3)	11	0.2
耳鳴	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
生殖系および乳房障害	1	(0.1)	1	<0.1	6	(0.4)	7	0.2	7	(0.2)	8	0.1
良性前立腺肥大症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
陰茎腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
亀頭包皮炎	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
子宮障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
女性化乳房	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
性器発疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
内分泌障害	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
甲状腺腫	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
甲状腺炎	0				1	(0.1)	1	0.1	0				0			
甲状腺機能低下症	0				0				1	(0.1)	1	0.1	0			
免疫系障害	0				0				1	(0.1)	1	0.1	0			
薬物過敏症	0				0				1	(0.1)	1	0.1	0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Adverse events possibly or probably related to trial product by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
甲状腺炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
甲状腺機能低下症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
免疫系障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
薬物過敏症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.25.2- 4　重度の有害事象（器官別大分類及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	823				819				819				825			
Exposure time (year)	1488.3				1443.9				1508.0				1526.8			
Events	185	(22.5)	359	24.1	185	(22.6)	332	23.0	186	(22.7)	358	23.7	180	(21.8)	371	24.3
心臓障害	46	(5.6)	63	4.2	42	(5.1)	60	4.2	54	(6.6)	64	4.2	58	(7.0)	85	5.6
急性心筋梗塞	9	(1.1)	9	0.6	5	(0.6)	5	0.3	9	(1.1)	9	0.6	18	(2.2)	19	1.2
うっ血性心不全	7	(0.9)	7	0.5	6	(0.7)	8	0.6	6	(0.7)	10	0.7	8	(1.0)	8	0.5
心筋梗塞	4	(0.5)	4	0.3	6	(0.7)	6	0.4	5	(0.6)	5	0.3	7	(0.8)	7	0.5
不安定狭心症	2	(0.2)	3	0.2	4	(0.5)	4	0.3	4	(0.5)	4	0.3	10	(1.2)	10	0.7
冠動脈疾患	4	(0.5)	4	0.3	6	(0.7)	6	0.4	6	(0.7)	7	0.5	0			
心不全	5	(0.6)	5	0.3	4	(0.5)	4	0.3	3	(0.4)	3	0.2	3	(0.4)	3	0.2
心房細動	3	(0.4)	3	0.2	3	(0.4)	3	0.2	2	(0.2)	2	0.1	6	(0.7)	6	0.4
狭心症	4	(0.5)	4	0.3	3	(0.4)	3	0.2	3	(0.4)	3	0.2	3	(0.4)	3	0.2
心停止	3	(0.4)	3	0.2	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
慢性心不全	4	(0.5)	4	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
心室性頻脈	0				5	(0.6)	5	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1
完全房室ブロック	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2
急性心不全	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
心原性ショック	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
心室細動	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
冠動脈狭窄	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
急性冠動脈症候群	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
不整脈	1	(0.1)	2	0.1	0				0				2	(0.2)	2	0.1
冠動脈閉塞	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
徐脈	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
心筋虚血	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
心肺停止	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
心房粗動	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	1642				1644				3286			
Exposure time (year)	2932.2				3034.8				5967.0			
Events	370	(22.5)	691	23.6	366	(22.3)	729	24.0	736	(22.4)	1420	23.8
心臓障害	88	(5.4)	123	4.2	112	(6.8)	149	4.9	200	(6.1)	272	4.6
急性心筋梗塞	14	(0.9)	14	0.5	27	(1.6)	28	0.9	41	(1.2)	42	0.7
うっ血性心不全	13	(0.8)	15	0.5	14	(0.9)	18	0.6	27	(0.8)	33	0.6
心筋梗塞	10	(0.6)	10	0.3	12	(0.7)	12	0.4	22	(0.7)	22	0.4
不安定狭心症	6	(0.4)	7	0.2	14	(0.9)	14	0.5	20	(0.6)	21	0.4
冠動脈疾患	10	(0.6)	10	0.3	6	(0.4)	7	0.2	16	(0.5)	17	0.3
心不全	9	(0.5)	9	0.3	6	(0.4)	6	0.2	15	(0.5)	15	0.3
心房細動	6	(0.4)	6	0.2	8	(0.5)	8	0.3	14	(0.4)	14	0.2
狭心症	7	(0.4)	7	0.2	6	(0.4)	6	0.2	13	(0.4)	13	0.2
心停止	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
慢性心不全	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
心室性頻脈	5	(0.3)	5	0.2	2	(0.1)	2	0.1	7	(0.2)	7	0.1
完全房室ブロック	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
急性心不全	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
心原性ショック	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
心室細動	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
冠動脈狭窄	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
急性冠動脈症候群	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
不整脈	1	(0.1)	2	0.1	2	(0.1)	2	0.1	3	(0.1)	4	0.1
冠動脈閉塞	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
徐脈	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
心筋虚血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心肺停止	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
心房粗動	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
洞性徐脈	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
うっ血性心筋症	0				0				0				1	(0.1)	1	0.1
右室不全	0				0				0				1	(0.1)	1	0.1
冠動脈硬化症	0				0				0				1	(0.1)	1	0.1
冠動脈入口部狭窄	0				0				1	(0.1)	1	0.1	0			
急性左室不全	0				0				0				1	(0.1)	1	0.1
高血圧性心筋症	0				0				0				1	(0.1)	1	0.1
左脚ブロック	0				0				0				1	(0.1)	1	0.1
左室肥大	0				0				1	(0.1)	1	0.1	0			
左室不全	0				0				0				1	(0.1)	1	0.1
三尖弁閉鎖不全症	1	(0.1)	1	0.1	0				0				0			
上室性期外収縮	0				1	(0.1)	1	0.1	0				0			
上室性頻脈	0				1	(0.1)	1	0.1	0				0			
心筋炎	1	(0.1)	1	0.1	0				0				0			
心血管不全	0				1	(0.1)	1	0.1	0				0			
心室血栓症	0				0				0				1	(0.1)	1	0.1
心室性頻脈性不整脈	1	(0.1)	1	0.1	0				0				0			
心室性不整脈	1	(0.1)	1	0.1	0				0				0			
心室無収縮	0				0				0				1	(0.1)	1	0.1
心臓性喘息	1	(0.1)	1	0.1	0				0				0			
心肺不全	0				0				1	(0.1)	1	0.1	0			
僧帽弁狭窄症	0				1	(0.1)	1	0.1	0				0			
僧帽弁閉鎖不全症	1	(0.1)	1	0.1	0				0				0			
大動脈弁狭窄	0				1	(0.1)	1	0.1	0				0			
大動脈弁疾患	1	(0.1)	1	0.1	0				0				0			
第二度房室ブロック	0				1	(0.1)	1	0.1	0				0			
頻脈	0				1	(0.1)	1	0.1	0				0			
房室ブロック	0				0				1	(0.1)	1	0.1	0			
感染症および寄生虫症	31	(3.8)	41	2.8	27	(3.3)	33	2.3	41	(5.0)	46	3.1	34	(4.1)	42	2.8

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
洞性徐脈	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
うっ血性心筋症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
右室不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
冠動脈硬化症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
冠動脈入口部狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性左室不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高血圧性心筋症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
左脚ブロック	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
左室肥大	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
左室不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
三尖弁閉鎖不全症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
上室性期外収縮	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
上室性頻脈	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心筋炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心血管不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心室血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心室性頻脈性不整脈	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心室性不整脈	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心室無収縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心臓性喘息	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心肺不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
僧帽弁狭窄症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
僧帽弁閉鎖不全症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大動脈弁狭窄	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大動脈弁疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
第二度房室ブロック	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頻脈	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
房室ブロック	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感染症および寄生虫症	58	(3.5)	74	2.5	75	(4.6)	88	2.9	133	(4.0)	162	2.7

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肺炎	6	(0.7)	6	0.4	6	(0.7)	7	0.5	9	(1.1)	9	0.6	5	(0.6)	5	0.3
蜂巣炎	6	(0.7)	6	0.4	2	(0.2)	2	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2
敗血症	5	(0.6)	5	0.3	2	(0.2)	2	0.1	0				4	(0.5)	4	0.3
尿路感染	2	(0.2)	2	0.1	0				5	(0.6)	5	0.3	1	(0.1)	1	0.1
敗血症性ショック	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	3	(0.4)	3	0.2
インフルエンザ	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
壊疽	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	2	(0.2)	2	0.1
胃腸炎	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
帯状疱疹	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
限局性感染	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
骨髄炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
術後創感染	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
大腸菌性敗血症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
虫垂炎	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
膀胱炎	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
ウイルス感染	2	(0.2)	2	0.1	0				0				0			
ウイルス性胃腸炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
ブドウ球菌性敗血症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
感染性大腸炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
気管支炎	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
憩室炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
処置後感染	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
食道カンジダ症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
腎盂腎炎	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
副鼻腔炎	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
ウイルス性消化管感染	1	(0.1)	1	0.1	0				0				0			
カンピロバクター胃腸炎	0				1	(0.1)	1	0.1	0				0			
クロストリジウム・ディフィシレ大腸炎	1	(0.1)	1	0.1	0				0				0			
サルモネラ菌性胃腸炎	0				1	(0.1)	1	0.1	0				0			

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肺炎	12	(0.7)	13	0.4	14	(0.9)	14	0.5	26	(0.8)	27	0.5
蜂巣炎	8	(0.5)	8	0.3	5	(0.3)	5	0.2	13	(0.4)	13	0.2
敗血症	7	(0.4)	7	0.2	4	(0.2)	4	0.1	11	(0.3)	11	0.2
尿路感染	2	(0.1)	2	0.1	6	(0.4)	6	0.2	8	(0.2)	8	0.1
敗血症性ショック	1	(0.1)	1	<0.1	6	(0.4)	6	0.2	7	(0.2)	7	0.1
インフルエンザ	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
壊疽	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
胃腸炎	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
帯状疱疹	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
限局性感染	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
骨髄炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
術後創感染	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
大腸菌性敗血症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
虫垂炎	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
膀胱炎	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
ウイルス感染	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
ウイルス性胃腸炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
ブドウ球菌性敗血症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
感染性大腸炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
気管支炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
憩室炎	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
処置後感染	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
食道カンジダ症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腎盂腎炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
副鼻腔炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
ウイルス性消化管感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
カンピロバクター胃腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
クロストリジウム・ディフィシレ大腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
サルモネラ菌性胃腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ブドウ球菌性骨髄炎	0				0				1	(0.1)	1	0.1	0			
ブドウ球菌性尿路感染	0				0				0				1	(0.1)	1	0.1
ボタン熱	0				0				1	(0.1)	1	0.1	0			
壊死性筋膜炎	0				0				1	(0.1)	1	0.1	0			
感染性腸炎	0				0				1	(0.1)	1	0.1	0			
感染性皮膚潰瘍	0				1	(0.1)	1	0.1	0				0			
肝膿瘍	1	(0.1)	1	0.1	0				0				0			
気道感染	0				1	(0.1)	1	0.1	0				0			
偽膜性大腸炎	0				0				1	(0.1)	1	0.1	0			
急性Ｂ型肝炎	1	(0.1)	1	0.1	0				0				0			
筋膿瘍	1	(0.1)	1	0.1	0				0				0			
四肢膿瘍	1	(0.1)	1	0.1	0				0				0			
歯膿瘍	1	(0.1)	1	0.1	0				0				0			
耳感染	1	(0.1)	1	0.1	0				0				0			
処置後肺炎	1	(0.1)	1	0.1	0				0				0			
上気道感染	0				0				1	(0.1)	1	0.1	0			
心内膜炎	0				0				1	(0.1)	1	0.1	0			
真菌性食道炎	0				1	(0.1)	1	0.1	0				0			
赤痢	0				1	(0.1)	1	0.1	0				0			
切開部位感染	0				0				1	(0.1)	1	0.1	0			
創傷感染	0				0				0				1	(0.1)	1	0.1
大腸菌感染	0				0				0				1	(0.1)	1	0.1
腸球菌感染	1	(0.1)	1	0.1	0				0				0			
爪囲炎	0				1	(0.1)	1	0.1	0				0			
糖尿病性足感染	0				0				0				1	(0.1)	1	0.1
軟部組織感染	0				0				0				1	(0.1)	1	0.1
膿瘍	0				0				1	(0.1)	1	0.1	0			
肺炎球菌性肺炎	0				0				1	(0.1)	1	0.1	0			
肺敗血症	1	(0.1)	1	0.1	0				0				0			
鼻咽頭炎	0				0				0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ブドウ球菌性骨髄炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ブドウ球菌性尿路感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ボタン熱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
壊死性筋膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感染性腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感染性皮膚潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
気道感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
偽膜性大腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性Ｂ型肝炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
筋膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
四肢膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
歯膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
耳感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
処置後肺炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
上気道感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心内膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
真菌性食道炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
赤痢	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
切開部位感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
創傷感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大腸菌感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸球菌感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
爪囲炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病性足感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
軟部組織感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺炎球菌性肺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺敗血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻咽頭炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腹膜炎	0				0				0				1	(0.1)	1	0.1
扁桃周囲膿瘍	0				0				0				1	(0.1)	1	0.1
脾臓膿瘍	0				0				0				1	(0.1)	1	0.1
胃腸障害	41	(5.0)	52	3.5	47	(5.7)	63	4.4	11	(1.3)	13	0.9	19	(2.3)	29	1.9
悪心	10	(1.2)	11	0.7	13	(1.6)	13	0.9	1	(0.1)	1	0.1	0			
嘔吐	5	(0.6)	6	0.4	11	(1.3)	12	0.8	3	(0.4)	3	0.2	2	(0.2)	5	0.3
下痢	7	(0.9)	9	0.6	7	(0.9)	7	0.5	2	(0.2)	2	0.1	2	(0.2)	2	0.1
腹痛	4	(0.5)	4	0.3	3	(0.4)	3	0.2	2	(0.2)	2	0.1	4	(0.5)	4	0.3
消化不良	4	(0.5)	4	0.3	4	(0.5)	5	0.3	0				0			
胃食道逆流性疾患	0				3	(0.4)	3	0.2	0				1	(0.1)	1	0.1
胃腸出血	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
胃腸障害	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0				0			
上腹部痛	0				4	(0.5)	4	0.3	0				0			
下腹部痛	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
急性膵炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
上部消化管出血	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
腹水	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
胃炎	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
胃排出不全	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
腹部不快感	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
便秘	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
嚥下障害	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
膵炎	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
鼠径ヘルニア	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
メレナ	0				1	(0.1)	1	0.1	0				0			
胃イレウス	0				0				0				1	(0.1)	1	0.1
胃障害	0				1	(0.1)	1	0.1	0				0			
胃腸虚血	0				0				0				1	(0.1)	1	0.1
下部消化管出血	1	(0.1)	1	0.1	0				0				0			

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腹膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
扁桃周囲膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脾臓膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胃腸障害	88	(5.4)	115	3.9	30	(1.8)	42	1.4	118	(3.6)	157	2.6
悪心	23	(1.4)	24	0.8	1	(0.1)	1	<0.1	24	(0.7)	25	0.4
嘔吐	16	(1.0)	18	0.6	5	(0.3)	8	0.3	21	(0.6)	26	0.4
下痢	14	(0.9)	16	0.5	4	(0.2)	4	0.1	18	(0.5)	20	0.3
腹痛	7	(0.4)	7	0.2	6	(0.4)	6	0.2	13	(0.4)	13	0.2
消化不良	8	(0.5)	9	0.3	0				8	(0.2)	9	0.2
胃食道逆流性疾患	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
胃腸出血	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
胃腸障害	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
上腹部痛	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
下腹部痛	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
急性膵炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
上部消化管出血	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
腹水	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
胃炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胃排出不全	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腹部不快感	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
便秘	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
嚥下障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
膵炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
鼠径ヘルニア	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
メレナ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃イレウス	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胃障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃腸虚血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
下部消化管出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
憩室	0				1	(0.1)	1	0.1	0				0			
口腔内潰瘍形成	1	(0.1)	1	0.1	0				0				0			
歯痛	0				1	(0.1)	1	0.1	0				0			
十二指腸炎	0				0				0				1	(0.1)	1	0.1
十二指腸潰瘍	0				0				0				1	(0.1)	1	0.1
出血性胃炎	1	(0.1)	1	0.1	0				0				0			
出血性胃潰瘍	1	(0.1)	1	0.1	0				0				0			
消化器痛	0				1	(0.1)	1	0.1	0				0			
食道静脈瘤	1	(0.1)	1	0.1	0				0				0			
舌浮腫	0				0				0				1	(0.1)	1	0.1
大腸出血	0				1	(0.1)	1	0.1	0				0			
腸出血	0				0				0				1	(0.1)	1	0.1
腸閉塞	1	(0.1)	1	0.1	0				0				0			
吐き戻し	1	(0.1)	1	0.1	0				0				0			
放屁	0				1	(0.1)	1	0.1	0				0			
裂孔ヘルニア	0				0				1	(0.1)	1	0.1	0			
臍ヘルニア	1	(0.1)	1	0.1	0				0				0			
神経系障害	27	(3.3)	28	1.9	18	(2.2)	29	2.0	27	(3.3)	39	2.6	21	(2.5)	29	1.9
虚血性脳卒中	5	(0.6)	5	0.3	4	(0.5)	5	0.3	5	(0.6)	5	0.3	1	(0.1)	1	0.1
低血糖性意識消失	4	(0.5)	4	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1	3	(0.4)	7	0.5
一過性脳虚血発作	1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2	2	(0.2)	2	0.1
失神	1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1	3	(0.4)	3	0.2
頭痛	1	(0.1)	1	0.1	3	(0.4)	3	0.2	4	(0.5)	7	0.5	1	(0.1)	1	0.1
脳血管発作	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	4	(0.5)	4	0.3
頚動脈狭窄	0				0				4	(0.5)	4	0.3	2	(0.2)	2	0.1
出血性卒中	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
失神寸前の状態	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
脳梗塞	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
神経根障害	0				0				2	(0.2)	2	0.1	0			

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
憩室	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔内潰瘍形成	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
歯痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
十二指腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
十二指腸潰瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性胃炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
出血性胃潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化器痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
食道静脈瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
舌浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大腸出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腸出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸閉塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
吐き戻し	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
放屁	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
裂孔ヘルニア	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
臍ヘルニア	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経系障害	45	(2.7)	57	1.9	48	(2.9)	68	2.2	93	(2.8)	125	2.1
虚血性脳卒中	9	(0.5)	10	0.3	6	(0.4)	6	0.2	15	(0.5)	16	0.3
低血糖性意識消失	8	(0.5)	8	0.3	5	(0.3)	9	0.3	13	(0.4)	17	0.3
一過性脳虚血発作	4	(0.2)	4	0.1	5	(0.3)	5	0.2	9	(0.3)	9	0.2
失神	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
頭痛	4	(0.2)	4	0.1	5	(0.3)	8	0.3	9	(0.3)	12	0.2
脳血管発作	2	(0.1)	2	0.1	6	(0.4)	6	0.2	8	(0.2)	8	0.1
頚動脈狭窄	0				6	(0.4)	6	0.2	6	(0.2)	6	0.1
出血性卒中	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
失神寸前の状態	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
脳梗塞	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
神経根障害	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
てんかん	0				1	(0.1)	1	0.1	0				0			
パーキンソニズム	1	(0.1)	1	0.1	0				0				0			
ラクナ梗塞	1	(0.1)	1	0.1	0				0				0			
意識変容状態	0				0				1	(0.1)	1	0.1	0			
感覚鈍麻	0				1	(0.1)	1	0.1	0				0			
肝性脳症	1	(0.1)	1	0.1	0				0				0			
記憶障害	0				0				1	(0.1)	1	0.1	0			
虚血性脳梗塞	0				0				0				1	(0.1)	1	0.1
血管性パーキンソニズム	1	(0.1)	1	0.1	0				0				0			
後頭神経痛	0				0				1	(0.1)	1	0.1	0			
構語障害	0				0				0				1	(0.1)	1	0.1
昏睡	0				1	(0.1)	2	0.1	0				0			
坐骨神経痛	1	(0.1)	1	0.1	0				0				0			
手根管症候群	1	(0.1)	1	0.1	0				0				0			
重症疾患多発ニューロパチー	0				0				0				1	(0.1)	1	0.1
小脳症候群	0				0				1	(0.1)	1	0.1	0			
神経根圧迫	1	(0.1)	1	0.1	0				0				0			
水頭症	0				0				0				1	(0.1)	1	0.1
舌下神経不全麻痺	0				0				0				1	(0.1)	1	0.1
代謝性脳症	1	(0.1)	1	0.1	0				0				0			
第７脳神経麻痺	0				0				1	(0.1)	1	0.1	0			
椎骨動脈閉塞	1	(0.1)	1	0.1	0				0				0			
低酸素性虚血性脳症	0				0				1	(0.1)	1	0.1	0			
頭蓋内動脈瘤	0				1	(0.1)	1	0.1	0				0			
脳圧低下	0				0				1	(0.1)	1	0.1	0			
脳幹梗塞	1	(0.1)	1	0.1	0				0				0			
脳虚血	0				0				0				1	(0.1)	1	0.1
脳室内出血	0				0				0				1	(0.1)	1	0.1
脳出血	1	(0.1)	1	0.1	0				0				0			

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
てんかん	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
パーキンソニズム	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ラクナ梗塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
意識変容状態	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感覚鈍麻	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝性脳症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
記憶障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
虚血性脳梗塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管性パーキンソニズム	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
後頭神経痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
構語障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
昏睡	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
坐骨神経痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
手根管症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
重症疾患多発ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
小脳症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経根圧迫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
水頭症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
舌下神経不全麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
代謝性脳症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
第７脳神経麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎骨動脈閉塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
低酸素性虚血性脳症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頭蓋内動脈瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳圧低下	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳幹梗塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳虚血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳室内出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脳神経麻痺	1	(0.1)	1	0.1	0				0				0			
脳脊髄液漏	0				0				1	(0.1)	1	0.1	0			
浮動性めまい	0				1	(0.1)	1	0.1	0				0			
片頭痛	0				0				1	(0.1)	1	0.1	0			
味覚異常	1	(0.1)	1	0.1	0				0				0			
痙攣発作	0				0				0				1	(0.1)	1	0.1
外科および内科処置	17	(2.1)	18	1.2	17	(2.1)	18	1.2	32	(3.9)	33	2.2	30	(3.6)	34	2.2
冠動脈バイパス	4	(0.5)	4	0.3	4	(0.5)	4	0.3	11	(1.3)	11	0.7	6	(0.7)	6	0.4
冠動脈ステント挿入	7	(0.9)	7	0.5	4	(0.5)	5	0.3	6	(0.7)	6	0.4	5	(0.6)	5	0.3
冠動脈血行再建	4	(0.5)	4	0.3	3	(0.4)	3	0.2	6	(0.7)	7	0.5	7	(0.8)	7	0.5
末梢血行再建	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	7	(0.8)	7	0.5
冠動脈形成	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2
経皮的冠インターベンション	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
ステント装着	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
頚動脈内膜剥離術	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
白内障手術	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
頚動脈血行再建	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
血管形成	1	(0.1)	1	0.1	0				0				0			
腹部ヘルニア修復	0				1	(0.1)	1	0.1	0				0			
筋骨格系および結合組織障害	10	(1.2)	14	0.9	13	(1.6)	13	0.9	20	(2.4)	31	2.1	21	(2.5)	24	1.6
背部痛	2	(0.2)	2	0.1	5	(0.6)	5	0.3	3	(0.4)	3	0.2	6	(0.7)	6	0.4
変形性関節症	1	(0.1)	1	0.1	3	(0.4)	3	0.2	4	(0.5)	5	0.3	6	(0.7)	6	0.4
関節痛	2	(0.2)	3	0.2	0				5	(0.6)	5	0.3	1	(0.1)	1	0.1
椎間板突出	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
筋骨格痛	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
腰部脊柱管狭窄症	0				0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
四肢痛	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脳神経麻痺	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳脊髄液漏	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
浮動性めまい	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
片頭痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
味覚異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
痙攣発作	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外科および内科処置	34	(2.1)	36	1.2	62	(3.8)	67	2.2	96	(2.9)	103	1.7
冠動脈バイパス	8	(0.5)	8	0.3	17	(1.0)	17	0.6	25	(0.8)	25	0.4
冠動脈ステント挿入	11	(0.7)	12	0.4	11	(0.7)	11	0.4	22	(0.7)	23	0.4
冠動脈血行再建	7	(0.4)	7	0.2	13	(0.8)	14	0.5	20	(0.6)	21	0.4
末梢血行再建	2	(0.1)	2	0.1	9	(0.5)	9	0.3	11	(0.3)	11	0.2
冠動脈形成	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
経皮的冠インターベンション	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
ステント装着	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
頚動脈内膜剥離術	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
白内障手術	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
頚動脈血行再建	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血管形成	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹部ヘルニア修復	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
筋骨格系および結合組織障害	23	(1.4)	27	0.9	41	(2.5)	55	1.8	64	(1.9)	82	1.4
背部痛	7	(0.4)	7	0.2	9	(0.5)	9	0.3	16	(0.5)	16	0.3
変形性関節症	4	(0.2)	4	0.1	10	(0.6)	11	0.4	14	(0.4)	15	0.3
関節痛	2	(0.1)	3	0.1	6	(0.4)	6	0.2	8	(0.2)	9	0.2
椎間板突出	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
筋骨格痛	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
腰部脊柱管狭窄症	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
四肢痛	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
滑液包炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
骨壊死	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
脊柱管狭窄症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
椎間関節症候群	0				0				2	(0.2)	3	0.2	0			
椎間板変性症	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
滑液嚢腫	0				0				1	(0.1)	1	0.1	0			
関節炎	0				1	(0.1)	1	0.1	0				0			
筋骨格系胸痛	0				0				1	(0.1)	1	0.1	0			
筋膜疼痛症候群	0				0				1	(0.1)	1	0.1	0			
筋痙縮	0				0				0				1	(0.1)	1	0.1
頚部痛	1	(0.1)	1	0.1	0				0				0			
肩回旋筋腱板症候群	0				1	(0.1)	1	0.1	0				0			
斜頚	0				0				1	(0.1)	1	0.1	0			
線維筋痛	0				0				1	(0.1)	1	0.1	0			
側腹部痛	0				1	(0.1)	1	0.1	0				0			
側弯症	1	(0.1)	1	0.1	0				0				0			
糖尿病性関節障害	0				0				1	(0.1)	1	0.1	0			
軟骨溶解	1	(0.1)	1	0.1	0				0				0			
瘻孔	0				0				0				1	(0.1)	1	0.1
鼠径部痛	0				0				1	(0.1)	1	0.1	0			
傷害、中毒および処置合併症	14	(1.7)	14	0.9	11	(1.3)	13	0.9	14	(1.7)	18	1.2	17	(2.1)	20	1.3
転倒	4	(0.5)	4	0.3	2	(0.2)	2	0.1	3	(0.4)	3	0.2	5	(0.6)	5	0.3
交通事故	0				4	(0.5)	4	0.3	3	(0.4)	3	0.2	2	(0.2)	3	0.2
各種物質毒性	0				0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
筋断裂	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
処置による疼痛	0				0				2	(0.2)	2	0.1	0			
上腕骨骨折	0				1	(0.1)	2	0.1	0				1	(0.1)	1	0.1
脊椎圧迫骨折	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
腱断裂	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
滑液包炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
骨壊死	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
脊柱管狭窄症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
椎間関節症候群	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
椎間板変性症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
滑液嚢腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
関節炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
筋骨格系胸痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋膜疼痛症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋痙縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頚部痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肩回旋筋腱板症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
斜頚	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
線維筋痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
側腹部痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
側弯症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病性関節障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
軟骨溶解	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
瘻孔	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鼠径部痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
傷害、中毒および処置合併症	25	(1.5)	27	0.9	31	(1.9)	38	1.3	56	(1.7)	65	1.1
転倒	6	(0.4)	6	0.2	8	(0.5)	8	0.3	14	(0.4)	14	0.2
交通事故	4	(0.2)	4	0.1	5	(0.3)	6	0.2	9	(0.3)	10	0.2
各種物質毒性	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
筋断裂	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
処置による疼痛	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
上腕骨骨折	1	(0.1)	2	0.1	1	(0.1)	1	<0.1	2	(0.1)	3	0.1
脊椎圧迫骨折	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腱断裂	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
移植血管閉塞	0				0				1	(0.1)	1	0.1	0			
下肢骨折	1	(0.1)	1	0.1	0				0				0			
過量投与	0				0				0				1	(0.1)	1	0.1
外傷性血胸	0				0				1	(0.1)	1	0.1	0			
外傷性潰瘍	0				1	(0.1)	1	0.1	0				0			
企図的過量投与	0				0				0				1	(0.1)	1	0.1
頚動脈再狭窄	1	(0.1)	1	0.1	0				0				0			
誤薬投与	1	(0.1)	1	0.1	0				0				0			
硬膜下血腫	0				1	(0.1)	1	0.1	0				0			
骨格損傷	0				0				1	(0.1)	1	0.1	0			
坐骨神経損傷	0				0				0				1	(0.1)	1	0.1
挫傷	0				0				1	(0.1)	1	0.1	0			
四肢損傷	0				0				1	(0.1)	1	0.1	0			
脂肪塞栓症	0				0				0				1	(0.1)	1	0.1
創壊死	0				0				1	(0.1)	1	0.1	0			
創傷	1	(0.1)	1	0.1	0				0				0			
足関節部骨折	1	(0.1)	1	0.1	0				0				0			
頭蓋骨骨折	0				0				0				1	(0.1)	1	0.1
頭部損傷	1	(0.1)	1	0.1	0				0				0			
軟骨損傷	1	(0.1)	1	0.1	0				0				0			
皮膚擦過傷	0				0				0				1	(0.1)	1	0.1
膝蓋骨骨折	1	(0.1)	1	0.1	0				0				0			
吻合不全	0				0				0				1	(0.1)	1	0.1
労働災害	1	(0.1)	1	0.1	0				0				0			
肋骨骨折	0				0				1	(0.1)	1	0.1	0			
橈骨骨折	0				1	(0.1)	1	0.1	0				0			
靭帯損傷	0				0				0				1	(0.1)	1	0.1
代謝および栄養障害	14	(1.7)	14	0.9	12	(1.5)	17	1.2	16	(2.0)	19	1.3	15	(1.8)	15	1.0
低血糖症	3	(0.4)	3	0.2	4	(0.5)	8	0.6	8	(1.0)	10	0.7	5	(0.6)	5	0.3

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
移植血管閉塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
下肢骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
過量投与	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外傷性血胸	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外傷性潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
企図的過量投与	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頚動脈再狭窄	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
誤薬投与	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
硬膜下血腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨格損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
坐骨神経損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
挫傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
四肢損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脂肪塞栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
創壊死	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
創傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
足関節部骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頭蓋骨骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頭部損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
軟骨損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮膚擦過傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膝蓋骨骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
吻合不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
労働災害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肋骨骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
橈骨骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
靭帯損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
代謝および栄養障害	26	(1.6)	31	1.1	31	(1.9)	34	1.1	57	(1.7)	65	1.1
低血糖症	7	(0.4)	11	0.4	13	(0.8)	15	0.5	20	(0.6)	26	0.4

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
高血糖	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2
高カリウム血症	0				1	(0.1)	1	0.1	3	(0.4)	4	0.3	1	(0.1)	1	0.1
脱水	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
食欲減退	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1	0			
水分過負荷	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
痛風	2	(0.2)	2	0.1	0				0				0			
糖尿病性ケトアシドーシス	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
アシドーシス	1	(0.1)	1	0.1	0				0				0			
コントロール不良の糖尿病	1	(0.1)	1	0.1	0				0				0			
ビタミンD欠乏	0				1	(0.1)	1	0.1	0				0			
高トリグリセリド血症	0				1	(0.1)	1	0.1	0				0			
高リパーゼ血症	0				0				0				1	(0.1)	1	0.1
高脂血症	0				0				0				1	(0.1)	1	0.1
成長障害	0				0				0				1	(0.1)	1	0.1
低カルシウム血症	0				1	(0.1)	1	0.1	0				0			
低マグネシウム血症	0				1	(0.1)	1	0.1	0				0			
糖尿病	0				1	(0.1)	1	0.1	0				0			
乳酸アシドーシス	0				0				0				1	(0.1)	1	0.1
肥満	0				0				1	(0.1)	1	0.1	0			
呼吸器、胸郭および縦隔障害	13	(1.6)	13	0.9	18	(2.2)	21	1.5	11	(1.3)	12	0.8	12	(1.5)	13	0.9
呼吸不全	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
呼吸困難	2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
慢性閉塞性肺疾患	1	(0.1)	1	0.1	4	(0.5)	4	0.3	0				1	(0.1)	1	0.1
肺塞栓症	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1
肺水腫	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
急性肺水腫	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				0			
急性呼吸不全	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
睡眠時無呼吸症候群	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
肺高血圧症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
高血糖	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
高カリウム血症	1	(0.1)	1	<0.1	4	(0.2)	5	0.2	5	(0.2)	6	0.1
脱水	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
食欲減退	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
水分過負荷	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
痛風	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
糖尿病性ケトアシドーシス	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
アシドーシス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
コントロール不良の糖尿病	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ビタミンD欠乏	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高トリグリセリド血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高リパーゼ血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高脂血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
成長障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
低カルシウム血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
低マグネシウム血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳酸アシドーシス	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肥満	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼吸器、胸郭および縦隔障害	31	(1.9)	34	1.2	23	(1.4)	25	0.8	54	(1.6)	59	1.0
呼吸不全	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
呼吸困難	5	(0.3)	5	0.2	2	(0.1)	2	0.1	7	(0.2)	7	0.1
慢性閉塞性肺疾患	5	(0.3)	5	0.2	1	(0.1)	1	<0.1	6	(0.2)	6	0.1
肺塞栓症	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
肺水腫	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
急性肺水腫	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
急性呼吸不全	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
睡眠時無呼吸症候群	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
肺高血圧症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
咳嗽	0				2	(0.2)	2	0.1	0				0			
気胸	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
鼻出血	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
胸水症	1	(0.1)	1	0.1	0				0				0			
呼吸窮迫	0				0				1	(0.1)	1	0.1	0			
呼吸停止	0				0				1	(0.1)	1	0.1	0			
誤嚥性肺炎	0				1	(0.1)	2	0.1	0				0			
喉頭狭窄	0				0				1	(0.1)	1	0.1	0			
肺うっ血	0				0				0				1	(0.1)	1	0.1
肺腫瘤	0				0				1	(0.1)	1	0.1	0			
喘息	0				0				0				1	(0.1)	1	0.1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	14	(1.7)	17	1.1	11	(1.3)	13	0.9	16	(2.0)	18	1.2	11	(1.3)	11	0.7
Ｂ細胞性リンパ腫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
結腸腺癌	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
小細胞肺癌	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
前立腺癌	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
気管支癌	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
直腸癌	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
肺の悪性新生物	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
膀胱移行上皮癌	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
Ｂ細胞性小リンパ球性リンパ腫	0				0				1	(0.1)	1	0.1	0			
ボーエン病	0				0				0				1	(0.1)	1	0.1
リンパ節転移	1	(0.1)	1	0.1	0				0				0			
悪性黒色腫	1	(0.1)	1	0.1	0				0				0			
胃癌	1	(0.1)	1	0.1	0				0				0			
胃腺癌	1	(0.1)	1	0.1	0				0				0			

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
咳嗽	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
気胸	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
鼻出血	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
胸水症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
呼吸窮迫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼吸停止	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
誤嚥性肺炎	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
喉頭狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺うっ血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺腫瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
喘息	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	25	(1.5)	30	1.0	27	(1.6)	29	1.0	52	(1.6)	59	1.0
Ｂ細胞性リンパ腫	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
結腸腺癌	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
小細胞肺癌	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
前立腺癌	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
気管支癌	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
直腸癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肺の悪性新生物	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
膀胱移行上皮癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
Ｂ細胞性小リンパ球性リンパ腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ボーエン病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
リンパ節転移	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
悪性黒色腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃腺癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
遠隔転移を伴う胃癌	1	(0.1)	1	0.1	0				0				0			
遠隔転移を伴う骨癌	0				1	(0.1)	1	0.1	0				0			
遠隔転移を伴う腎癌	1	(0.1)	1	0.1	0				0				0			
遠隔転移を伴う前立腺癌	0				1	(0.1)	1	0.1	0				0			
遠隔転移を伴う膵癌	0				0				1	(0.1)	1	0.1	0			
肝癌	1	(0.1)	1	0.1	0				0				0			
肝転移	1	(0.1)	1	0.1	0				0				0			
肝内胆管癌	0				0				1	(0.1)	2	0.1	0			
急性骨髄性白血病	0				0				1	(0.1)	1	0.1	0			
結腸癌	0				0				1	(0.1)	1	0.1	0			
喉頭扁平上皮癌	1	(0.1)	1	0.1	0				0				0			
再発膀胱移行上皮癌	0				0				0				1	(0.1)	1	0.1
浸潤性乳管癌	0				0				1	(0.1)	1	0.1	0			
真珠腫	0				0				1	(0.1)	1	0.1	0			
腎細胞癌	0				1	(0.1)	1	0.1	0				0			
成長ホルモン産生性下垂体腫瘍	0				0				0				1	(0.1)	1	0.1
節外周辺帯Ｂ細胞リンパ腫（ＭＡＬＴ型）	1	(0.1)	1	0.1	0				0				0			
退形成星細胞腫	0				0				0				1	(0.1)	1	0.1
胆嚢腺癌	0				0				1	(0.1)	1	0.1	0			
中枢神経系転移	0				1	(0.1)	1	0.1	0				0			
乳癌	0				1	(0.1)	1	0.1	0				0			
乳癌第３期	0				0				0				1	(0.1)	1	0.1
肺癌第４期、細胞タイプ不明	0				1	(0.1)	1	0.1	0				0			
肺腺癌第４期	0				1	(0.1)	1	0.1	0				0			
肺転移	1	(0.1)	1	0.1	0				0				0			
慢性リンパ性白血病	0				0				1	(0.1)	1	0.1	0			
脈絡膜黒色腫	1	(0.1)	1	0.1	0				0				0			

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
遠隔転移を伴う胃癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う骨癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う腎癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う前立腺癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う膵癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝転移	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝内胆管癌	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
急性骨髄性白血病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結腸癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
喉頭扁平上皮癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
再発膀胱移行上皮癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
浸潤性乳管癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
真珠腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎細胞癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
成長ホルモン産生性下垂体腫瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
節外周辺帯Ｂ細胞リンパ腫（ＭＡＬＴ型）	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
退形成星細胞腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆嚢腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
中枢神経系転移	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳癌第３期	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺癌第４期、細胞タイプ不明	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺腺癌第４期	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺転移	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
慢性リンパ性白血病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脈絡膜黒色腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
卵巣上皮癌	1	(0.1)	1	0.1	0				0				0			
卵巣胚細胞良性奇形腫	1	(0.1)	1	0.1	0				0				0			
膀胱移行上皮癌第２期	0				1	(0.1)	1	0.1	0				0			
膵癌	0				0				0				1	(0.1)	1	0.1
膵腺癌	0				0				0				1	(0.1)	1	0.1
腎および尿路障害	11	(1.3)	11	0.7	12	(1.5)	13	0.9	17	(2.1)	18	1.2	13	(1.6)	15	1.0
急性腎不全	4	(0.5)	4	0.3	5	(0.6)	5	0.3	6	(0.7)	6	0.4	6	(0.7)	7	0.5
慢性腎臓病	3	(0.4)	3	0.2	2	(0.2)	2	0.1	6	(0.7)	7	0.5	3	(0.4)	3	0.2
腎結石症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
腎症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
腎嚢胞	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
腎不全	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
蛋白尿	0				0				2	(0.2)	2	0.1	0			
尿管結石	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
急性腎前性腎不全	1	(0.1)	1	0.1	0				0				0			
腎機能障害	0				0				0				1	(0.1)	1	0.1
水腎症	0				0				0				1	(0.1)	1	0.1
糖尿病性腎症	0				1	(0.1)	1	0.1	0				0			
尿失禁	0				0				1	(0.1)	1	0.1	0			
膀胱ポリープ	0				0				0				1	(0.1)	1	0.1
血管障害	13	(1.6)	13	0.9	3	(0.4)	3	0.2	7	(0.9)	7	0.5	14	(1.7)	14	0.9
低血圧	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
末梢動脈閉塞性疾患	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2
高血圧	0				0				0				3	(0.4)	3	0.2
高血圧クリーゼ	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
高血圧緊急症	3	(0.4)	3	0.2	0				0				0			
末梢血管障害	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
大動脈狭窄	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
卵巣上皮癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
卵巣胚細胞良性奇形腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱移行上皮癌第２期	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膵腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎および尿路障害	23	(1.4)	24	0.8	30	(1.8)	33	1.1	53	(1.6)	57	1.0
急性腎不全	9	(0.5)	9	0.3	12	(0.7)	13	0.4	21	(0.6)	22	0.4
慢性腎臓病	5	(0.3)	5	0.2	9	(0.5)	10	0.3	14	(0.4)	15	0.3
腎結石症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
腎症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
腎嚢胞	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腎不全	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
蛋白尿	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
尿管結石	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
急性腎前性腎不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎機能障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
水腎症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糖尿病性腎症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿失禁	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膀胱ポリープ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管障害	16	(1.0)	16	0.5	21	(1.3)	21	0.7	37	(1.1)	37	0.6
低血圧	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
末梢動脈閉塞性疾患	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
高血圧	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
高血圧クリーゼ	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
高血圧緊急症	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
末梢血管障害	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
大動脈狭窄	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
末梢動脈血栓症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
リンパ浮腫	1	(0.1)	1	0.1	0				0				0			
起立性低血圧	1	(0.1)	1	0.1	0				0				0			
四肢壊死	0				0				0				1	(0.1)	1	0.1
出血性ショック	0				0				1	(0.1)	1	0.1	0			
循環虚脱	1	(0.1)	1	0.1	0				0				0			
側頭動脈炎	1	(0.1)	1	0.1	0				0				0			
大腿動脈閉塞	0				1	(0.1)	1	0.1	0				0			
大動脈解離	0				0				0				1	(0.1)	1	0.1
大動脈瘤	1	(0.1)	1	0.1	0				0				0			
腹腔内血腫	1	(0.1)	1	0.1	0				0				0			
末梢動脈狭窄	0				0				0				1	(0.1)	1	0.1
臨床検査	8	(1.0)	11	0.7	6	(0.7)	6	0.4	8	(1.0)	10	0.7	2	(0.2)	2	0.1
リパーゼ増加	4	(0.5)	5	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
体重減少	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
血中カリウム増加	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
トランスアミナーゼ上昇	0				0				1	(0.1)	1	0.1	0			
眼圧検査	0				0				1	(0.1)	1	0.1	0			
血圧上昇	0				0				0				1	(0.1)	1	0.1
血中アルカリホスファターゼ増加	0				0				1	(0.1)	1	0.1	0			
血中カルシトニン増加	1	(0.1)	1	0.1	0				0				0			
血中トリグリセリド異常	0				0				0				1	(0.1)	1	0.1
血中ビリルビン増加	0				0				1	(0.1)	1	0.1	0			
血中ブドウ糖増加	1	(0.1)	3	0.2	0				0				0			
血中プロインスリン増加	0				1	(0.1)	1	0.1	0				0			
国際標準比増加	0				0				1	(0.1)	1	0.1	0			
心カテーテル検査	0				0				1	(0.1)	1	0.1	0			
末梢血管造影	0				0				1	(0.1)	1	0.1	0			

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
末梢動脈血栓症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
リンパ浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
起立性低血圧	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
四肢壊死	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性ショック	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
循環虚脱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
側頭動脈炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大腿動脈閉塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大動脈解離	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大動脈瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹腔内血腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
末梢動脈狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
臨床検査	14	(0.9)	17	0.6	10	(0.6)	12	0.4	24	(0.7)	29	0.5
リパーゼ増加	6	(0.4)	7	0.2	2	(0.1)	2	0.1	8	(0.2)	9	0.2
体重減少	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
血中カリウム増加	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
トランスアミナーゼ上昇	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼圧検査	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血圧上昇	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中アルカリホスファターゼ増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中カルシトニン増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中トリグリセリド異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中ビリルビン増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中ブドウ糖増加	1	(0.1)	3	0.1	0				1	(<0.1)	3	0.1
血中プロインスリン増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
国際標準比増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心カテーテル検査	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢血管造影	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
膵酵素増加	1	(0.1)	1	0.1	0				0				0			
一般・全身障害および投与部位の状態	7	(0.9)	7	0.5	8	(1.0)	8	0.6	7	(0.9)	7	0.5	6	(0.7)	6	0.4
死亡	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
非心臓性胸痛	0				2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
胸痛	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
多臓器不全	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
突然死	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
悪性高熱	0				1	(0.1)	1	0.1	0				0			
心突然死	1	(0.1)	1	0.1	0				0				0			
先行疾患の改善	0				1	(0.1)	1	0.1	0				0			
全身性浮腫	1	(0.1)	1	0.1	0				0				0			
潰瘍	0				1	(0.1)	1	0.1	0				0			
発熱	0				0				1	(0.1)	1	0.1	0			
疲労	0				1	(0.1)	1	0.1	0				0			
歩行障害	0				0				0				1	(0.1)	1	0.1
末梢性浮腫	0				0				1	(0.1)	1	0.1	0			
無力症	1	(0.1)	1	0.1	0				0				0			
肝胆道系障害	10	(1.2)	11	0.7	4	(0.5)	5	0.3	5	(0.6)	6	0.4	5	(0.6)	6	0.4
急性胆嚢炎	3	(0.4)	3	0.2	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
胆石症	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
胆嚢炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
肝硬変	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
虚血性肝炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
黄疸	1	(0.1)	1	0.1	0				0				0			
脂肪肝	1	(0.1)	1	0.1	0				0				0			
胆管炎	1	(0.1)	1	0.1	0				0				0			
胆汁性肝硬変	0				1	(0.1)	1	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
膵酵素増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
一般・全身障害および投与部位の状態	15	(0.9)	15	0.5	13	(0.8)	13	0.4	28	(0.9)	28	0.5
死亡	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
非心臓性胸痛	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
胸痛	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
多臓器不全	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
突然死	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
悪性高熱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心突然死	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
先行疾患の改善	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
全身性浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
発熱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
疲労	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
歩行障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢性浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
無力症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝胆道系障害	14	(0.9)	16	0.5	10	(0.6)	12	0.4	24	(0.7)	28	0.5
急性胆嚢炎	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
胆石症	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
胆嚢炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
肝硬変	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
虚血性肝炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
黄疸	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脂肪肝	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆管炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆汁性肝硬変	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胆道仙痛	1	(0.1)	1	0.1	0				0				0			
胆嚢壊死	0				0				1	(0.1)	1	0.1	0			
閉塞性胆石症	1	(0.1)	1	0.1	0				0				0			
慢性胆嚢炎	0				0				0				1	(0.1)	1	0.1
眼障害	8	(1.0)	9	0.6	7	(0.9)	7	0.5	5	(0.6)	5	0.3	7	(0.8)	7	0.5
糖尿病網膜症	4	(0.5)	4	0.3	3	(0.4)	3	0.2	2	(0.2)	2	0.1	4	(0.5)	4	0.3
白内障	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
硝子体出血	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
眼瞼下垂	0				0				1	(0.1)	1	0.1	0			
虚血性視神経症	0				1	(0.1)	1	0.1	0				0			
失明	1	(0.1)	1	0.1	0				0				0			
出血性網膜症	1	(0.1)	1	0.1	0				0				0			
虹彩毛様体炎	0				0				0				1	(0.1)	1	0.1
嚢胞様黄斑浮腫	1	(0.1)	1	0.1	0				0				0			
片側失明	0				1	(0.1)	1	0.1	0				0			
網膜剥離	0				0				0				1	(0.1)	1	0.1
皮膚および皮下組織障害	10	(1.2)	12	0.8	2	(0.2)	2	0.1	4	(0.5)	4	0.3	4	(0.5)	6	0.4
糖尿病性足病変	5	(0.6)	6	0.4	2	(0.2)	2	0.1	3	(0.4)	3	0.2	4	(0.5)	6	0.4
皮膚潰瘍	2	(0.2)	2	0.1	0				0				0			
スティーブンス・ジョンソン症候群	1	(0.1)	1	0.1	0				0				0			
丘疹性皮疹	0				0				1	(0.1)	1	0.1	0			
脱毛症	1	(0.1)	1	0.1	0				0				0			
発疹	1	(0.1)	1	0.1	0				0				0			
褥瘡性潰瘍	1	(0.1)	1	0.1	0				0				0			
血液およびリンパ系障害	4	(0.5)	4	0.3	2	(0.2)	2	0.1	5	(0.6)	5	0.3	5	(0.6)	5	0.3
貧血	3	(0.4)	3	0.2	1	(0.1)	1	0.1	4	(0.5)	4	0.3	0			

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胆道仙痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆嚢壊死	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
閉塞性胆石症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
慢性胆嚢炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼障害	15	(0.9)	16	0.5	12	(0.7)	12	0.4	27	(0.8)	28	0.5
糖尿病網膜症	7	(0.4)	7	0.2	6	(0.4)	6	0.2	13	(0.4)	13	0.2
白内障	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
硝子体出血	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
眼瞼下垂	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
虚血性視神経症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
失明	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
出血性網膜症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
虹彩毛様体炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
嚢胞様黄斑浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
片側失明	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
網膜剥離	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚および皮下組織障害	12	(0.7)	14	0.5	8	(0.5)	10	0.3	20	(0.6)	24	0.4
糖尿病性足病変	7	(0.4)	8	0.3	7	(0.4)	9	0.3	14	(0.4)	17	0.3
皮膚潰瘍	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
スティーブンス・ジョンソン症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
丘疹性皮疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脱毛症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
発疹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
褥瘡性潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血液およびリンパ系障害	6	(0.4)	6	0.2	10	(0.6)	10	0.3	16	(0.5)	16	0.3
貧血	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
出血性貧血	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
血小板減少症	0				0				0				1	(0.1)	1	0.1
縦隔リンパ節腫脹	0				0				1	(0.1)	1	0.1	0			
小球性貧血	0				0				0				1	(0.1)	1	0.1
脾腫	0				0				0				1	(0.1)	1	0.1
脾静脈血栓症	0				0				0				1	(0.1)	1	0.1
精神障害	3	(0.4)	4	0.3	5	(0.6)	5	0.3	0				4	(0.5)	4	0.3
うつ病	2	(0.2)	2	0.1	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1
精神状態変化	0				0				0				2	(0.2)	2	0.1
不眠症	2	(0.2)	2	0.1	0				0				0			
錯乱状態	0				1	(0.1)	1	0.1	0				0			
不安障害	0				0				0				1	(0.1)	1	0.1
譫妄	0				1	(0.1)	1	0.1	0				0			
耳および迷路障害	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
回転性めまい	0				0				1	(0.1)	1	0.1	0			
感音性難聴	0				0				1	(0.1)	1	0.1	0			
鼓膜穿孔	0				1	(0.1)	1	0.1	0				0			
聴力低下	0				0				0				1	(0.1)	1	0.1
免疫系障害	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
アナフィラキシーショック	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
アナフィラキシー反応	0				0				0				1	(0.1)	1	0.1
過敏症	1	(0.1)	1	0.1	0				0				0			
生殖系および乳房障害	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
前立腺腫大	0				0				0				1	(0.1)	1	0.1
良性前立腺肥大症	1	(0.1)	1	0.1	0				0				0			

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
出血性貧血	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
血小板減少症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
縦隔リンパ節腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
小球性貧血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脾腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脾静脈血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精神障害	8	(0.5)	9	0.3	4	(0.2)	4	0.1	12	(0.4)	13	0.2
うつ病	5	(0.3)	5	0.2	1	(0.1)	1	<0.1	6	(0.2)	6	0.1
精神状態変化	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
不眠症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
錯乱状態	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
不安障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
譫妄	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
耳および迷路障害	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
回転性めまい	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感音性難聴	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鼓膜穿孔	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
聴力低下	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
免疫系障害	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
アナフィラキシーショック	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
アナフィラキシー反応	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
過敏症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
生殖系および乳房障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
前立腺腫大	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性前立腺肥大症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
内分泌障害	0				0				0				1	(0.1)	1	0.1
甲状腺機能低下症	0				0				0				1	(0.1)	1	0.1

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Severe adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
内分泌障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
甲状腺機能低下症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.25.2- 5　中等度の有害事象（器官別大分類及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	823				819				819				825			
Exposure time (year)	1488.3				1443.9				1508.0				1526.8			
Events	476	(57.8)	1522	102.3	476	(58.1)	1657	114.8	466	(56.9)	1560	103.4	468	(56.7)	1513	99.1
胃腸障害	172	(20.9)	326	21.9	187	(22.8)	441	30.5	111	(13.6)	177	11.7	100	(12.1)	165	10.8
下痢	51	(6.2)	80	5.4	53	(6.5)	81	5.6	37	(4.5)	47	3.1	33	(4.0)	38	2.5
悪心	35	(4.3)	46	3.1	64	(7.8)	78	5.4	19	(2.3)	20	1.3	16	(1.9)	17	1.1
嘔吐	33	(4.0)	38	2.6	49	(6.0)	60	4.2	15	(1.8)	18	1.2	11	(1.3)	13	0.9
腹痛	16	(1.9)	18	1.2	17	(2.1)	18	1.2	14	(1.7)	14	0.9	8	(1.0)	8	0.5
便秘	10	(1.2)	11	0.7	25	(3.1)	30	2.1	11	(1.3)	11	0.7	9	(1.1)	9	0.6
消化不良	14	(1.7)	15	1.0	26	(3.2)	33	2.3	5	(0.6)	5	0.3	2	(0.2)	2	0.1
上腹部痛	16	(1.9)	16	1.1	15	(1.8)	18	1.2	5	(0.6)	5	0.3	6	(0.7)	9	0.6
胃食道逆流性疾患	11	(1.3)	11	0.7	15	(1.8)	18	1.2	5	(0.6)	5	0.3	7	(0.8)	8	0.5
胃炎	9	(1.1)	9	0.6	11	(1.3)	11	0.8	4	(0.5)	5	0.3	5	(0.6)	5	0.3
腹部不快感	6	(0.7)	18	1.2	12	(1.5)	18	1.2	6	(0.7)	7	0.5	2	(0.2)	2	0.1
腹部膨満	2	(0.2)	2	0.1	8	(1.0)	9	0.6	3	(0.4)	3	0.2	4	(0.5)	4	0.3
おくび	3	(0.4)	3	0.2	9	(1.1)	10	0.7	0				0			
歯痛	1	(0.1)	1	0.1	2	(0.2)	2	0.1	6	(0.7)	6	0.4	2	(0.2)	2	0.1
放屁	3	(0.4)	5	0.3	6	(0.7)	6	0.4	1	(0.1)	1	0.1	1	(0.1)	1	0.1
痔核	3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
大腸ポリープ	0				4	(0.5)	4	0.3	1	(0.1)	1	0.1	3	(0.4)	3	0.2
憩室	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
齲歯	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
心窩部不快感	3	(0.4)	3	0.2	3	(0.4)	4	0.3	0				0			
膵炎	3	(0.4)	3	0.2	0				0				3	(0.4)	3	0.2
胃腸出血	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
胃潰瘍	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	4	0.3
過敏性腸症候群	3	(0.4)	3	0.2	2	(0.2)	2	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	1642				1644				3286			
Exposure time (year)	2932.2				3034.8				5967.0			
Events	952	(58.0)	3179	108.4	934	(56.8)	3073	101.3	1886	(57.4)	6252	104.8
胃腸障害	359	(21.9)	767	26.2	211	(12.8)	342	11.3	570	(17.3)	1109	18.6
下痢	104	(6.3)	161	5.5	70	(4.3)	85	2.8	174	(5.3)	246	4.1
悪心	99	(6.0)	124	4.2	35	(2.1)	37	1.2	134	(4.1)	161	2.7
嘔吐	82	(5.0)	98	3.3	26	(1.6)	31	1.0	108	(3.3)	129	2.2
腹痛	33	(2.0)	36	1.2	22	(1.3)	22	0.7	55	(1.7)	58	1.0
便秘	35	(2.1)	41	1.4	20	(1.2)	20	0.7	55	(1.7)	61	1.0
消化不良	40	(2.4)	48	1.6	7	(0.4)	7	0.2	47	(1.4)	55	0.9
上腹部痛	31	(1.9)	34	1.2	11	(0.7)	14	0.5	42	(1.3)	48	0.8
胃食道逆流性疾患	26	(1.6)	29	1.0	12	(0.7)	13	0.4	38	(1.2)	42	0.7
胃炎	20	(1.2)	20	0.7	9	(0.5)	10	0.3	29	(0.9)	30	0.5
腹部不快感	18	(1.1)	36	1.2	8	(0.5)	9	0.3	26	(0.8)	45	0.8
腹部膨満	10	(0.6)	11	0.4	7	(0.4)	7	0.2	17	(0.5)	18	0.3
おくび	12	(0.7)	13	0.4	0				12	(0.4)	13	0.2
歯痛	3	(0.2)	3	0.1	8	(0.5)	8	0.3	11	(0.3)	11	0.2
放屁	9	(0.5)	11	0.4	2	(0.1)	2	0.1	11	(0.3)	13	0.2
痔核	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
大腸ポリープ	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
憩室	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
齲歯	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
心窩部不快感	6	(0.4)	7	0.2	0				6	(0.2)	7	0.1
膵炎	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
胃腸出血	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
胃潰瘍	2	(0.1)	2	0.1	3	(0.2)	5	0.2	5	(0.2)	7	0.1
過敏性腸症候群	5	(0.3)	5	0.2	0				5	(0.2)	5	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胃腸障害	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0				0			
消化性潰瘍	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
食中毒	0				2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
大腸炎	4	(0.5)	4	0.3	0				0				0			
慢性胃炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
嚥下障害	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1	0			
びらん性胃炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
胃ポリープ	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
急性膵炎	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
十二指腸炎	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
十二指腸潰瘍	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
裂孔ヘルニア	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
鼠径ヘルニア	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
バレット食道	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
胃十二指腸炎	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
胃排出不全	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
呼気臭	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
口内乾燥	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
歯周病	2	(0.2)	2	0.1	0				0				0			
小腸閉塞	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
上部消化管出血	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
腸憩室	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
変色便	0				0				0				2	(0.2)	2	0.1
臍ヘルニア	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
びらん性食道炎	1	(0.1)	1	0.1	0				0				0			
イレウス	1	(0.1)	1	0.1	0				0				0			
クローン病	0				0				0				1	(0.1)	1	0.1
メレナ	0				1	(0.1)	1	0.1	0				0			
レッチング	0				1	(0.1)	1	0.1	0				0			
胃食道括約筋機能不全	0				0				1	(0.1)	1	0.1	0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胃腸障害	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
消化性潰瘍	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
食中毒	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
大腸炎	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
慢性胃炎	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
嚥下障害	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
びらん性胃炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
胃ポリープ	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
急性膵炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
十二指腸炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
十二指腸潰瘍	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
裂孔ヘルニア	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
鼠径ヘルニア	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
バレット食道	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胃十二指腸炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胃排出不全	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
呼気臭	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
口内乾燥	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
歯周病	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
小腸閉塞	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
上部消化管出血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腸憩室	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
変色便	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
臍ヘルニア	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
びらん性食道炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
イレウス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
クローン病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
メレナ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
レッチング	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃食道括約筋機能不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胃腸の炎症	0				0				1	(0.1)	1	0.1	0			
胃腸音異常	0				1	(0.1)	1	0.1	0				0			
下腹部痛	0				0				0				1	(0.1)	1	0.1
虚血性大腸炎	0				0				0				1	(0.1)	1	0.1
口腔内潰瘍形成	0				0				1	(0.1)	1	0.1	0			
痔瘻	0				0				0				1	(0.1)	1	0.1
出血性胃炎	0				1	(0.1)	1	0.1	0				0			
出血性胃潰瘍	1	(0.1)	1	0.1	0				0				0			
出血性十二指腸潰瘍	0				1	(0.1)	1	0.1	0				0			
出血性大腸潰瘍	0				0				1	(0.1)	1	0.1	0			
出血性腸炎	0				0				0				1	(0.1)	1	0.1
出血性直腸炎	0				0				1	(0.1)	1	0.1	0			
小腸炎	1	(0.1)	1	0.1	0				0				0			
小腸捻転	0				1	(0.1)	1	0.1	0				0			
消化管運動過剰	1	(0.1)	1	0.1	0				0				0			
食道炎	0				0				1	(0.1)	1	0.1	0			
食道狭窄	0				0				0				1	(0.1)	1	0.1
舌腫脹	0				1	(0.1)	1	0.1	0				0			
舌痛	0				0				1	(0.1)	1	0.1	0			
腸炎	0				0				0				1	(0.1)	1	0.1
腸管ポリープ	0				0				0				1	(0.1)	1	0.1
腸管虚血	0				1	(0.1)	1	0.1	0				0			
腸閉塞	1	(0.1)	1	0.1	0				0				0			
直腸出血	0				0				0				1	(0.1)	1	0.1
直腸脱	1	(0.1)	1	0.1	0				0				0			
吐き戻し	0				1	(0.1)	2	0.1	0				0			
吐血	0				1	(0.1)	1	0.1	0				0			
糖尿病性胃不全麻痺	0				1	(0.1)	1	0.1	0				0			
排便回数減少	0				1	(0.1)	1	0.1	0				0			
腹水	0				1	(0.1)	1	0.1	0				0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胃腸の炎症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胃腸音異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
下腹部痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
虚血性大腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口腔内潰瘍形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
痔瘻	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性胃炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
出血性胃潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
出血性十二指腸潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
出血性大腸潰瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性直腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
小腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
小腸捻転	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管運動過剰	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
食道炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
食道狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
舌腫脹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
舌痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸管ポリープ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸管虚血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腸閉塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
直腸出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
直腸脱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
吐き戻し	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
吐血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病性胃不全麻痺	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
排便回数減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹水	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腹部ヘルニア	0				0				0				1	(0.1)	1	0.1
腹部硬直	0				0				0				1	(0.1)	1	0.1
腹部腫瘤	0				1	(0.1)	1	0.1	0				0			
腹膜出血	1	(0.1)	1	0.1	0				0				0			
噴出性嘔吐	0				1	(0.1)	1	0.1	0				0			
麻痺性イレウス	1	(0.1)	1	0.1	0				0				0			
埋伏歯	0				0				0				1	(0.1)	1	0.1
慢性膵炎	0				1	(0.1)	1	0.1	0				0			
嚥下痛	0				0				1	(0.1)	1	0.1	0			
肛門周囲痛	1	(0.1)	1	0.1	0				0				0			
脾臓動脈瘤	0				0				0				1	(0.1)	1	0.1
膵萎縮	0				1	(0.1)	1	0.1	0				0			
膵石症	0				1	(0.1)	1	0.1	0				0			
膵臓障害	0				0				0				1	(0.1)	1	0.1
膵嚢胞	1	(0.1)	1	0.1	0				0				0			
感染症および寄生虫症	158	(19.2)	249	16.7	162	(19.8)	247	17.1	171	(20.9)	302	20.0	171	(20.7)	283	18.5
尿路感染	23	(2.8)	26	1.7	29	(3.5)	33	2.3	21	(2.6)	26	1.7	23	(2.8)	29	1.9
気管支炎	24	(2.9)	25	1.7	21	(2.6)	24	1.7	24	(2.9)	25	1.7	22	(2.7)	28	1.8
上気道感染	17	(2.1)	18	1.2	19	(2.3)	21	1.5	21	(2.6)	22	1.5	26	(3.2)	31	2.0
インフルエンザ	17	(2.1)	18	1.2	13	(1.6)	13	0.9	20	(2.4)	24	1.6	17	(2.1)	21	1.4
肺炎	12	(1.5)	12	0.8	12	(1.5)	12	0.8	18	(2.2)	22	1.5	17	(2.1)	18	1.2
副鼻腔炎	9	(1.1)	9	0.6	12	(1.5)	21	1.5	17	(2.1)	22	1.5	8	(1.0)	10	0.7
鼻咽頭炎	9	(1.1)	11	0.7	11	(1.3)	13	0.9	16	(2.0)	18	1.2	9	(1.1)	9	0.6
蜂巣炎	10	(1.2)	11	0.7	3	(0.4)	3	0.2	12	(1.5)	12	0.8	14	(1.7)	16	1.0
胃腸炎	8	(1.0)	10	0.7	13	(1.6)	14	1.0	9	(1.1)	10	0.7	7	(0.8)	8	0.5
限局性感染	4	(0.5)	5	0.3	5	(0.6)	6	0.4	8	(1.0)	10	0.7	6	(0.7)	8	0.5
帯状疱疹	6	(0.7)	6	0.4	1	(0.1)	1	0.1	7	(0.9)	7	0.5	8	(1.0)	8	0.5
咽頭炎	4	(0.5)	4	0.3	8	(1.0)	8	0.6	3	(0.4)	3	0.2	4	(0.5)	4	0.3
下気道感染	3	(0.4)	4	0.3	3	(0.4)	3	0.2	3	(0.4)	3	0.2	5	(0.6)	5	0.3

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System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腹部ヘルニア	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腹部硬直	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腹部腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹膜出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
噴出性嘔吐	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
麻痺性イレウス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
埋伏歯	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
慢性膵炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
嚥下痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肛門周囲痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脾臓動脈瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膵萎縮	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵石症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵臓障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膵嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染症および寄生虫症	320	(19.5)	496	16.9	342	(20.8)	585	19.3	662	(20.1)	1081	18.1
尿路感染	52	(3.2)	59	2.0	44	(2.7)	55	1.8	96	(2.9)	114	1.9
気管支炎	45	(2.7)	49	1.7	46	(2.8)	53	1.7	91	(2.8)	102	1.7
上気道感染	36	(2.2)	39	1.3	47	(2.9)	53	1.7	83	(2.5)	92	1.5
インフルエンザ	30	(1.8)	31	1.1	37	(2.3)	45	1.5	67	(2.0)	76	1.3
肺炎	24	(1.5)	24	0.8	35	(2.1)	40	1.3	59	(1.8)	64	1.1
副鼻腔炎	21	(1.3)	30	1.0	25	(1.5)	32	1.1	46	(1.4)	62	1.0
鼻咽頭炎	20	(1.2)	24	0.8	25	(1.5)	27	0.9	45	(1.4)	51	0.9
蜂巣炎	13	(0.8)	14	0.5	26	(1.6)	28	0.9	39	(1.2)	42	0.7
胃腸炎	21	(1.3)	24	0.8	16	(1.0)	18	0.6	37	(1.1)	42	0.7
限局性感染	9	(0.5)	11	0.4	14	(0.9)	18	0.6	23	(0.7)	29	0.5
帯状疱疹	7	(0.4)	7	0.2	15	(0.9)	15	0.5	22	(0.7)	22	0.4
咽頭炎	12	(0.7)	12	0.4	7	(0.4)	7	0.2	19	(0.6)	19	0.3
下気道感染	6	(0.4)	7	0.2	8	(0.5)	8	0.3	14	(0.4)	15	0.3

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System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
急性副鼻腔炎	6	(0.7)	8	0.5	1	(0.1)	1	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3
膀胱炎	4	(0.5)	5	0.3	1	(0.1)	1	0.1	7	(0.9)	9	0.6	2	(0.2)	3	0.2
ウイルス感染	5	(0.6)	6	0.4	3	(0.4)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	3	0.2
歯膿瘍	0				3	(0.4)	3	0.2	5	(0.6)	5	0.3	4	(0.5)	4	0.3
ウイルス性胃腸炎	4	(0.5)	4	0.3	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1
外陰部腟カンジダ症	2	(0.2)	2	0.1	2	(0.2)	2	0.1	3	(0.4)	4	0.3	3	(0.4)	3	0.2
憩室炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	4	(0.5)	6	0.4	3	(0.4)	3	0.2
骨髄炎	5	(0.6)	7	0.5	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
せつ	3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
ヘリコバクター感染	0				3	(0.4)	3	0.2	0				3	(0.4)	3	0.2
外陰腟真菌感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
中耳炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
ブドウ球菌感染	2	(0.2)	2	0.1	0				0				3	(0.4)	3	0.2
外耳炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
歯感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
真菌感染	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
創傷感染	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	2	0.1
足部白癬	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
敗血症	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
慢性腎盂腎炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1	2	(0.2)	2	0.1
ウイルス性上気道感染	0				2	(0.2)	2	0.1	2	(0.2)	3	0.2	0			
急性中耳炎	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
尿路性敗血症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
皮下組織膿瘍	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
鼻炎	0				0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
扁桃炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
ウイルス性消化管感染	0				3	(0.4)	3	0.2	0				0			
カンジダ感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
レンサ球菌性咽頭炎	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
眼感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			

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System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
急性副鼻腔炎	7	(0.4)	9	0.3	7	(0.4)	7	0.2	14	(0.4)	16	0.3
膀胱炎	5	(0.3)	6	0.2	9	(0.5)	12	0.4	14	(0.4)	18	0.3
ウイルス感染	8	(0.5)	9	0.3	4	(0.2)	4	0.1	12	(0.4)	13	0.2
歯膿瘍	3	(0.2)	3	0.1	9	(0.5)	9	0.3	12	(0.4)	12	0.2
ウイルス性胃腸炎	7	(0.4)	7	0.2	4	(0.2)	4	0.1	11	(0.3)	11	0.2
外陰部腟カンジダ症	4	(0.2)	4	0.1	6	(0.4)	7	0.2	10	(0.3)	11	0.2
憩室炎	3	(0.2)	3	0.1	7	(0.4)	9	0.3	10	(0.3)	12	0.2
骨髄炎	5	(0.3)	7	0.2	4	(0.2)	4	0.1	9	(0.3)	11	0.2
せつ	5	(0.3)	5	0.2	2	(0.1)	2	0.1	7	(0.2)	7	0.1
ヘリコバクター感染	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
外陰腟真菌感染	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
中耳炎	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
ブドウ球菌感染	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
外耳炎	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
歯感染	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
真菌感染	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
創傷感染	2	(0.1)	2	0.1	3	(0.2)	4	0.1	5	(0.2)	6	0.1
足部白癬	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
敗血症	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
慢性腎盂腎炎	2	(0.1)	2	0.1	3	(0.2)	4	0.1	5	(0.2)	6	0.1
ウイルス性上気道感染	2	(0.1)	2	0.1	2	(0.1)	3	0.1	4	(0.1)	5	0.1
急性中耳炎	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
尿路性敗血症	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
皮下組織膿瘍	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
鼻炎	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
扁桃炎	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
ウイルス性消化管感染	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
カンジダ感染	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
レンサ球菌性咽頭炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
眼感染	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
気管支肺炎	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
気道感染	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
結膜炎	0				3	(0.4)	4	0.3	0				0			
口腔カンジダ症	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
喉頭炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
四肢膿瘍	2	(0.2)	3	0.2	0				0				1	(0.1)	1	0.1
歯肉炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
耳感染	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
術後創感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
体部白癬	1	(0.1)	1	0.1	0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
大葉性肺炎	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
爪囲炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
爪真菌症	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
皮膚真菌感染	2	(0.2)	4	0.3	0				1	(0.1)	1	0.1	0			
迷路炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
咬傷感染	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
ウイルス性耳感染	0				0				2	(0.2)	2	0.1	0			
カンジダ性亀頭炎	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
クロストリジウム・ディフィシレ大腸炎	0				0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
デング熱	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
ロタウイルス胃腸炎	0				0				2	(0.2)	3	0.2	0			
医療機器関連感染	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
感染性皮膚潰瘍	0				0				0				2	(0.2)	4	0.3
急性腎盂腎炎	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
結核	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
細菌性膣症	0				1	(0.1)	2	0.1	0				1	(0.1)	1	0.1
腎盂腎炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
切開部位感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
丹毒	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
気管支肺炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
気道感染	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
結膜炎	3	(0.2)	4	0.1	0				3	(0.1)	4	0.1
口腔カンジダ症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
喉頭炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
四肢膿瘍	2	(0.1)	3	0.1	1	(0.1)	1	<0.1	3	(0.1)	4	0.1
歯肉炎	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
耳感染	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
術後創感染	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
体部白癬	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
大葉性肺炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
爪囲炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
爪真菌症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
皮膚真菌感染	2	(0.1)	4	0.1	1	(0.1)	1	<0.1	3	(0.1)	5	0.1
迷路炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
咬傷感染	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
ウイルス性耳感染	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
カンジダ性亀頭炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
クロストリジウム・ディフィシレ大腸炎	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
デング熱	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
ロタウイルス胃腸炎	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
医療機器関連感染	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
感染性皮膚潰瘍	0				2	(0.1)	4	0.1	2	(0.1)	4	0.1
急性腎盂腎炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
結核	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
細菌性膣症	1	(0.1)	2	0.1	1	(0.1)	1	<0.1	2	(0.1)	3	0.1
腎盂腎炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
切開部位感染	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
丹毒	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
虫垂部膿瘍	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
アデノウイルス結膜炎	0				0				1	(0.1)	1	0.1	0			
ウイルス性咽頭炎	0				0				1	(0.1)	1	0.1	0			
ウイルス性角膜炎	0				1	(0.1)	1	0.1	0				0			
ウイルス性気道感染	1	(0.1)	1	0.1	0				0				0			
ウイルス性結膜炎	0				1	(0.1)	1	0.1	0				0			
ウエストナイルウイルス感染	1	(0.1)	1	0.1	0				0				0			
カテーテル留置部位蜂巣炎	0				0				1	(0.1)	1	0.1	0			
シュードモナス性尿路感染	0				1	(0.1)	1	0.1	0				0			
ヘルペスウイルス感染	1	(0.1)	1	0.1	0				0				0			
ライム病	0				0				0				1	(0.1)	1	0.1
医療機器関連敗血症	0				0				1	(0.1)	1	0.1	0			
感染	1	(0.1)	1	0.1	0				0				0			
感染による慢性閉塞性気道疾患の増悪	1	(0.1)	1	0.1	0				0				0			
感染性関節炎	1	(0.1)	1	0.1	0				0				0			
感染性皮膚嚢腫	0				0				0				1	(0.1)	1	0.1
股部白癬	0				1	(0.1)	1	0.1	0				0			
口腔ヘルペス	0				1	(0.1)	1	0.1	0				0			
口腔膿瘍	0				0				1	(0.1)	1	0.1	0			
細気管支炎	0				0				0				1	(0.1)	1	0.1
細菌性咽頭炎	0				1	(0.1)	1	0.1	0				0			
細菌性髄膜炎	0				1	(0.1)	1	0.1	0				0			
細菌性尿路感染	0				0				1	(0.1)	2	0.1	0			
細菌尿	0				0				1	(0.1)	1	0.1	0			
歯周炎	0				0				0				1	(0.1)	1	0.1
歯槽骨炎	0				0				0				1	(0.1)	1	0.1
歯肉膿瘍	0				1	(0.1)	1	0.1	0				0			
処置後感染	0				0				1	(0.1)	1	0.1	0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
鼻径部膿瘍	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
アデノウイルス結膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ウイルス性咽頭炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ウイルス性角膜炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ウイルス性気道感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ウイルス性結膜炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ウエストナイルウイルス感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
カテーテル留置部位蜂巣炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
シュードモナス性尿路感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ヘルペスウイルス感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ライム病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
医療機器関連敗血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染による慢性閉塞性気道疾患の増悪	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染性関節炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染性皮膚嚢腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
股部白癬	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔ヘルペス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細気管支炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性咽頭炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
細菌性髄膜炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
細菌性尿路感染	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
細菌尿	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯周炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯槽骨炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯肉膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
処置後感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
小腸内細菌過剰増殖	0				1	(0.1)	1	0.1	0				0			
消化管感染	0				0				1	(0.1)	1	0.1	0			
真菌性尿路感染	1	(0.1)	1	0.1	0				0				0			
腎感染	0				0				0				1	(0.1)	1	0.1
性器カンジダ症	0				0				1	(0.1)	1	0.1	0			
性器膿瘍	0				0				0				1	(0.1)	1	0.1
精巣上体炎	0				0				0				1	(0.1)	1	0.1
赤痢	0				1	(0.1)	1	0.1	0				0			
大腸菌性敗血症	0				1	(0.1)	1	0.1	0				0			
単純ヘルペス	1	(0.1)	2	0.1	0				0				0			
直腸周囲膿瘍	0				1	(0.1)	1	0.1	0				0			
糖尿病性足感染	0				0				1	(0.1)	1	0.1	0			
軟部組織感染	0				0				0				1	(0.1)	1	0.1
乳房膿瘍	0				0				0				1	(0.1)	1	0.1
膿痂疹	0				0				0				1	(0.1)	1	0.1
膿疱性皮疹	0				1	(0.1)	1	0.1	0				0			
膿瘍	1	(0.1)	1	0.1	0				0				0			
百日咳	0				0				0				1	(0.1)	1	0.1
腹膜炎	0				1	(0.1)	1	0.1	0				0			
埋込み部位感染	0				0				1	(0.1)	1	0.1	0			
慢性Ｃ型肝炎	0				0				0				1	(0.1)	1	0.1
慢性中耳炎	1	(0.1)	1	0.1	0				0				0			
慢性副鼻腔炎	1	(0.1)	2	0.1	0				0				0			
癰	1	(0.1)	1	0.1	0				0				0			
肛門膿瘍	1	(0.1)	1	0.1	0				0				0			
膣感染	0				0				0				1	(0.1)	1	0.1
臍帯周囲膿瘍	0				0				0				1	(0.1)	1	0.1
筋骨格系および結合組織障害	87	(10.6)	111	7.5	90	(11.0)	136	9.4	100	(12.2)	160	10.6	114	(13.8)	160	10.5
関節痛	11	(1.3)	12	0.8	13	(1.6)	16	1.1	24	(2.9)	28	1.9	23	(2.8)	24	1.6

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
小腸内細菌過剰増殖	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
真菌性尿路感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
性器カンジダ症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
性器膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精巣上体炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
赤痢	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大腸菌性敗血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
単純ヘルペス	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
直腸周囲膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病性足感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
軟部組織感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳房膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膿痂疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膿疱性皮疹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
百日咳	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腹膜炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
埋込み部位感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
慢性Ｃ型肝炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
慢性中耳炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
慢性副鼻腔炎	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
癰	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肛門膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膣感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
臍帯周囲膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋骨格系および結合組織障害	177	(10.8)	247	8.4	214	(13.0)	320	10.5	391	(11.9)	567	9.5
関節痛	24	(1.5)	28	1.0	47	(2.9)	52	1.7	71	(2.2)	80	1.3

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
背部痛	11	(1.3)	11	0.7	19	(2.3)	21	1.5	17	(2.1)	22	1.5	21	(2.5)	21	1.4
変形性関節症	22	(2.7)	25	1.7	13	(1.6)	14	1.0	12	(1.5)	13	0.9	12	(1.5)	13	0.9
四肢痛	12	(1.5)	14	0.9	12	(1.5)	13	0.9	15	(1.8)	18	1.2	15	(1.8)	16	1.0
筋骨格痛	8	(1.0)	9	0.6	9	(1.1)	11	0.8	6	(0.7)	7	0.5	11	(1.3)	11	0.7
筋骨格系胸痛	1	(0.1)	1	0.1	4	(0.5)	4	0.3	9	(1.1)	11	0.7	5	(0.6)	5	0.3
筋肉痛	3	(0.4)	3	0.2	5	(0.6)	7	0.5	3	(0.4)	4	0.3	3	(0.4)	4	0.3
筋痙縮	2	(0.2)	3	0.2	1	(0.1)	1	0.1	6	(0.7)	6	0.4	4	(0.5)	4	0.3
椎間板突出	5	(0.6)	5	0.3	2	(0.2)	2	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
関節炎	3	(0.4)	3	0.2	4	(0.5)	6	0.4	2	(0.2)	2	0.1	3	(0.4)	3	0.2
変形性脊椎症	0				3	(0.4)	3	0.2	3	(0.4)	3	0.2	6	(0.7)	7	0.5
滑液包炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	6	(0.7)	6	0.4	3	(0.4)	3	0.2
頚部痛	2	(0.2)	2	0.1	2	(0.2)	2	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2
関節腫脹	0				1	(0.1)	1	0.1	5	(0.6)	5	0.3	3	(0.4)	3	0.2
肩回旋筋腱板症候群	2	(0.2)	3	0.2	3	(0.4)	3	0.2	1	(0.1)	1	0.1	2	(0.2)	2	0.1
外骨腫	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2
腱炎	1	(0.1)	1	0.1	3	(0.4)	4	0.3	3	(0.4)	3	0.2	0			
弾発指	1	(0.1)	1	0.1	1	(0.1)	2	0.1	0				4	(0.5)	4	0.3
滑液嚢腫	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
筋力低下	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
椎間板障害	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
肋軟骨炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
腰部脊柱管狭窄症	0				0				1	(0.1)	1	0.1	3	(0.4)	3	0.2
側腹部痛	0				3	(0.4)	3	0.2	0				1	(0.1)	1	0.1
足底筋膜炎	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
関節リウマチ	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
関節周囲炎	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
関節滲出液	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
骨端症	0				0				0				3	(0.4)	3	0.2
鼡径部痛	0				0				0				3	(0.4)	3	0.2
骨粗鬆症	0				0				2	(0.2)	2	0.1	0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
背部痛	30	(1.8)	32	1.1	38	(2.3)	43	1.4	68	(2.1)	75	1.3
変形性関節症	35	(2.1)	39	1.3	24	(1.5)	26	0.9	59	(1.8)	65	1.1
四肢痛	24	(1.5)	27	0.9	30	(1.8)	34	1.1	54	(1.6)	61	1.0
筋骨格痛	17	(1.0)	20	0.7	17	(1.0)	18	0.6	34	(1.0)	38	0.6
筋骨格系胸痛	5	(0.3)	5	0.2	14	(0.9)	16	0.5	19	(0.6)	21	0.4
筋肉痛	8	(0.5)	10	0.3	6	(0.4)	8	0.3	14	(0.4)	18	0.3
筋痙縮	3	(0.2)	4	0.1	10	(0.6)	10	0.3	13	(0.4)	14	0.2
椎間板突出	7	(0.4)	7	0.2	6	(0.4)	6	0.2	13	(0.4)	13	0.2
関節炎	7	(0.4)	9	0.3	5	(0.3)	5	0.2	12	(0.4)	14	0.2
変形性脊椎症	3	(0.2)	3	0.1	9	(0.5)	10	0.3	12	(0.4)	13	0.2
滑液包炎	2	(0.1)	2	0.1	9	(0.5)	9	0.3	11	(0.3)	11	0.2
頚部痛	4	(0.2)	4	0.1	7	(0.4)	7	0.2	11	(0.3)	11	0.2
関節腫脹	1	(0.1)	1	<0.1	8	(0.5)	8	0.3	9	(0.3)	9	0.2
肩回旋筋腱板症候群	5	(0.3)	6	0.2	3	(0.2)	3	0.1	8	(0.2)	9	0.2
外骨腫	2	(0.1)	2	0.1	5	(0.3)	5	0.2	7	(0.2)	7	0.1
腱炎	4	(0.2)	5	0.2	3	(0.2)	3	0.1	7	(0.2)	8	0.1
弾発指	2	(0.1)	3	0.1	4	(0.2)	4	0.1	6	(0.2)	7	0.1
滑液嚢腫	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
筋力低下	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
椎間板障害	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
肋軟骨炎	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
腰部脊柱管狭窄症	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
側腹部痛	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
足底筋膜炎	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
関節リウマチ	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
関節周囲炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
関節滲出液	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
骨端症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
肩径部痛	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
骨粗鬆症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脊柱管狭窄症	0				0				2	(0.2)	4	0.3	0			
脊椎痛	0				2	(0.2)	2	0.1	0				0			
椎間関節症候群	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
椎間板変性症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
痛風性関節炎	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
腱障害	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
腱鞘炎	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
デュプイトラン拘縮	0				0				0				1	(0.1)	1	0.1
ピロリン酸カルシウム結晶性軟骨石灰化症	0				0				0				1	(0.1)	1	0.1
リウマチ性多発筋痛	0				0				1	(0.1)	1	0.1	0			
運動性低下	0				0				0				1	(0.1)	1	0.1
横紋筋融解症	1	(0.1)	1	0.1	0				0				0			
下肢腫瘤	0				1	(0.1)	1	0.1	0				0			
顎痛	0				1	(0.1)	1	0.1	0				0			
関節拘縮	0				0				0				1	(0.1)	1	0.1
関節摩擦音	0				0				0				1	(0.1)	1	0.1
筋膜疼痛症候群	0				0				1	(0.1)	1	0.1	0			
筋攣縮	0				1	(0.1)	1	0.1	0				0			
骨関節障害	1	(0.1)	1	0.1	0				0				0			
骨減少症	1	(0.1)	1	0.1	0				0				0			
骨障害	0				1	(0.1)	1	0.1	0				0			
骨痛	0				1	(0.1)	1	0.1	0				0			
骨軟骨炎	0				1	(0.1)	2	0.1	0				0			
骨溶解	0				1	(0.1)	1	0.1	0				0			
神経障害性関節症	1	(0.1)	1	0.1	0				0				0			
脊柱変形	0				1	(0.1)	1	0.1	0				0			
足変形	0				1	(0.1)	1	0.1	0				0			
多発性関節炎	1	(0.1)	1	0.1	0				0				0			
単関節炎	0				1	(0.1)	1	0.1	0				0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脊柱管狭窄症	0				2	(0.1)	4	0.1	2	(0.1)	4	0.1
脊椎痛	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
椎間関節症候群	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
椎間板変性症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
痛風性関節炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腱障害	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
腱鞘炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
デュプイトラン拘縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ピロリン酸カルシウム結晶性軟骨石灰化症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
リウマチ性多発筋痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
運動性低下	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
横紋筋融解症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
下肢腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
顎痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
関節拘縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
関節摩擦音	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋膜疼痛症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋攣縮	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨関節障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨減少症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨軟骨炎	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
骨溶解	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経障害性関節症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脊柱変形	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
足変形	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
多発性関節炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
単関節炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
椎間板圧迫	0				0				0				1	(0.1)	1	0.1
椎間板偏位	0				0				0				1	(0.1)	1	0.1
軟部組織障害	0				0				0				1	(0.1)	1	0.1
膝蓋大腿関節痛症候群	0				0				0				1	(0.1)	1	0.1
腱石灰化	1	(0.1)	1	0.1	0				0				0			
神経系障害	68	(8.3)	87	5.8	84	(10.3)	107	7.4	81	(9.9)	109	7.2	75	(9.1)	94	6.2
頭痛	14	(1.7)	20	1.3	21	(2.6)	33	2.3	18	(2.2)	26	1.7	21	(2.5)	23	1.5
浮動性めまい	6	(0.7)	6	0.4	12	(1.5)	13	0.9	8	(1.0)	9	0.6	11	(1.3)	12	0.8
一過性脳虚血発作	6	(0.7)	7	0.5	3	(0.4)	3	0.2	7	(0.9)	8	0.5	4	(0.5)	4	0.3
失神	4	(0.5)	4	0.3	4	(0.5)	4	0.3	5	(0.6)	6	0.4	3	(0.4)	3	0.2
末梢性ニューロパチー	6	(0.7)	7	0.5	1	(0.1)	1	0.1	4	(0.5)	4	0.3	5	(0.6)	5	0.3
虚血性脳卒中	3	(0.4)	3	0.2	2	(0.2)	2	0.1	7	(0.9)	7	0.5	2	(0.2)	2	0.1
坐骨神経痛	5	(0.6)	6	0.4	3	(0.4)	3	0.2	0				4	(0.5)	4	0.3
頚動脈狭窄	3	(0.4)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
糖尿病性ニューロパチー	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
手根管症候群	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
脳血管発作	0				2	(0.2)	2	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1
片頭痛	0				3	(0.4)	3	0.2	3	(0.4)	3	0.2	0			
腰髄神経根障害	0				1	(0.1)	1	0.1	4	(0.5)	4	0.3	0			
嗜眠	2	(0.2)	3	0.2	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
感覚鈍麻	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	0			
錯感覚	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
失神寸前の状態	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1
神経圧迫	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
神経痛	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1	0			
脳血管障害	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
副鼻腔炎に伴う頭痛	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
健忘	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
神経根圧迫	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
椎間板圧迫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎間板偏位	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
軟部組織障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膝蓋大腿関節痛症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腱石灰化	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経系障害	152	(9.3)	194	6.6	156	(9.5)	203	6.7	308	(9.4)	397	6.7
頭痛	35	(2.1)	53	1.8	39	(2.4)	49	1.6	74	(2.3)	102	1.7
浮動性めまい	18	(1.1)	19	0.6	19	(1.2)	21	0.7	37	(1.1)	40	0.7
一過性脳虚血発作	9	(0.5)	10	0.3	11	(0.7)	12	0.4	20	(0.6)	22	0.4
失神	8	(0.5)	8	0.3	8	(0.5)	9	0.3	16	(0.5)	17	0.3
末梢性ニューロパチー	7	(0.4)	8	0.3	9	(0.5)	9	0.3	16	(0.5)	17	0.3
虚血性脳卒中	5	(0.3)	5	0.2	9	(0.5)	9	0.3	14	(0.4)	14	0.2
坐骨神経痛	8	(0.5)	9	0.3	4	(0.2)	4	0.1	12	(0.4)	13	0.2
頚動脈狭窄	4	(0.2)	4	0.1	5	(0.3)	5	0.2	9	(0.3)	9	0.2
糖尿病性ニューロパチー	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2
手根管症候群	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
脳血管発作	2	(0.1)	2	0.1	5	(0.3)	5	0.2	7	(0.2)	7	0.1
片頭痛	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
腰髄神経根障害	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
嗜眠	4	(0.2)	5	0.2	1	(0.1)	1	<0.1	5	(0.2)	6	0.1
感覚鈍麻	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
錯感覚	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
失神寸前の状態	2	(0.1)	2	0.1	2	(0.1)	3	0.1	4	(0.1)	5	0.1
神経圧迫	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
神経痛	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
脳血管障害	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
副鼻腔炎に伴う頭痛	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
健忘	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
神経根圧迫	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
神経根障害	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
第７脳神経麻痺	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
味覚異常	0				3	(0.4)	3	0.2	0				0			
てんかん	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
パーキンソン病	0				2	(0.2)	2	0.1	0				0			
視野欠損	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
振戦	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
多発ニューロパチー	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
糖尿病性単ニューロパチー	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
頭蓋内動脈瘤	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
脳虚血	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
脳症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
部分発作	0				0				2	(0.2)	2	0.1	0			
平衡障害	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
痙攣発作	0				0				0				2	(0.2)	2	0.1
ジストニア振戦	0				1	(0.1)	1	0.1	0				0			
トンネル状視野	0				1	(0.1)	1	0.1	0				0			
パーキンソニズム	0				1	(0.1)	1	0.1	0				0			
ヘルペス後神経痛	1	(0.1)	1	0.1	0				0				0			
モートン神経痛	1	(0.1)	1	0.1	0				0				0			
ラクナ梗塞	0				0				0				1	(0.1)	1	0.1
意識消失	0				1	(0.1)	1	0.1	0				0			
運動障害	0				0				1	(0.1)	1	0.1	0			
概日リズム睡眠障害	0				1	(0.1)	1	0.1	0				0			
感覚異常性大腿神経痛	0				1	(0.1)	1	0.1	0				0			
肝性脳症	1	(0.1)	1	0.1	0				0				0			
起立障害	0				0				0				1	(0.1)	1	0.1
虚血性脳小血管疾患	0				0				0				1	(0.1)	1	0.1
協調運動異常	0				0				0				1	(0.1)	1	0.1
傾眠	0				1	(0.1)	1	0.1	0				0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
神経根障害	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
第７脳神経麻痺	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
味覚異常	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
てんかん	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
パーキンソン病	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
視野欠損	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
振戦	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
多発ニューロパチー	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
糖尿病性単ニューロパチー	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
頭蓋内動脈瘤	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
脳虚血	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
脳症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
部分発作	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
平衡障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
痙攣発作	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
ジストニア振戦	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
トンネル状視野	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
パーキンソニズム	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ヘルペス後神経痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
モートン神経痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ラクナ梗塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
意識消失	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
運動障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
概日リズム睡眠障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感覚異常性大腿神経痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝性脳症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
起立障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
虚血性脳小血管疾患	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
協調運動異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
傾眠	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
頚髄症	0				0				0				1	(0.1)	1	0.1
頚髄神経根障害	0				1	(0.1)	1	0.1	0				0			
頚動脈硬化症	0				0				0				1	(0.1)	1	0.1
頚動脈閉塞	0				0				1	(0.1)	1	0.1	0			
頚腕症候群	0				1	(0.1)	1	0.1	0				0			
硬膜下ヒグローマ	0				0				1	(0.1)	1	0.1	0			
高血圧性脳症	0				0				0				1	(0.1)	1	0.1
三叉神経痛	0				0				0				1	(0.1)	1	0.1
視床梗塞	0				1	(0.1)	1	0.1	0				0			
軸索型ニューロパチー	0				0				1	(0.1)	1	0.1	0			
失語症	0				1	(0.1)	1	0.1	0				0			
灼熱感	0				0				1	(0.1)	1	0.1	0			
小脳出血	0				0				1	(0.1)	1	0.1	0			
神経炎	0				0				1	(0.1)	1	0.1	0			
神経系障害	0				0				1	(0.1)	1	0.1	0			
水頭症	0				1	(0.1)	1	0.1	0				0			
脊髄圧迫	0				0				1	(0.1)	1	0.1	0			
脊髄性跛行症	0				1	(0.1)	1	0.1	0				0			
体位性めまい	0				0				0				1	(0.1)	1	0.1
代謝性脳症	1	(0.1)	1	0.1	0				0				0			
大脳萎縮	0				0				0				1	(0.1)	1	0.1
第３脳神経不全麻痺	0				0				0				1	(0.1)	1	0.1
第６脳神経障害	1	(0.1)	1	0.1	0				0				0			
注意力障害	0				0				0				1	(0.1)	1	0.1
低血糖性意識消失	1	(0.1)	1	0.1	0				0				0			
頭蓋内出血	0				0				0				1	(0.1)	1	0.1
認知症	0				1	(0.1)	1	0.1	0				0			
認知障害	0				1	(0.1)	1	0.1	0				0			
脳血管不全	0				1	(0.1)	1	0.1	0				0			
脳梗塞	0				1	(0.1)	1	0.1	0				0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
頚髄症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頚髄神経根障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頚動脈硬化症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頚動脈閉塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頚腕症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
硬膜下ヒグローマ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高血圧性脳症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
三叉神経痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
視床梗塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
軸索型ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
失語症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
灼熱感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
小脳出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経系障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
水頭症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脊髄圧迫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脊髄性跛行症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
体位性めまい	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
代謝性脳症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大脳萎縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
第３脳神経不全麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
第６脳神経障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
注意力障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
低血糖性意識消失	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頭蓋内出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
認知症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
認知障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳血管不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脳梗塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg			Sema 1.0 mg			Placebo 0.5 mg			Placebo 1.0 mg		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脳脊髄液漏	0				0				1	(0.1)	1	0.1	0			
脳浮腫	0				0				0				1	(0.1)	1	0.1
発作様現象	0				0				1	(0.1)	1	0.1	0			
本態性振戦	0				0				1	(0.1)	1	0.1	0			
末梢性感覚運動ニューロパチー	0				0				0				1	(0.1)	1	0.1
梨状筋症候群	0				0				1	(0.1)	1	0.1	0			
老年認知症	0				0				1	(0.1)	1	0.1	0			
肋間神経痛	0				0				0				1	(0.1)	1	0.1
腓骨神経麻痺	0				0				0				1	(0.1)	1	0.1
心臓障害	71	(8.6)	87	5.8	53	(6.5)	80	5.5	83	(10.1)	106	7.0	76	(9.2)	99	6.5
心房細動	9	(1.1)	9	0.6	12	(1.5)	14	1.0	18	(2.2)	19	1.3	11	(1.3)	12	0.8
狭心症	10	(1.2)	10	0.7	4	(0.5)	4	0.3	12	(1.5)	13	0.9	16	(1.9)	17	1.1
不安定狭心症	9	(1.1)	9	0.6	9	(1.1)	10	0.7	13	(1.6)	13	0.9	11	(1.3)	12	0.8
うっ血性心不全	8	(1.0)	8	0.5	5	(0.6)	5	0.3	10	(1.2)	11	0.7	9	(1.1)	11	0.7
急性心筋梗塞	4	(0.5)	5	0.3	4	(0.5)	4	0.3	4	(0.5)	4	0.3	5	(0.6)	5	0.3
心不全	7	(0.9)	7	0.5	5	(0.6)	5	0.3	3	(0.4)	3	0.2	1	(0.1)	1	0.1
心筋梗塞	0				2	(0.2)	2	0.1	4	(0.5)	5	0.3	6	(0.7)	7	0.5
冠動脈疾患	6	(0.7)	6	0.4	0				3	(0.4)	3	0.2	2	(0.2)	2	0.1
慢性心不全	3	(0.4)	3	0.2	3	(0.4)	3	0.2	4	(0.5)	4	0.3	1	(0.1)	1	0.1
心筋虚血	3	(0.4)	3	0.2	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
冠動脈狭窄	4	(0.5)	4	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
左脚ブロック	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				3	(0.4)	4	0.3
徐脈	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
上室性頻脈	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	4	0.3	1	(0.1)	1	0.1
心房粗動	0				0				5	(0.6)	5	0.3	1	(0.1)	1	0.1
不整脈	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3
三尖弁閉鎖不全症	4	(0.5)	4	0.3	0				0				1	(0.1)	1	0.1
左室機能不全	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1

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System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脳脊髄液漏	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
発作様現象	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
本態性振戦	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢性感覚運動ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
梨状筋症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
老年認知症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肋間神経痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腓骨神経麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心臓障害	124	(7.6)	167	5.7	159	(9.7)	205	6.8	283	(8.6)	372	6.2
心房細動	21	(1.3)	23	0.8	29	(1.8)	31	1.0	50	(1.5)	54	0.9
狭心症	14	(0.9)	14	0.5	28	(1.7)	30	1.0	42	(1.3)	44	0.7
不安定狭心症	18	(1.1)	19	0.6	24	(1.5)	25	0.8	42	(1.3)	44	0.7
うっ血性心不全	13	(0.8)	13	0.4	19	(1.2)	22	0.7	32	(1.0)	35	0.6
急性心筋梗塞	8	(0.5)	9	0.3	9	(0.5)	9	0.3	17	(0.5)	18	0.3
心不全	12	(0.7)	12	0.4	4	(0.2)	4	0.1	16	(0.5)	16	0.3
心筋梗塞	2	(0.1)	2	0.1	10	(0.6)	12	0.4	12	(0.4)	14	0.2
冠動脈疾患	6	(0.4)	6	0.2	5	(0.3)	5	0.2	11	(0.3)	11	0.2
慢性心不全	6	(0.4)	6	0.2	5	(0.3)	5	0.2	11	(0.3)	11	0.2
心筋虚血	5	(0.3)	5	0.2	5	(0.3)	5	0.2	10	(0.3)	10	0.2
冠動脈狭窄	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
左脚ブロック	3	(0.2)	3	0.1	3	(0.2)	4	0.1	6	(0.2)	7	0.1
徐脈	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
上室性頻脈	2	(0.1)	2	0.1	4	(0.2)	5	0.2	6	(0.2)	7	0.1
心房粗動	0				6	(0.4)	6	0.2	6	(0.2)	6	0.1
不整脈	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
三尖弁閉鎖不全症	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
左室機能不全	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1

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System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心室性頻脈	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
僧帽弁閉鎖不全症	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0				0			
虚血性心筋症	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
動悸	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
頻脈	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
右脚ブロック	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
冠動脈硬化症	0				0				0				2	(0.2)	2	0.1
心筋線維症	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
心室性期外収縮	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
心室壁運動低下	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
第一度房室ブロック	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
第二度房室ブロック	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
洞結節機能不全	0				2	(0.2)	2	0.1	0				0			
洞性頻脈	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
無症候性心筋梗塞	0				0				2	(0.2)	2	0.1	0			
うっ血性心筋症	1	(0.1)	1	0.1	0				0				0			
拡張機能障害	0				0				1	(0.1)	1	0.1	0			
冠動脈不全	1	(0.1)	1	0.1	0				0				0			
冠動脈閉塞	0				1	(0.1)	1	0.1	0				0			
期外収縮	0				0				1	(0.1)	1	0.1	0			
急性冠動脈症候群	0				0				0				1	(0.1)	1	0.1
急性心不全	0				0				1	(0.1)	1	0.1	0			
結節性調律	0				1	(0.1)	1	0.1	0				0			
高血圧性心筋症	0				1	(0.1)	1	0.1	0				0			
上室性期外収縮	0				1	(0.1)	1	0.1	0				0			
心タンポナーデ	1	(0.1)	1	0.1	0				0				0			
心拡大	0				1	(0.1)	1	0.1	0				0			
心筋症	0				1	(0.1)	1	0.1	0				0			
心室血栓症	0				0				1	(0.1)	1	0.1	0			
心臓弁石灰化	0				1	(0.1)	1	0.1	0				0			

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	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心室性頻脈	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
僧帽弁閉鎖不全症	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
虚血性心筋症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
動悸	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
頻脈	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
右脚ブロック	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
冠動脈硬化症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
心筋線維症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心室性期外収縮	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心室壁運動低下	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
第一度房室ブロック	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
第二度房室ブロック	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
洞結節機能不全	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
洞性頻脈	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
無症候性心筋梗塞	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
うっ血性心筋症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
拡張機能障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
冠動脈不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
冠動脈閉塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
期外収縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性冠動脈症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性心不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結節性調律	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高血圧性心筋症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
上室性期外収縮	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心タンポナーデ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心拡大	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心筋症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心室血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心臓弁石灰化	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心臓瘤	0				0				0				1	(0.1)	1	0.1
心停止	0				1	(0.1)	1	0.1	0				0			
心嚢液貯留	1	(0.1)	1	0.1	0				0				0			
心房血栓症	0				1	(0.1)	1	0.1	0				0			
心膜炎	1	(0.1)	1	0.1	0				0				0			
心膜石灰化	0				1	(0.1)	1	0.1	0				0			
大動脈弁閉鎖不全症	0				1	(0.1)	1	0.1	0				0			
糖尿病性心筋症	0				0				0				1	(0.1)	1	0.1
洞性徐脈	0				0				0				1	(0.1)	1	0.1
洞性不整脈	0				0				1	(0.1)	1	0.1	0			
変性僧帽弁疾患	0				1	(0.1)	1	0.1	0				0			
変性大動脈弁疾患	0				1	(0.1)	1	0.1	0				0			
房室ブロック	0				0				0				1	(0.1)	1	0.1
臨床検査	56	(6.8)	90	6.0	54	(6.6)	93	6.4	57	(7.0)	93	6.2	47	(5.7)	69	4.5
リパーゼ増加	25	(3.0)	29	1.9	26	(3.2)	35	2.4	15	(1.8)	17	1.1	14	(1.7)	17	1.1
アミラーゼ増加	9	(1.1)	11	0.7	10	(1.2)	13	0.9	4	(0.5)	4	0.3	5	(0.6)	6	0.4
血中クレアチニン増加	5	(0.6)	5	0.3	2	(0.2)	2	0.1	9	(1.1)	9	0.6	4	(0.5)	4	0.3
血圧上昇	3	(0.4)	7	0.5	3	(0.4)	3	0.2	3	(0.4)	4	0.3	4	(0.5)	5	0.3
体重減少	5	(0.6)	6	0.4	4	(0.5)	4	0.3	2	(0.2)	2	0.1	1	(0.1)	1	0.1
血中ブドウ糖増加	1	(0.1)	3	0.2	1	(0.1)	1	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2
血中カルシトニン増加	0				3	(0.4)	3	0.2	3	(0.4)	3	0.2	2	(0.2)	2	0.1
膵酵素増加	5	(0.6)	5	0.3	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
ヘモグロビン減少	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2
血中カリウム増加	2	(0.2)	2	0.1	2	(0.2)	2	0.1	3	(0.4)	4	0.3	0			
グリコヘモグロビン増加	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
血中トリグリセリド増加	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	0			
アスパラギン酸アミノトランスフェラーゼ増加	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	0			
血中カルシウム増加	1	(0.1)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心臓瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心停止	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心嚢液貯留	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心房血栓症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心膜炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心膜石灰化	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大動脈弁閉鎖不全症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病性心筋症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
洞性徐脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
洞性不整脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
変性僧帽弁疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
変性大動脈弁疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
房室ブロック	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
臨床検査	110	(6.7)	183	6.2	104	(6.3)	162	5.3	214	(6.5)	345	5.8
リパーゼ増加	51	(3.1)	64	2.2	29	(1.8)	34	1.1	80	(2.4)	98	1.6
アミラーゼ増加	19	(1.2)	24	0.8	9	(0.5)	10	0.3	28	(0.9)	34	0.6
血中クレアチニン増加	7	(0.4)	7	0.2	13	(0.8)	13	0.4	20	(0.6)	20	0.3
血圧上昇	6	(0.4)	10	0.3	7	(0.4)	9	0.3	13	(0.4)	19	0.3
体重減少	9	(0.5)	10	0.3	3	(0.2)	3	0.1	12	(0.4)	13	0.2
血中ブドウ糖増加	2	(0.1)	4	0.1	7	(0.4)	7	0.2	9	(0.3)	11	0.2
血中カルシトニン増加	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
膵酵素増加	7	(0.4)	7	0.2	1	(0.1)	1	<0.1	8	(0.2)	8	0.1
ヘモグロビン減少	2	(0.1)	2	0.1	5	(0.3)	5	0.2	7	(0.2)	7	0.1
血中カリウム増加	4	(0.2)	4	0.1	3	(0.2)	4	0.1	7	(0.2)	8	0.1
グリコヘモグロビン増加	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
血中トリグリセリド増加	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
アスパラギン酸アミノトランスフェラーゼ増加	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
血中カルシウム増加	2	(0.1)	3	0.1	2	(0.1)	2	0.1	4	(0.1)	5	0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
血中ビリルビン増加	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
白血球数増加	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
アラニンアミノトランスフェラーゼ増加	2	(0.2)	2	0.1	0				1	(0.1)	2	0.1	0			
ヘマトクリット減少	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
心電図Ｔ波逆転	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
赤血球分布幅増加	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
尿中アルブミン	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
尿中ブドウ糖陽性	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
冠血管造影	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
肝機能検査異常	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
肝酵素上昇	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
血中アルカリホスファターゼ増加	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
血中クレアチンホスホキナーゼ増加	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
血中プロインスリン増加	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
血中尿素増加	0				0				2	(0.2)	2	0.1	0			
好中球数増加	0				2	(0.2)	2	0.1	0				0			
心電図ＱＴ延長	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
体重増加	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
尿中アルブミン／クレアチニン比増加	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
ウエスト周囲径増加	0				1	(0.1)	1	0.1	0				0			
トロポニンＩ増加	0				0				1	(0.1)	1	0.1	0			
トロポニン増加	0				1	(0.1)	1	0.1	0				0			
眼圧上昇	0				0				1	(0.1)	1	0.1	0			
胸部Ｘ線異常	0				0				0				1	(0.1)	1	0.1
駆出率減少	0				0				0				1	(0.1)	1	0.1
血圧異常	0				0				1	(0.1)	1	0.1	0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
血中ビリルビン増加	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
白血球数増加	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
アラニンアミノトランスフェラーゼ増加	2	(0.1)	2	0.1	1	(0.1)	2	0.1	3	(0.1)	4	0.1
ヘマトクリット減少	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
心電図Ｔ波逆転	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
赤血球分布幅増加	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
尿中アルブミン	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
尿中ブドウ糖陽性	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
冠血管造影	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肝機能検査異常	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
肝酵素上昇	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
血中アルカリホスファターゼ増加	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
血中クレアチンホスホキナーゼ増加	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
血中プロインスリン増加	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
血中尿素増加	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
好中球数増加	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
心電図ＱＴ延長	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
体重増加	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
尿中アルブミン／クレアチニン比増加	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
ウエスト周囲径増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
トロポニンＩ増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
トロポニン増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼圧上昇	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胸部Ｘ線異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
駆出率減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血圧異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
血小板数減少	0				0				1	(0.1)	2	0.1	0			
血小板数増加	0				0				1	(0.1)	1	0.1	0			
血中アルブミン増加	0				0				0				1	(0.1)	1	0.1
血中カリウム減少	0				0				0				1	(0.1)	1	0.1
血中クレアチン増加	0				0				1	(0.1)	1	0.1	0			
血中コレステロール増加	0				0				0				1	(0.1)	1	0.1
血中テストステロン減少	0				0				1	(0.1)	1	0.1	0			
血中トリグリセリド異常	0				0				0				1	(0.1)	1	0.1
血中亜鉛減少	1	(0.1)	1	0.1	0				0				0			
血中甲状腺刺激ホルモン減少	0				1	(0.1)	1	0.1	0				0			
血中成長ホルモン増加	0				0				0				1	(0.1)	1	0.1
血中卵胞刺激ホルモン	0				0				0				1	(0.1)	1	0.1
呼吸音異常	0				1	(0.1)	1	0.1	0				0			
好塩基球数増加	0				0				0				1	(0.1)	1	0.1
国際標準比増加	0				1	(0.1)	1	0.1	0				0			
細菌検査陽性	0				0				0				1	(0.1)	1	0.1
糸球体濾過率減少	0				0				1	(0.1)	1	0.1	0			
糸球体濾過率増加	0				1	(0.1)	1	0.1	0				0			
心カテーテル検査	0				1	(0.1)	1	0.1	0				0			
心電図２相性Ｔ波	0				1	(0.1)	1	0.1	0				0			
心電図ＳＴ部分異常	0				0				1	(0.1)	1	0.1	0			
心電図Ｔ波振幅減少	0				0				0				1	(0.1)	1	0.1
心電図異常Ｑ波	0				1	(0.1)	1	0.1	0				0			
心電図変化	0				0				0				1	(0.1)	1	0.1
赤血球数減少	0				0				1	(0.1)	1	0.1	0			
赤血球数増加	1	(0.1)	1	0.1	0				0				0			
前立腺生検	1	(0.1)	1	0.1	0				0				0			
足脈拍減少	0				1	(0.1)	1	0.1	0				0			
単球数増加	0				1	(0.1)	1	0.1	0				0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
血小板数減少	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
血小板数増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中アルブミン増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中カリウム減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中クレアチン増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中コレステロール増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中テストステロン減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中トリグリセリド異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中亜鉛減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中甲状腺刺激ホルモン減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中成長ホルモン増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中卵胞刺激ホルモン	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼吸音異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
好塩基球数増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
国際標準比増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
細菌検査陽性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糸球体濾過率減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糸球体濾過率増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心カテーテル検査	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心電図２相性Ｔ波	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心電図ＳＴ部分異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図Ｔ波振幅減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図異常Ｑ波	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心電図変化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
赤血球数減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
赤血球数増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
前立腺生検	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
足脈拍減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
単球数増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
低比重リポ蛋白増加	1	(0.1)	1	0.1	0				0				0			
尿検査異常	0				0				0				1	(0.1)	1	0.1
尿蛋白	0				1	(0.1)	1	0.1	0				0			
尿中アルブミン陽性	0				1	(0.1)	1	0.1	0				0			
尿中ビリルビン	0				1	(0.1)	1	0.1	0				0			
尿中ヘモグロビン陽性	0				0				1	(0.1)	1	0.1	0			
尿中血	0				0				0				1	(0.1)	1	0.1
尿中血陽性	0				1	(0.1)	1	0.1	0				0			
尿中蛋白陽性	1	(0.1)	1	0.1	0				0				0			
尿中白血球陽性	0				0				1	(0.1)	1	0.1	0			
平均赤血球ヘモグロビン減少	0				0				1	(0.1)	1	0.1	0			
遊離脂肪酸増加	1	(0.1)	1	0.1	0				0				0			
代謝および栄養障害	73	(8.9)	95	6.4	43	(5.3)	49	3.4	69	(8.4)	82	5.4	61	(7.4)	78	5.1
食欲減退	22	(2.7)	24	1.6	18	(2.2)	18	1.2	3	(0.4)	3	0.2	4	(0.5)	5	0.3
高血糖	10	(1.2)	15	1.0	3	(0.4)	3	0.2	12	(1.5)	12	0.8	9	(1.1)	9	0.6
痛風	11	(1.3)	13	0.9	3	(0.4)	4	0.3	6	(0.7)	6	0.4	7	(0.8)	8	0.5
糖尿病	7	(0.9)	7	0.5	3	(0.4)	3	0.2	12	(1.5)	15	1.0	4	(0.5)	4	0.3
コントロール不良の糖尿病	2	(0.2)	2	0.1	3	(0.4)	3	0.2	7	(0.9)	9	0.6	8	(1.0)	9	0.6
低血糖症	8	(1.0)	11	0.7	1	(0.1)	1	0.1	1	(0.1)	2	0.1	9	(1.1)	11	0.7
脂質異常症	3	(0.4)	3	0.2	3	(0.4)	3	0.2	4	(0.5)	4	0.3	3	(0.4)	3	0.2
高カリウム血症	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	6	(0.7)	7	0.5
脱水	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	4	(0.5)	5	0.3
ビタミンＤ欠乏	2	(0.2)	2	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
高トリグリセリド血症	1	(0.1)	1	0.1	0				4	(0.5)	4	0.3	3	(0.4)	3	0.2
低カリウム血症	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1
低ナトリウム血症	1	(0.1)	1	0.1	0				4	(0.5)	5	0.3	1	(0.1)	1	0.1
２型糖尿病	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
ビタミンＢ１２欠乏	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
低比重リポ蛋白増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿検査異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿蛋白	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中アルブミン陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中ビリルビン	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中ヘモグロビン陽性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿中血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿中血陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中蛋白陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中白血球陽性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
平均赤血球ヘモグロビン減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
遊離脂肪酸増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
代謝および栄養障害	116	(7.1)	144	4.9	130	(7.9)	160	5.3	246	(7.5)	304	5.1
食欲減退	40	(2.4)	42	1.4	7	(0.4)	8	0.3	47	(1.4)	50	0.8
高血糖	13	(0.8)	18	0.6	21	(1.3)	21	0.7	34	(1.0)	39	0.7
痛風	14	(0.9)	17	0.6	13	(0.8)	14	0.5	27	(0.8)	31	0.5
糖尿病	10	(0.6)	10	0.3	16	(1.0)	19	0.6	26	(0.8)	29	0.5
コントロール不良の糖尿病	5	(0.3)	5	0.2	15	(0.9)	18	0.6	20	(0.6)	23	0.4
低血糖症	9	(0.5)	12	0.4	10	(0.6)	13	0.4	19	(0.6)	25	0.4
脂質異常症	6	(0.4)	6	0.2	7	(0.4)	7	0.2	13	(0.4)	13	0.2
高カリウム血症	3	(0.2)	3	0.1	9	(0.5)	10	0.3	12	(0.4)	13	0.2
脱水	3	(0.2)	3	0.1	7	(0.4)	8	0.3	10	(0.3)	11	0.2
ビタミンＤ欠乏	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
高トリグリセリド血症	1	(0.1)	1	<0.1	7	(0.4)	7	0.2	8	(0.2)	8	0.1
低カリウム血症	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
低ナトリウム血症	1	(0.1)	1	<0.1	5	(0.3)	6	0.2	6	(0.2)	7	0.1
２型糖尿病	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
ビタミンＢ１２欠乏	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
高コレステロール血症	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
高リパーゼ血症	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
低マグネシウム血症	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
乳酸アシドーシス	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
高カルシウム血症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
高脂血症	0				0				2	(0.2)	2	0.1	0			
食欲亢進	0				2	(0.2)	2	0.1	0				0			
水分過負荷	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
電解質失調	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
糖尿病性ケトアシドーシス	1	(0.1)	2	0.1	0				1	(0.1)	1	0.1	0			
ケトーシス	1	(0.1)	1	0.1	0				0				0			
過小食	0				0				0				1	(0.1)	1	0.1
血液量減少症	1	(0.1)	1	0.1	0				0				0			
水分摂取量減少	0				0				1	(0.1)	1	0.1	0			
多飲症	1	(0.1)	2	0.1	0				0				0			
体液貯留	0				0				0				1	(0.1)	1	0.1
低カルシウム血症	0				0				0				1	(0.1)	1	0.1
鉄欠乏	1	(0.1)	1	0.1	0				0				0			
傷害、中毒および処置合併症	59	(7.2)	75	5.0	50	(6.1)	63	4.4	60	(7.3)	82	5.4	63	(7.6)	82	5.4
転倒	12	(1.5)	12	0.8	11	(1.3)	15	1.0	16	(2.0)	21	1.4	12	(1.5)	14	0.9
挫傷	2	(0.2)	2	0.1	6	(0.7)	6	0.4	4	(0.5)	4	0.3	2	(0.2)	2	0.1
処置による疼痛	1	(0.1)	1	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3	6	(0.7)	7	0.5
靱帯捻挫	4	(0.5)	5	0.3	3	(0.4)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	3	0.2
創傷	0				1	(0.1)	1	0.1	5	(0.6)	5	0.3	4	(0.5)	4	0.3
肋骨骨折	1	(0.1)	1	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3
交通事故	1	(0.1)	2	0.1	4	(0.5)	4	0.3	2	(0.2)	3	0.2	2	(0.2)	2	0.1
肉離れ	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
半月板損傷	4	(0.5)	4	0.3	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
裂傷	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0				4	(0.5)	4	0.3

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
高コレステロール血症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
高リパーゼ血症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
低マグネシウム血症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
乳酸アシドーシス	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
高カルシウム血症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
高脂血症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
食欲亢進	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
水分過負荷	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
電解質失調	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
糖尿病性ケトアシドーシス	1	(0.1)	2	0.1	1	(0.1)	1	<0.1	2	(0.1)	3	0.1
ケトーシス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
過小食	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血液量減少症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
水分摂取量減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
多飲症	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
体液貯留	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
低カルシウム血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鉄欠乏	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
傷害、中毒および処置合併症	109	(6.6)	138	4.7	123	(7.5)	164	5.4	232	(7.1)	302	5.1
転倒	23	(1.4)	27	0.9	28	(1.7)	35	1.2	51	(1.6)	62	1.0
挫傷	8	(0.5)	8	0.3	6	(0.4)	6	0.2	14	(0.4)	14	0.2
処置による疼痛	4	(0.2)	4	0.1	10	(0.6)	11	0.4	14	(0.4)	15	0.3
靱帯捻挫	7	(0.4)	8	0.3	4	(0.2)	4	0.1	11	(0.3)	12	0.2
創傷	1	(0.1)	1	<0.1	9	(0.5)	9	0.3	10	(0.3)	10	0.2
肋骨骨折	2	(0.1)	2	0.1	8	(0.5)	8	0.3	10	(0.3)	10	0.2
交通事故	5	(0.3)	6	0.2	4	(0.2)	5	0.2	9	(0.3)	11	0.2
肉離れ	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
半月板損傷	6	(0.4)	6	0.2	2	(0.1)	2	0.1	8	(0.2)	8	0.1
裂傷	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
手首関節骨折	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
熱傷	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
四肢損傷	3	(0.4)	4	0.3	1	(0.1)	1	0.1	1	(0.1)	2	0.1	0			
節足動物咬傷	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
動物咬傷	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
腱断裂	0				2	(0.2)	2	0.1	0				3	(0.4)	3	0.2
関節損傷	0				0				3	(0.4)	4	0.3	1	(0.1)	1	0.1
歯牙破折	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
上肢骨折	2	(0.2)	2	0.1	0				0				2	(0.2)	2	0.1
切開部位痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
上腕骨骨折	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
足骨折	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
第２度熱傷	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1
頭部損傷	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
橈骨骨折	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
眼窩周囲出血	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
胸椎骨折	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
筋断裂	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
偶発的過量投与	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
硬膜下血腫	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
手骨折	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
処置後浮腫	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
脊椎圧迫骨折	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
足関節部骨折	2	(0.2)	2	0.1	0				0				0			
損傷	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
大腿骨骨折	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
腸脛靱帯症候群	0				1	(0.1)	1	0.1	1	(0.1)	2	0.1	0			
背部損傷	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
皮膚擦過傷	0				0				0				2	(0.2)	2	0.1
粉砕骨折	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
手首関節骨折	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
熱傷	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
四肢損傷	4	(0.2)	5	0.2	1	(0.1)	2	0.1	5	(0.2)	7	0.1
節足動物咬傷	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
動物咬傷	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
腱断裂	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
関節損傷	0				4	(0.2)	5	0.2	4	(0.1)	5	0.1
歯牙破折	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
上肢骨折	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
切開部位痛	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
上腕骨骨折	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
足骨折	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
第２度熱傷	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
頭部損傷	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
橈骨骨折	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
眼窩周囲出血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胸椎骨折	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
筋断裂	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
偶発的過量投与	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
硬膜下血腫	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
手骨折	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
処置後浮腫	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
脊椎圧迫骨折	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
足関節部骨折	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
損傷	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
大腿骨骨折	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
腸脛靱帯症候群	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
背部損傷	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
皮膚擦過傷	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
粉砕骨折	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脛骨骨折	2	(0.2)	2	0.1	0				0				0			
靭帯断裂	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
ストレス骨折	0				0				1	(0.1)	1	0.1	0			
過量投与	0				1	(0.1)	1	0.1	0				0			
外傷後疼痛	0				0				1	(0.1)	1	0.1	0			
外傷性骨折	1	(0.1)	1	0.1	0				0				0			
角膜擦過傷	0				1	(0.1)	1	0.1	0				0			
関節脱臼	0				0				0				1	(0.1)	1	0.1
眼の擦過傷	0				1	(0.1)	1	0.1	0				0			
眼外傷	0				0				0				1	(0.1)	1	0.1
顔面骨骨折	1	(0.1)	1	0.1	0				0				0			
気圧性中耳炎	1	(0.1)	1	0.1	0				0				0			
胸部損傷	0				0				1	(0.1)	1	0.1	0			
頚椎骨折	0				0				1	(0.1)	1	0.1	0			
血管偽動脈瘤	1	(0.1)	1	0.1	0				0				0			
肩甲骨骨折	1	(0.1)	1	0.1	0				0				0			
誤用量投与	1	(0.1)	2	0.1	0				0				0			
硬膜裂傷	0				0				1	(0.1)	1	0.1	0			
骨格損傷	0				0				0				1	(0.1)	1	0.1
骨亀裂	1	(0.1)	1	0.1	0				0				0			
擦過傷	0				0				0				1	(0.1)	1	0.1
蛇咬傷	0				0				1	(0.1)	1	0.1	0			
尺骨骨折	0				0				0				1	(0.1)	1	0.1
術後イレウス	0				1	(0.1)	1	0.1	0				0			
術後呼吸不全	1	(0.1)	1	0.1	0				0				0			
処置による悪心	0				0				0				1	(0.1)	1	0.1
処置後血腫	0				0				0				1	(0.1)	1	0.1
処置後合併症	0				0				0				1	(0.1)	1	0.1
処置後便秘	0				1	(0.1)	1	0.1	0				0			
上顎炎	0				0				1	(0.1)	1	0.1	0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脛骨骨折	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
靭帯断裂	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
ストレス骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
過量投与	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
外傷後疼痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外傷性骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
角膜擦過傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
関節脱臼	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼の擦過傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼外傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
顔面骨骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
気圧性中耳炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胸部損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頚椎骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管偽動脈瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肩甲骨骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
誤用量投与	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
硬膜裂傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
骨格損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
骨亀裂	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
擦過傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
蛇咬傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尺骨骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
術後イレウス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
術後呼吸不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
処置による悪心	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
処置後血腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
処置後合併症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
処置後便秘	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
上顎炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
食道熱傷	1	(0.1)	1	0.1	0				0				0			
節足動物刺傷	1	(0.1)	1	0.1	0				0				0			
創傷血腫	0				1	(0.1)	1	0.1	0				0			
体内異物	0				0				1	(0.1)	1	0.1	0			
椎弓切除後症候群	0				0				1	(0.1)	1	0.1	0			
脳振盪	1	(0.1)	1	0.1	0				0				0			
皮下血腫	0				0				0				1	(0.1)	1	0.1
膝蓋骨骨折	0				0				1	(0.1)	1	0.1	0			
末梢動脈再狭窄	0				0				1	(0.1)	1	0.1	0			
労働災害	0				0				1	(0.1)	1	0.1	0			
漿液腫	0				0				1	(0.1)	1	0.1	0			
腓骨骨折	0				0				0				1	(0.1)	1	0.1
腎および尿路障害	45	(5.5)	54	3.6	49	(6.0)	63	4.4	70	(8.5)	79	5.2	46	(5.6)	56	3.7
急性腎不全	8	(1.0)	8	0.5	5	(0.6)	5	0.3	11	(1.3)	11	0.7	9	(1.1)	9	0.6
慢性腎臓病	7	(0.9)	7	0.5	2	(0.2)	2	0.1	13	(1.6)	16	1.1	4	(0.5)	4	0.3
腎結石症	6	(0.7)	7	0.5	9	(1.1)	9	0.6	4	(0.5)	5	0.3	2	(0.2)	2	0.1
ミクロアルブミン尿	2	(0.2)	3	0.2	5	(0.6)	5	0.3	8	(1.0)	8	0.5	3	(0.4)	3	0.2
蛋白尿	3	(0.4)	3	0.2	4	(0.5)	4	0.3	2	(0.2)	2	0.1	4	(0.5)	4	0.3
腎症	2	(0.2)	2	0.1	3	(0.4)	3	0.2	6	(0.7)	6	0.4	1	(0.1)	1	0.1
腎嚢胞	2	(0.2)	2	0.1	1	(0.1)	1	0.1	5	(0.6)	5	0.3	3	(0.4)	3	0.2
腎機能障害	3	(0.4)	3	0.2	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1
糖尿病性腎症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3
血尿	1	(0.1)	1	0.1	4	(0.5)	5	0.3	1	(0.1)	1	0.1	3	(0.4)	3	0.2
尿閉	2	(0.2)	4	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1	0			
腎不全	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
尿失禁	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1
排尿困難	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
水腎症	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0				0			
尿管結石	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
食道熱傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
節足動物刺傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
創傷血腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
体内異物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎弓切除後症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳振盪	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮下血腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膝蓋骨骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈再狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
労働災害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
漿液腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腓骨骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎および尿路障害	94	(5.7)	117	4.0	116	(7.1)	135	4.4	210	(6.4)	252	4.2
急性腎不全	13	(0.8)	13	0.4	20	(1.2)	20	0.7	33	(1.0)	33	0.6
慢性腎臓病	9	(0.5)	9	0.3	17	(1.0)	20	0.7	26	(0.8)	29	0.5
腎結石症	15	(0.9)	16	0.5	6	(0.4)	7	0.2	21	(0.6)	23	0.4
ミクロアルブミン尿	7	(0.4)	8	0.3	11	(0.7)	11	0.4	18	(0.5)	19	0.3
蛋白尿	7	(0.4)	7	0.2	6	(0.4)	6	0.2	13	(0.4)	13	0.2
腎症	5	(0.3)	5	0.2	7	(0.4)	7	0.2	12	(0.4)	12	0.2
腎嚢胞	3	(0.2)	3	0.1	8	(0.5)	8	0.3	11	(0.3)	11	0.2
腎機能障害	6	(0.4)	6	0.2	4	(0.2)	4	0.1	10	(0.3)	10	0.2
糖尿病性腎症	2	(0.1)	2	0.1	8	(0.5)	8	0.3	10	(0.3)	10	0.2
血尿	5	(0.3)	6	0.2	4	(0.2)	4	0.1	9	(0.3)	10	0.2
尿閉	6	(0.4)	8	0.3	2	(0.1)	2	0.1	8	(0.2)	10	0.2
腎不全	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
尿失禁	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
排尿困難	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
水腎症	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
尿管結石	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腎仙痛	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
糖尿	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
尿路結石	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
夜間頻尿	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
アルブミン尿	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
ケトン尿	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
ネフローゼ症候群	0				0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
高窒素血症	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
腎臓痛	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
膀胱肉柱形成	0				0				2	(0.2)	2	0.1	0			
間質性膀胱炎	0				0				0				1	(0.1)	1	0.1
急性腎前性腎不全	0				0				0				1	(0.1)	1	0.1
緊張性膀胱	0				0				1	(0.1)	1	0.1	0			
失禁	1	(0.1)	1	0.1	0				0				0			
出血性膀胱炎	1	(0.1)	1	0.1	0				0				0			
腎下垂症	1	(0.1)	1	0.1	0				0				0			
腎梗塞	0				0				0				1	(0.1)	1	0.1
腎腫瘤	0				0				0				1	(0.1)	1	0.1
腎障害	0				1	(0.1)	1	0.1	0				0			
腎動脈の動脈硬化症	0				1	(0.1)	1	0.1	0				0			
腎動脈瘤	0				0				0				1	(0.1)	1	0.1
腎嚢胞出血	0				0				0				1	(0.1)	1	0.1
腎盂腎杯拡張症	0				0				0				1	(0.1)	1	0.1
多尿	1	(0.1)	2	0.1	0				0				0			
着色尿	0				0				0				1	(0.1)	1	0.1
尿意切迫	0				0				0				1	(0.1)	1	0.1
尿管狭窄	0				1	(0.1)	1	0.1	0				0			
尿道狭窄	0				0				0				1	(0.1)	1	0.1
排尿異常	0				1	(0.1)	1	0.1	0				0			
頻尿	0				0				0				1	(0.1)	1	0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腎仙痛	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
糖尿	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
尿路結石	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
夜間頻尿	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
アルブミン尿	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
ケトン尿	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
ネフローゼ症候群	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
高窒素血症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腎臓痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
膀胱肉柱形成	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
間質性膀胱炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性腎前性腎不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
緊張性膀胱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
失禁	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
出血性膀胱炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎下垂症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎梗塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎腫瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎動脈の動脈硬化症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎動脈瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎嚢胞出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎盂腎杯拡張症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
多尿	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
着色尿	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿意切迫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿管狭窄	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿道狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
排尿異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頻尿	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
膀胱ポリープ	0				0				1	(0.1)	1	0.1	0			
膀胱痙縮	0				0				1	(0.1)	1	0.1	0			
呼吸器、胸郭および縦隔障害	41	(5.0)	53	3.6	47	(5.7)	65	4.5	37	(4.5)	43	2.9	50	(6.1)	69	4.5
咳嗽	9	(1.1)	9	0.6	12	(1.5)	12	0.8	9	(1.1)	9	0.6	8	(1.0)	9	0.6
呼吸困難	7	(0.9)	8	0.5	8	(1.0)	10	0.7	8	(1.0)	9	0.6	7	(0.8)	7	0.5
慢性閉塞性肺疾患	2	(0.2)	2	0.1	2	(0.2)	4	0.3	6	(0.7)	6	0.4	9	(1.1)	13	0.9
睡眠時無呼吸症候群	1	(0.1)	1	0.1	2	(0.2)	2	0.1	5	(0.6)	5	0.3	5	(0.6)	5	0.3
アレルギー性鼻炎	2	(0.2)	2	0.1	5	(0.6)	5	0.3	0				1	(0.1)	2	0.1
口腔咽頭痛	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1	4	(0.5)	5	0.3
喘息	3	(0.4)	4	0.3	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
胸水	0				3	(0.4)	3	0.2	3	(0.4)	4	0.3	0			
しゃっくり	1	(0.1)	3	0.2	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1
呼吸不全	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
肺水腫	0				1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
無気肺	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
労作性呼吸困難	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
低酸素症	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
肺塞栓症	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
発声障害	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
胸水症	0				0				0				2	(0.2)	2	0.1
胸膜痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
肺高血圧症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
肺腫瘤	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
鼻出血	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
鼻茸	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
鼻閉	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
鼻漏	0				2	(0.2)	2	0.1	0				0			
副鼻腔うっ血	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
慢性気管支炎	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
膀胱ポリープ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膀胱痙縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼吸器、胸郭および縦隔障害	88	(5.4)	118	4.0	87	(5.3)	112	3.7	175	(5.3)	230	3.9
咳嗽	21	(1.3)	21	0.7	17	(1.0)	18	0.6	38	(1.2)	39	0.7
呼吸困難	15	(0.9)	18	0.6	15	(0.9)	16	0.5	30	(0.9)	34	0.6
慢性閉塞性肺疾患	4	(0.2)	6	0.2	15	(0.9)	19	0.6	19	(0.6)	25	0.4
睡眠時無呼吸症候群	3	(0.2)	3	0.1	10	(0.6)	10	0.3	13	(0.4)	13	0.2
アレルギー性鼻炎	7	(0.4)	7	0.2	1	(0.1)	2	0.1	8	(0.2)	9	0.2
口腔咽頭痛	3	(0.2)	3	0.1	5	(0.3)	6	0.2	8	(0.2)	9	0.2
喘息	5	(0.3)	6	0.2	2	(0.1)	2	0.1	7	(0.2)	8	0.1
胸水	3	(0.2)	3	0.1	3	(0.2)	4	0.1	6	(0.2)	7	0.1
しゃっくり	4	(0.2)	6	0.2	1	(0.1)	1	<0.1	5	(0.2)	7	0.1
呼吸不全	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
肺水腫	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
無気肺	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
労作性呼吸困難	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
低酸素症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
肺塞栓症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
発声障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
胸水症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
胸膜痛	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
肺高血圧症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
肺腫瘤	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
鼻出血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
鼻茸	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
鼻閉	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
鼻漏	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
副鼻腔うっ血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
慢性気管支炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ピックウィック症候群	1	(0.1)	1	0.1	0				0				0			
安静時呼吸困難	0				0				1	(0.1)	1	0.1	0			
過換気	0				1	(0.1)	1	0.1	0				0			
器質化肺炎	0				0				0				1	(0.1)	1	0.1
気管支反応性亢進	0				1	(0.1)	1	0.1	0				0			
気管支痙攣	0				0				0				1	(0.1)	1	0.1
気胸	1	(0.1)	1	0.1	0				0				0			
急性呼吸不全	1	(0.1)	1	0.1	0				0				0			
急性肺水腫	0				0				0				1	(0.1)	1	0.1
胸膜炎	0				1	(0.1)	1	0.1	0				0			
胸膜障害	1	(0.1)	1	0.1	0				0				0			
胸膜線維症	1	(0.1)	1	0.1	0				0				0			
呼吸障害	1	(0.1)	1	0.1	0				0				0			
後天性横隔膜性内臓転位	1	(0.1)	1	0.1	0				0				0			
誤嚥性肺炎	0				1	(0.1)	1	0.1	0				0			
拘束性肺疾患	1	(0.1)	1	0.1	0				0				0			
高炭酸ガス血症	1	(0.1)	1	0.1	0				0				0			
湿性咳嗽	0				0				0				1	(0.1)	1	0.1
上気道うっ血	0				1	(0.1)	1	0.1	0				0			
肺うっ血	0				0				1	(0.1)	1	0.1	0			
肺気腫	0				0				0				1	(0.1)	1	0.1
肺障害	0				0				0				1	(0.1)	2	0.1
肺線維症	0				0				0				1	(0.1)	1	0.1
肺嚢胞	1	(0.1)	1	0.1	0				0				0			
鼻中隔障害	0				1	(0.1)	1	0.1	0				0			
鼻中隔穿孔	0				1	(0.1)	1	0.1	0				0			
副鼻腔不快感	0				0				0				1	(0.1)	1	0.1
副鼻腔分泌過多	1	(0.1)	1	0.1	0				0				0			
喀血	0				1	(0.1)	3	0.2	0				0			
喘息クリーゼ	1	(0.1)	1	0.1	0				0				0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ピックウィック症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
安静時呼吸困難	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
過換気	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
器質化肺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
気管支反応性亢進	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
気管支痙攣	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
気胸	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
急性呼吸不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
急性肺水腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胸膜炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胸膜障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胸膜線維症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
呼吸障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
後天性横隔膜性内臓転位	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
誤嚥性肺炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
拘束性肺疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高炭酸ガス血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
湿性咳嗽	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
上気道うっ血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺うっ血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺気腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺障害	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
肺線維症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻中隔障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻中隔穿孔	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
副鼻腔不快感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副鼻腔分泌過多	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
喀血	1	(0.1)	3	0.1	0				1	(<0.1)	3	0.1
喘息クリーゼ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
一般・全身障害および投与部位の状態	42	(5.1)	51	3.4	46	(5.6)	63	4.4	48	(5.9)	57	3.8	41	(5.0)	50	3.3
非心臓性胸痛	8	(1.0)	8	0.5	4	(0.5)	4	0.3	10	(1.2)	10	0.7	8	(1.0)	8	0.5
疲労	3	(0.4)	5	0.3	11	(1.3)	11	0.8	6	(0.7)	6	0.4	9	(1.1)	9	0.6
胸痛	1	(0.1)	1	0.1	6	(0.7)	11	0.8	7	(0.9)	8	0.5	6	(0.7)	6	0.4
末梢性浮腫	4	(0.5)	4	0.3	2	(0.2)	2	0.1	7	(0.9)	7	0.5	6	(0.7)	6	0.4
無力症	3	(0.4)	3	0.2	7	(0.9)	8	0.6	4	(0.5)	5	0.3	4	(0.5)	6	0.4
発熱	7	(0.9)	7	0.5	4	(0.5)	5	0.3	4	(0.5)	4	0.3	0			
胸部不快感	4	(0.5)	4	0.3	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
末梢腫脹	4	(0.5)	4	0.3	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
疼痛	0				3	(0.4)	3	0.2	3	(0.4)	3	0.2	3	(0.4)	3	0.2
インフルエンザ様疾患	0				1	(0.1)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
歩行障害	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
悪寒	0				1	(0.1)	1	0.1	2	(0.2)	3	0.2	0			
小結節	1	(0.1)	3	0.2	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
浮腫	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
治癒不良	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
カテーテル留置部位炎症	0				1	(0.1)	1	0.1	0				0			
ポリープ	1	(0.1)	1	0.1	0				0				0			
医薬品副作用	0				1	(0.1)	1	0.1	0				0			
医療機器関連の血栓症	0				0				0				1	(0.1)	1	0.1
医療機器機能不良	1	(0.1)	1	0.1	0				0				0			
炎症	0				1	(0.1)	1	0.1	0				0			
壊死	1	(0.1)	1	0.1	0				0				0			
顔面痛	1	(0.1)	1	0.1	0				0				0			
倦怠感	1	(0.1)	1	0.1	0				0				0			
限局性浮腫	1	(0.1)	1	0.1	0				0				0			
口渇	0				0				0				1	(0.1)	1	0.1
硬結	1	(0.1)	1	0.1	0				0				0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
一般・全身障害および投与部位の状態	88	(5.4)	114	3.9	89	(5.4)	107	3.5	177	(5.4)	221	3.7
非心臓性胸痛	12	(0.7)	12	0.4	18	(1.1)	18	0.6	30	(0.9)	30	0.5
疲労	14	(0.9)	16	0.5	15	(0.9)	15	0.5	29	(0.9)	31	0.5
胸痛	7	(0.4)	12	0.4	13	(0.8)	14	0.5	20	(0.6)	26	0.4
末梢性浮腫	6	(0.4)	6	0.2	13	(0.8)	13	0.4	19	(0.6)	19	0.3
無力症	10	(0.6)	11	0.4	8	(0.5)	11	0.4	18	(0.5)	22	0.4
発熱	11	(0.7)	12	0.4	4	(0.2)	4	0.1	15	(0.5)	16	0.3
胸部不快感	6	(0.4)	6	0.2	5	(0.3)	5	0.2	11	(0.3)	11	0.2
末梢腫脹	6	(0.4)	6	0.2	5	(0.3)	5	0.2	11	(0.3)	11	0.2
疼痛	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2
インフルエンザ様疾患	1	(0.1)	2	0.1	3	(0.2)	3	0.1	4	(0.1)	5	0.1
歩行障害	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
悪寒	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
小結節	2	(0.1)	4	0.1	1	(0.1)	1	<0.1	3	(0.1)	5	0.1
浮腫	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
治癒不良	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
カテーテル留置部位炎症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ポリープ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
医薬品副作用	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
医療機器関連の血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
医療機器機能不良	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
炎症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
壊死	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
顔面痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
倦怠感	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
限局性浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口渇	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
硬結	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腫脹	1	(0.1)	1	0.1	0				0				0			
腫瘤	0				1	(0.1)	1	0.1	0				0			
先行疾患の改善	1	(0.1)	1	0.1	0				0				0			
早期満腹	0				1	(0.1)	1	0.1	0				0			
多臓器不全	0				0				1	(0.1)	1	0.1	0			
注射部位内出血	0				1	(0.1)	1	0.1	0				0			
注射部位疼痛	0				1	(0.1)	1	0.1	0				0			
潰瘍	0				1	(0.1)	1	0.1	0				0			
軟部組織の炎症	0				0				0				1	(0.1)	1	0.1
嚢胞	0				1	(0.1)	1	0.1	0				0			
薬剤離脱症候群	0				1	(0.1)	1	0.1	0				0			
血管障害	38	(4.6)	41	2.8	41	(5.0)	47	3.3	42	(5.1)	57	3.8	52	(6.3)	59	3.9
高血圧	8	(1.0)	8	0.5	15	(1.8)	17	1.2	16	(2.0)	20	1.3	13	(1.6)	14	0.9
低血圧	6	(0.7)	7	0.5	7	(0.9)	7	0.5	3	(0.4)	8	0.5	6	(0.7)	7	0.5
末梢動脈閉塞性疾患	2	(0.2)	2	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2	5	(0.6)	5	0.3
高血圧クリーゼ	1	(0.1)	1	0.1	2	(0.2)	2	0.1	2	(0.2)	3	0.2	3	(0.4)	5	0.3
起立性低血圧	2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
深部静脈血栓症	3	(0.4)	3	0.2	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
末梢血管障害	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	3	0.2
末梢静脈疾患	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2
間欠性跛行	0				0				1	(0.1)	1	0.1	4	(0.5)	4	0.3
血腫	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
大動脈硬化症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
糖尿病性血管障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
動脈硬化症	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	0			
末梢動脈狭窄	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
虚血	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
血栓性静脈炎	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
静脈瘤	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腫脹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
先行疾患の改善	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
早期満腹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
多臓器不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
注射部位内出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
注射部位疼痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
軟部組織の炎症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
薬剤離脱症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管障害	79	(4.8)	88	3.0	94	(5.7)	116	3.8	173	(5.3)	204	3.4
高血圧	23	(1.4)	25	0.9	29	(1.8)	34	1.1	52	(1.6)	59	1.0
低血圧	13	(0.8)	14	0.5	9	(0.5)	15	0.5	22	(0.7)	29	0.5
末梢動脈閉塞性疾患	6	(0.4)	6	0.2	8	(0.5)	8	0.3	14	(0.4)	14	0.2
高血圧クリーゼ	3	(0.2)	3	0.1	5	(0.3)	8	0.3	8	(0.2)	11	0.2
起立性低血圧	5	(0.3)	5	0.2	2	(0.1)	2	0.1	7	(0.2)	7	0.1
深部静脈血栓症	5	(0.3)	5	0.2	2	(0.1)	2	0.1	7	(0.2)	7	0.1
末梢血管障害	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
末梢静脈疾患	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
間欠性跛行	0				5	(0.3)	5	0.2	5	(0.2)	5	0.1
血腫	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
大動脈硬化症	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
糖尿病性血管障害	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
動脈硬化症	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
末梢動脈狭窄	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
虚血	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
血栓性静脈炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
静脈瘤	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
大動脈狭窄	3	(0.4)	3	0.2	0				0				0			
鎖骨下動脈狭窄	0				0				0				2	(0.2)	2	0.1
静脈炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
静脈瘤性潰瘍	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
大動脈瘤	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
ほてり	0				0				1	(0.1)	1	0.1	0			
リンパ浮腫	1	(0.1)	1	0.1	0				0				0			
血管炎	0				0				1	(0.1)	1	0.1	0			
血管石灰化	0				0				0				1	(0.1)	1	0.1
血管破裂	0				0				0				1	(0.1)	1	0.1
血栓症	0				0				1	(0.1)	1	0.1	0			
高血圧性血管障害	1	(0.1)	1	0.1	0				0				0			
四肢壊死	1	(0.1)	1	0.1	0				0				0			
収縮期高血圧	0				0				1	(0.1)	1	0.1	0			
静脈血栓症	0				0				1	(0.1)	1	0.1	0			
大腿動脈閉塞	1	(0.1)	1	0.1	0				0				0			
大動脈拡張	0				0				1	(0.1)	1	0.1	0			
糖尿病性大血管障害	0				0				0				1	(0.1)	1	0.1
糖尿病性微小血管症	0				0				1	(0.1)	1	0.1	0			
動脈不全	0				0				1	(0.1)	1	0.1	0			
末梢性虚血	0				0				1	(0.1)	1	0.1	0			
末梢動脈血栓症	0				0				1	(0.1)	1	0.1	0			
末梢動脈瘤	1	(0.1)	1	0.1	0				0				0			
眼障害	41	(5.0)	51	3.4	41	(5.0)	47	3.3	40	(4.9)	47	3.1	40	(4.8)	49	3.2
糖尿病網膜症	18	(2.2)	18	1.2	14	(1.7)	14	1.0	12	(1.5)	12	0.8	7	(0.8)	7	0.5
白内障	14	(1.7)	15	1.0	8	(1.0)	9	0.6	9	(1.1)	9	0.6	14	(1.7)	15	1.0
緑内障	1	(0.1)	1	0.1	2	(0.2)	2	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1
黄斑浮腫	0				2	(0.2)	3	0.2	2	(0.2)	2	0.1	0			
視力低下	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
大動脈狭窄	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
鎖骨下動脈狭窄	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
静脈炎	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
静脈瘤性潰瘍	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
大動脈瘤	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
ほてり	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
リンパ浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管石灰化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管破裂	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高血圧性血管障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
四肢壊死	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
収縮期高血圧	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
静脈血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大腿動脈閉塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大動脈拡張	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糖尿病性大血管障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糖尿病性微小血管症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
動脈不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢性虚血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼障害	82	(5.0)	98	3.3	80	(4.9)	96	3.2	162	(4.9)	194	3.3
糖尿病網膜症	32	(1.9)	32	1.1	19	(1.2)	19	0.6	51	(1.6)	51	0.9
白内障	22	(1.3)	24	0.8	23	(1.4)	24	0.8	45	(1.4)	48	0.8
緑内障	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2
黄斑浮腫	2	(0.1)	3	0.1	2	(0.1)	2	0.1	4	(0.1)	5	0.1
視力低下	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
硝子体出血	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
網膜出血	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
網膜剥離	1	(0.1)	2	0.1	0				0				3	(0.4)	3	0.2
糖尿病性網膜浮腫	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
アレルギー性結膜炎	0				0				2	(0.2)	3	0.2	0			
黄斑症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
加齢黄斑変性	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
開放隅角緑内障	0				0				1	(0.1)	1	0.1	1	(0.1)	2	0.1
角膜混濁	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
高血圧性網膜症	0				0				0				2	(0.2)	2	0.1
出血性網膜症	2	(0.2)	2	0.1	0				0				0			
硝子体浮遊物	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
動脈硬化性網膜症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
嚢胞様黄斑浮腫	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
複視	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
霧視	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
網膜血管瘤	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
網膜障害	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
網膜動脈閉塞	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
網膜裂孔	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
一過性黒内障	0				0				1	(0.1)	1	0.1	0			
遠視	0				1	(0.1)	1	0.1	0				0			
黄斑線維症	0				1	(0.1)	1	0.1	0				0			
眼そう痒症	1	(0.1)	1	0.1	0				0				0			
眼球浮腫	0				1	(0.1)	1	0.1	0				0			
眼刺激	1	(0.1)	1	0.1	0				0				0			
眼充血	0				0				0				1	(0.1)	1	0.1
眼痛	1	(0.1)	1	0.1	0				0				0			
眼部腫脹	0				0				1	(0.1)	1	0.1	0			
眼瞼炎	0				0				1	(0.1)	1	0.1	0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
硝子体出血	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
網膜出血	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
網膜剥離	1	(0.1)	2	0.1	3	(0.2)	3	0.1	4	(0.1)	5	0.1
糖尿病性網膜浮腫	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
アレルギー性結膜炎	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
黄斑症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
加齢黄斑変性	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
開放隅角緑内障	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
角膜混濁	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
高血圧性網膜症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
出血性網膜症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
硝子体浮遊物	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
動脈硬化性網膜症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
嚢胞様黄斑浮腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
複視	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
霧視	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
網膜血管瘤	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
網膜障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
網膜動脈閉塞	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
網膜裂孔	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
一過性黒内障	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
遠視	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
黄斑線維症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼そう痒症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼球浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼刺激	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼充血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼部腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼瞼炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
眼瞼下垂	0				1	(0.1)	1	0.1	0				0			
虚血性視神経症	0				1	(0.1)	1	0.1	0				0			
視神経萎縮	0				0				1	(0.1)	1	0.1	0			
視神経乳頭出血	0				1	(0.1)	1	0.1	0				0			
視神経乳頭障害	1	(0.1)	1	0.1	0				0				0			
視力障害	0				0				0				1	(0.1)	1	0.1
失明	0				0				1	(0.1)	1	0.1	0			
硝子体障害	0				0				0				1	(0.1)	1	0.1
硝子体変性	0				0				0				1	(0.1)	1	0.1
前房狭隅角	0				0				1	(0.1)	1	0.1	0			
増殖性網膜症	0				0				0				1	(0.1)	1	0.1
嚢下白内障	0				0				1	(0.1)	1	0.1	0			
網膜症	1	(0.1)	1	0.1	0				0				0			
網膜静脈閉塞	0				1	(0.1)	1	0.1	0				0			
網膜滲出物	0				0				0				1	(0.1)	1	0.1
乱視	0				1	(0.1)	1	0.1	0				0			
老視	0				1	(0.1)	1	0.1	0				0			
外科および内科処置	29	(3.5)	34	2.3	18	(2.2)	18	1.2	37	(4.5)	41	2.7	36	(4.4)	42	2.8
冠動脈ステント挿入	6	(0.7)	6	0.4	2	(0.2)	2	0.1	10	(1.2)	11	0.7	11	(1.3)	13	0.9
冠動脈血行再建	10	(1.2)	11	0.7	2	(0.2)	2	0.1	8	(1.0)	8	0.5	3	(0.4)	3	0.2
白内障手術	1	(0.1)	1	0.1	5	(0.6)	5	0.3	2	(0.2)	2	0.1	1	(0.1)	1	0.1
末梢血行再建	1	(0.1)	1	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2
冠動脈バイパス	4	(0.5)	4	0.3	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
経皮的冠インターベンション	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	3	0.2	3	(0.4)	3	0.2
末梢動脈形成	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
冠動脈形成	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
末梢動脈ステント挿入	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
抜歯	0				1	(0.1)	1	0.1	0				2	(0.2)	3	0.2

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
眼瞼下垂	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
虚血性視神経症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
視神経萎縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
視神経乳頭出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
視神経乳頭障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
視力障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
失明	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
硝子体障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
硝子体変性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
前房狭隅角	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
増殖性網膜症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
嚢下白内障	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
網膜症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
網膜静脈閉塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
網膜滲出物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乱視	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
老視	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
外科および内科処置	47	(2.9)	52	1.8	73	(4.4)	83	2.7	120	(3.7)	135	2.3
冠動脈ステント挿入	8	(0.5)	8	0.3	21	(1.3)	24	0.8	29	(0.9)	32	0.5
冠動脈血行再建	12	(0.7)	13	0.4	11	(0.7)	11	0.4	23	(0.7)	24	0.4
白内障手術	6	(0.4)	6	0.2	3	(0.2)	3	0.1	9	(0.3)	9	0.2
末梢血行再建	2	(0.1)	2	0.1	7	(0.4)	7	0.2	9	(0.3)	9	0.2
冠動脈バイパス	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
経皮的冠インターベンション	2	(0.1)	2	0.1	5	(0.3)	6	0.2	7	(0.2)	8	0.1
末梢動脈形成	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
冠動脈形成	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
末梢動脈ステント挿入	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
抜歯	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ステント装着	2	(0.2)	2	0.1	0				0				0			
頚動脈内膜剥離術	0				0				2	(0.2)	2	0.1	0			
血管形成	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
開腹	1	(0.1)	1	0.1	0				0				0			
外科的脊椎固定	0				0				0				1	(0.1)	1	0.1
眼瞼形成	0				0				0				1	(0.1)	1	0.1
機械的換気	1	(0.1)	1	0.1	0				0				0			
近距離照射療法	0				0				0				1	(0.1)	1	0.1
頚動脈ステント挿入	0				1	(0.1)	1	0.1	0				0			
頚動脈形成	0				0				0				1	(0.1)	1	0.1
頚動脈血行再建	1	(0.1)	1	0.1	0				0				0			
肩回旋筋腱板修復	1	(0.1)	1	0.1	0				0				0			
手根管除圧	0				0				0				1	(0.1)	1	0.1
植皮	0				1	(0.1)	1	0.1	0				0			
静脈切除術	0				0				0				1	(0.1)	1	0.1
椎間板手術	0				0				1	(0.1)	1	0.1	0			
動静脈瘻手術	0				0				1	(0.1)	1	0.1	0			
内固定除去	0				0				1	(0.1)	1	0.1	0			
末梢動脈バイパス	0				0				0				1	(0.1)	1	0.1
末梢動脈内膜剥離術	0				1	(0.1)	1	0.1	0				0			
網膜レーザー凝固	0				0				1	(0.1)	1	0.1	0			
瘻修復	0				0				1	(0.1)	1	0.1	0			
臍ヘルニア修復	0				1	(0.1)	1	0.1	0				0			
皮膚および皮下組織障害	27	(3.3)	31	2.1	23	(2.8)	24	1.7	25	(3.1)	29	1.9	41	(5.0)	49	3.2
皮膚潰瘍	5	(0.6)	7	0.5	3	(0.4)	3	0.2	5	(0.6)	5	0.3	7	(0.8)	10	0.7
糖尿病性足病変	3	(0.4)	5	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1	5	(0.6)	5	0.3
発疹	4	(0.5)	4	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1
蕁麻疹	0				3	(0.4)	3	0.2	3	(0.4)	3	0.2	1	(0.1)	1	0.1
過角化	1	(0.1)	1	0.1	0				4	(0.5)	4	0.3	0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ステント装着	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
頚動脈内膜剥離術	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
血管形成	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
開腹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
外科的脊椎固定	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼瞼形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
機械的換気	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
近距離照射療法	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頚動脈ステント挿入	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頚動脈形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頚動脈血行再建	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肩回旋筋腱板修復	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
手根管除圧	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
植皮	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
静脈切除術	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎間板手術	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
動静脈瘻手術	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
内固定除去	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈バイパス	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈内膜剥離術	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
網膜レーザー凝固	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
瘻修復	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
臍ヘルニア修復	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮膚および皮下組織障害	50	(3.0)	55	1.9	66	(4.0)	78	2.6	116	(3.5)	133	2.2
皮膚潰瘍	8	(0.5)	10	0.3	12	(0.7)	15	0.5	20	(0.6)	25	0.4
糖尿病性足病変	4	(0.2)	6	0.2	7	(0.4)	7	0.2	11	(0.3)	13	0.2
発疹	6	(0.4)	6	0.2	4	(0.2)	4	0.1	10	(0.3)	10	0.2
蕁麻疹	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
過角化	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg			Sema 1.0 mg			Placebo 0.5 mg			Placebo 1.0 mg		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
乾癬	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
皮膚病変	0				0				2	(0.2)	2	0.1	3	(0.4)	3	0.2
そう痒症	0				0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
日光角化症	0				0				0				4	(0.5)	6	0.4
嵌入爪	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
全身性そう痒症	0				0				0				3	(0.4)	3	0.2
全身性皮疹	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
多汗症	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
アトピー性皮膚炎	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
血管浮腫	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
脂漏性皮膚炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
接触性皮膚炎	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
脱毛症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
皮膚壊死	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
褥瘡性潰瘍	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
ざ瘡	0				1	(0.1)	1	0.1	0				0			
アレルギー性皮膚炎	0				0				0				1	(0.1)	1	0.1
間擦疹	0				0				0				1	(0.1)	2	0.1
血性水疱	1	(0.1)	1	0.1	0				0				0			
硬化性苔癬	0				1	(0.1)	1	0.1	0				0			
紅斑	1	(0.1)	1	0.1	0				0				0			
脂肪肥大症	0				0				0				1	(0.1)	1	0.1
湿疹	1	(0.1)	1	0.1	0				0				0			
酒さ	0				0				1	(0.1)	1	0.1	0			
寝汗	1	(0.1)	1	0.1	0				0				0			
神経障害性潰瘍	0				0				1	(0.1)	1	0.1	0			
神経皮膚炎	0				0				0				1	(0.1)	1	0.1
水疱	0				0				1	(0.1)	1	0.1	0			
中毒性皮疹	1	(0.1)	1	0.1	0				0				0			
点状出血	1	(0.1)	1	0.1	0				0				0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
乾癬	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
皮膚病変	0				5	(0.3)	5	0.2	5	(0.2)	5	0.1
そう痒症	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
日光角化症	0				4	(0.2)	6	0.2	4	(0.1)	6	0.1
嵌入爪	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
全身性そう痒症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
全身性皮疹	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
多汗症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
アトピー性皮膚炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血管浮腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
脂漏性皮膚炎	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
接触性皮膚炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
脱毛症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
皮膚壊死	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
褥瘡性潰瘍	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
ざ瘡	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
アレルギー性皮膚炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
間擦疹	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
血性水疱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
硬化性苔癬	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
紅斑	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脂肪肥大症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
湿疹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
酒さ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
寝汗	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経障害性潰瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経皮膚炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
水疱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
中毒性皮疹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
点状出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg			Sema 1.0 mg			Placebo 0.5 mg			Placebo 1.0 mg		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
斑状丘疹状皮疹	0				0				0				1	(0.1)	1	0.1
斑状出血	0				0				0				1	(0.1)	1	0.1
斑状皮疹	0				0				1	(0.1)	1	0.1	0			
皮膚局面	0				1	(0.1)	2	0.1	0				0			
皮膚障害	0				1	(0.1)	1	0.1	0				0			
皮膚嚢腫	0				0				0				1	(0.1)	2	0.1
皮膚剥脱	0				1	(0.1)	1	0.1	0				0			
冷汗	0				1	(0.1)	1	0.1	0				0			
精神障害	18	(2.2)	24	1.6	22	(2.7)	22	1.5	19	(2.3)	21	1.4	17	(2.1)	24	1.6
うつ病	7	(0.9)	7	0.5	7	(0.9)	7	0.5	7	(0.9)	7	0.5	7	(0.8)	9	0.6
不眠症	5	(0.6)	5	0.3	8	(1.0)	8	0.6	5	(0.6)	5	0.3	2	(0.2)	2	0.1
不安	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2
ストレス	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
錯乱状態	1	(0.1)	2	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
精神状態変化	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
激越	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
大うつ病	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
抑うつ気分	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
リビドー減退	0				1	(0.1)	1	0.1	0				0			
感情的苦悩	0				0				0				1	(0.1)	1	0.1
幻視	0				1	(0.1)	1	0.1	0				0			
心的外傷後ストレス障害	0				0				1	(0.1)	1	0.1	0			
神経症	0				1	(0.1)	1	0.1	0				0			
睡眠時驚愕	1	(0.1)	1	0.1	0				0				0			
睡眠障害	0				0				0				1	(0.1)	1	0.1
絶望感	0				0				1	(0.1)	1	0.1	0			
統合失調感情障害	0				1	(0.1)	1	0.1	0				0			
抑うつ症状	1	(0.1)	2	0.1	0				0				0			
落ち着きのなさ	0				0				0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
斑状丘疹状皮疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
斑状出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
斑状皮疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚局面	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
皮膚障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮膚嚢腫	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
皮膚剥脱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
冷汗	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
精神障害	40	(2.4)	46	1.6	36	(2.2)	45	1.5	76	(2.3)	91	1.5
うつ病	14	(0.9)	14	0.5	14	(0.9)	16	0.5	28	(0.9)	30	0.5
不眠症	13	(0.8)	13	0.4	7	(0.4)	7	0.2	20	(0.6)	20	0.3
不安	4	(0.2)	4	0.1	5	(0.3)	5	0.2	9	(0.3)	9	0.2
ストレス	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
錯乱状態	1	(0.1)	2	0.1	3	(0.2)	3	0.1	4	(0.1)	5	0.1
精神状態変化	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
激越	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
大うつ病	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
抑うつ気分	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
リビドー減退	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感情的苦悩	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
幻視	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心的外傷後ストレス障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
睡眠時驚愕	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
睡眠障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
絶望感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
統合失調感情障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
抑うつ症状	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
落ち着きのなさ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg			Sema 1.0 mg			Placebo 0.5 mg			Placebo 1.0 mg		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
譫妄	0				0				1	(0.1)	1	0.1	0			
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	10	(1.2)	11	0.7	22	(2.7)	27	1.9	15	(1.8)	15	1.0	25	(3.0)	25	1.6
基底細胞癌	1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1
前立腺癌	3	(0.4)	3	0.2	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
良性副甲状腺腫瘍	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
甲状腺の良性新生物	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
大腸腺腫	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
皮膚乳頭腫	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
子宮平滑筋腫	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
真珠腫	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
前立腺腺腫	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
肺腺癌	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
肛門性器疣贅	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
Ｂ細胞性リンパ腫	0				0				0				1	(0.1)	1	0.1
アクロコルドン	0				0				1	(0.1)	1	0.1	0			
カルチノイド腫瘍	0				1	(0.1)	1	0.1	0				0			
グロームス腫瘍	0				1	(0.1)	1	0.1	0				0			
異形成母斑	0				1	(0.1)	1	0.1	0				0			
移行上皮癌	1	(0.1)	1	0.1	0				0				0			
胃腺癌	1	(0.1)	1	0.1	0				0				0			
遠隔転移を伴う結腸癌	0				0				0				1	(0.1)	1	0.1
褐色細胞腫	1	(0.1)	1	0.1	0				0				0			
肝新生物	0				1	(0.1)	1	0.1	0				0			
肝腺腫	0				0				1	(0.1)	1	0.1	0			
急性リンパ性白血病	0				0				0				1	(0.1)	1	0.1
形質細胞性骨髄腫	0				0				0				1	(0.1)	1	0.1
結腸癌	0				1	(0.1)	1	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
譫妄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	32	(1.9)	38	1.3	40	(2.4)	40	1.3	72	(2.2)	78	1.3
基底細胞癌	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
前立腺癌	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
良性副甲状腺腫瘍	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
甲状腺の良性新生物	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
大腸腺腫	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
皮膚乳頭腫	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
子宮平滑筋腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
真珠腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
前立腺腺腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肺腺癌	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肛門性器疣贅	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
Ｂ細胞性リンパ腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
アクロコルドン	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
カルチノイド腫瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
グロームス腫瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
異形成母斑	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
移行上皮癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃腺癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
遠隔転移を伴う結腸癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
褐色細胞腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝腺腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性リンパ性白血病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
形質細胞性骨髄腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結腸癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
結腸新生物	0				0				1	(0.1)	1	0.1	0			
結腸直腸癌	0				0				1	(0.1)	1	0.1	0			
血管の良性新生物	0				1	(0.1)	1	0.1	0				0			
口腔線維腫	0				0				1	(0.1)	1	0.1	0			
喉頭扁平上皮癌	0				0				0				1	(0.1)	1	0.1
子宮内膜肉腫	0				0				0				1	(0.1)	1	0.1
脂漏性角化症	0				1	(0.1)	1	0.1	0				0			
十二指腸新生物	0				0				0				1	(0.1)	1	0.1
小細胞肺癌	0				0				1	(0.1)	1	0.1	0			
消化器新生物	0				0				0				1	(0.1)	1	0.1
浸潤性乳管癌	0				1	(0.1)	1	0.1	0				0			
腎癌第１期	0				0				0				1	(0.1)	1	0.1
腎明細胞癌	0				0				0				1	(0.1)	1	0.1
成長ホルモン産生性下垂体腫瘍	0				1	(0.1)	1	0.1	0				0			
前立腺癌第１期	0				0				0				1	(0.1)	1	0.1
前立腺癌第３期	0				0				0				1	(0.1)	1	0.1
虫垂新生物	0				1	(0.1)	1	0.1	0				0			
尿管癌	0				1	(0.1)	1	0.1	0				0			
皮膚の新生物	0				1	(0.1)	1	0.1	0				0			
皮膚有棘細胞癌	0				1	(0.1)	1	0.1	0				0			
非小細胞肺癌	0				0				0				1	(0.1)	1	0.1
傍神経節新生物	1	(0.1)	1	0.1	0				0				0			
卵巣莢膜細胞腫	1	(0.1)	1	0.1	0				0				0			
良性髄膜腫	0				0				1	(0.1)	1	0.1	0			
扁平上皮癌	0				1	(0.1)	1	0.1	0				0			
膀胱移行上皮癌	0				0				1	(0.1)	1	0.1	0			
膀胱新生物	0				0				0				1	(0.1)	1	0.1
血液およびリンパ系障害	18	(2.2)	18	1.2	17	(2.1)	17	1.2	12	(1.5)	12	0.8	16	(1.9)	18	1.2

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
結腸新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結腸直腸癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管の良性新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔線維腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
喉頭扁平上皮癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮内膜肉腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脂漏性角化症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
十二指腸新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
小細胞肺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
消化器新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
浸潤性乳管癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎癌第１期	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎明細胞癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
成長ホルモン産生性下垂体腫瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
前立腺癌第１期	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
前立腺癌第３期	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
虫垂新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿管癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮膚の新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮膚有棘細胞癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
非小細胞肺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
傍神経節新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
卵巣莢膜細胞腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性髄膜腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
扁平上皮癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱移行上皮癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膀胱新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血液およびリンパ系障害	35	(2.1)	35	1.2	28	(1.7)	30	1.0	63	(1.9)	65	1.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
貧血	7	(0.9)	7	0.5	10	(1.2)	10	0.7	8	(1.0)	8	0.5	10	(1.2)	10	0.7
白血球増加症	2	(0.2)	2	0.1	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
血小板減少症	2	(0.2)	2	0.1	0				0				2	(0.2)	2	0.1
出血性貧血	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
白血球減少症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
正色素性正球性貧血	2	(0.2)	2	0.1	0				0				0			
鉄欠乏性貧血	2	(0.2)	2	0.1	0				0				0			
ヘパリン起因性血小板減少症	0				0				0				1	(0.1)	1	0.1
リンパ節症	0				0				0				1	(0.1)	1	0.1
凝固因子異常	1	(0.1)	1	0.1	0				0				0			
血小板増加症	0				1	(0.1)	1	0.1	0				0			
縦隔リンパ節腫脹	0				1	(0.1)	1	0.1	0				0			
腎性貧血	1	(0.1)	1	0.1	0				0				0			
赤血球増加症	0				0				0				1	(0.1)	1	0.1
汎血球減少症	1	(0.1)	1	0.1	0				0				0			
慢性疾患の貧血	0				1	(0.1)	1	0.1	0				0			
脾腫	0				1	(0.1)	1	0.1	0				0			
肝胆道系障害	8	(1.0)	9	0.6	17	(2.1)	19	1.3	16	(2.0)	20	1.3	11	(1.3)	13	0.9
脂肪肝	2	(0.2)	2	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3	6	(0.7)	6	0.4
胆石症	3	(0.4)	3	0.2	7	(0.9)	7	0.5	3	(0.4)	3	0.2	1	(0.1)	1	0.1
急性胆嚢炎	0				0				4	(0.5)	4	0.3	0			
胆管結石	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
胆道仙痛	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1	0			
肝障害	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
肝嚢胞	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
胆嚢炎	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
慢性胆嚢炎	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
肝硬変	0				1	(0.1)	1	0.1	0				0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
貧血	17	(1.0)	17	0.6	18	(1.1)	18	0.6	35	(1.1)	35	0.6
白血球増加症	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
血小板減少症	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
出血性貧血	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
白血球減少症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
正色素性正球性貧血	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
鉄欠乏性貧血	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
ヘパリン起因性血小板減少症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
リンパ節症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
凝固因子異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血小板増加症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
縦隔リンパ節腫脹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎性貧血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
赤血球増加症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
汎血球減少症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
慢性疾患の貧血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脾腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝胆道系障害	25	(1.5)	28	1.0	27	(1.6)	33	1.1	52	(1.6)	61	1.0
脂肪肝	6	(0.4)	6	0.2	10	(0.6)	10	0.3	16	(0.5)	16	0.3
胆石症	10	(0.6)	10	0.3	4	(0.2)	4	0.1	14	(0.4)	14	0.2
急性胆嚢炎	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
胆管結石	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
胆道仙痛	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
肝障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肝嚢胞	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胆嚢炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
慢性胆嚢炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
肝硬変	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肝腫大	1	(0.1)	1	0.1	0				0				0			
肝石灰化	0				0				1	(0.1)	1	0.1	0			
肝臓うっ血	0				0				0				1	(0.1)	1	0.1
肝脾腫大	1	(0.1)	1	0.1	0				0				0			
心臓性肝硬変	1	(0.1)	1	0.1	0				0				0			
水腫性胆嚢炎	1	(0.1)	1	0.1	0				0				0			
胆管炎	0				0				0				1	(0.1)	1	0.1
胆汁うっ滞	0				0				1	(0.1)	1	0.1	0			
胆道障害	0				1	(0.1)	1	0.1	0				0			
胆嚢ポリープ	0				0				1	(0.1)	1	0.1	0			
生殖系および乳房障害	12	(1.5)	12	0.8	10	(1.2)	11	0.8	9	(1.1)	12	0.8	10	(1.2)	10	0.7
良性前立腺肥大症	5	(0.6)	5	0.3	3	(0.4)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	3	0.2
前立腺腫大	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
膀胱瘤	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
膣脱	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
乳房痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
勃起不全	0				2	(0.2)	2	0.1	0				0			
萎縮性外陰膣炎	0				0				0				1	(0.1)	1	0.1
外陰膣そう痒症	0				0				0				1	(0.1)	1	0.1
外陰膣痛	0				0				1	(0.1)	1	0.1	0			
月経過多	0				1	(0.1)	1	0.1	0				0			
子宮ポリープ	0				0				1	(0.1)	1	0.1	0			
子宮障害	1	(0.1)	1	0.1	0				0				0			
子宮脱	0				0				1	(0.1)	1	0.1	0			
子宮内膜増殖症	0				0				1	(0.1)	1	0.1	0			
子宮付属器嚢胞	0				0				0				1	(0.1)	1	0.1
子宮膣脱	0				1	(0.1)	1	0.1	0				0			
女性化乳房	0				0				0				1	(0.1)	1	0.1
性器脱	0				0				1	(0.1)	1	0.1	0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肝腫大	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝石灰化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝臓うっ血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝脾腫大	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心臓性肝硬変	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
水腫性胆嚢炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆管炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆汁うっ滞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆道障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆嚢ポリープ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
生殖系および乳房障害	22	(1.3)	23	0.8	19	(1.2)	22	0.7	41	(1.2)	45	0.8
良性前立腺肥大症	8	(0.5)	8	0.3	4	(0.2)	4	0.1	12	(0.4)	12	0.2
前立腺腫大	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
膀胱瘤	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
膣脱	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
乳房痛	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
勃起不全	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
萎縮性外陰膣炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外陰膣そう痒症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外陰膣痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
月経過多	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
子宮ポリープ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
子宮脱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮内膜増殖症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮付属器嚢胞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮膣脱	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
女性化乳房	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
性器脱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
性機能不全	0				0				1	(0.1)	1	0.1	0			
精巣上体圧痛	0				0				1	(0.1)	1	0.1	0			
前立腺炎	0				0				0				1	(0.1)	1	0.1
前立腺閉塞	0				0				1	(0.1)	1	0.1	0			
乳房圧痛	1	(0.1)	1	0.1	0				0				0			
閉経後出血	1	(0.1)	1	0.1	0				0				0			
卵巣嚢胞	0				0				0				1	(0.1)	1	0.1
腟瘤	0				0				1	(0.1)	1	0.1	0			
耳および迷路障害	7	(0.9)	8	0.5	11	(1.3)	11	0.8	6	(0.7)	6	0.4	10	(1.2)	11	0.7
回転性めまい	2	(0.2)	2	0.1	5	(0.6)	5	0.3	4	(0.5)	4	0.3	5	(0.6)	5	0.3
耳垢栓塞	1	(0.1)	1	0.1	0				0				3	(0.4)	3	0.2
聴力低下	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
耳鳴	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
難聴	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
メニエール病	1	(0.1)	1	0.1	0				0				0			
鼓膜穿孔	1	(0.1)	1	0.1	0				0				0			
耳管機能障害	1	(0.1)	1	0.1	0				0				0			
耳硬化症	0				0				1	(0.1)	1	0.1	0			
耳痛	0				1	(0.1)	1	0.1	0				0			
前庭障害	0				1	(0.1)	1	0.1	0				0			
中耳の炎症	1	(0.1)	1	0.1	0				0				0			
頭位性回転性めまい	0				0				0				1	(0.1)	1	0.1
両耳難聴	0				1	(0.1)	1	0.1	0				0			
内分泌障害	2	(0.2)	2	0.1	2	(0.2)	2	0.1	6	(0.7)	6	0.4	4	(0.5)	4	0.3
甲状腺機能低下症	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	0			
甲状腺腫	0				0				3	(0.4)	3	0.2	3	(0.4)	3	0.2
原発性甲状腺機能低下症	0				0				0				1	(0.1)	1	0.1
甲状腺機能亢進症	1	(0.1)	1	0.1	0				0				0			

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
性機能不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精巣上体圧痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
前立腺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
前立腺閉塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳房圧痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
閉経後出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
卵巣嚢胞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腟瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
耳および迷路障害	18	(1.1)	19	0.6	16	(1.0)	17	0.6	34	(1.0)	36	0.6
回転性めまい	7	(0.4)	7	0.2	9	(0.5)	9	0.3	16	(0.5)	16	0.3
耳垢栓塞	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
聴力低下	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
耳鳴	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
難聴	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
メニエール病	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼓膜穿孔	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
耳管機能障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
耳硬化症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
耳痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
前庭障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
中耳の炎症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頭位性回転性めまい	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
両耳難聴	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
内分泌障害	4	(0.2)	4	0.1	10	(0.6)	10	0.3	14	(0.4)	14	0.2
甲状腺機能低下症	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
甲状腺腫	0				6	(0.4)	6	0.2	6	(0.2)	6	0.1
原発性甲状腺機能低下症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
甲状腺機能亢進症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
免疫系障害	3	(0.4)	3	0.2	2	(0.2)	2	0.1	3	(0.4)	4	0.3	3	(0.4)	3	0.2
薬物過敏症	1	(0.1)	1	0.1	0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
季節性アレルギー	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
食物アレルギー	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
過敏症	1	(0.1)	1	0.1	0				0				0			
香料過敏症	0				1	(0.1)	1	0.1	0				0			
節足動物咬傷アレルギー	0				0				1	(0.1)	1	0.1	0			
動物アレルギー	0				0				0				1	(0.1)	1	0.1
先天性、家族性および遺伝性障害	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
α１抗トリプシン欠損症	0				0				0				1	(0.1)	1	0.1
色覚異常	0				1	(0.1)	1	0.1	0				0			
包茎	0				1	(0.1)	1	0.1	0				0			
社会環境	0				1	(0.1)	1	0.1	0				0			
運動不能	0				1	(0.1)	1	0.1	0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Moderate adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
免疫系障害	5	(0.3)	5	0.2	6	(0.4)	7	0.2	11	(0.3)	12	0.2
薬物過敏症	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
季節性アレルギー	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
食物アレルギー	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
過敏症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
香料過敏症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
節足動物咬傷アレルギー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
動物アレルギー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
先天性、家族性および遺伝性障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
α１抗トリプシン欠損症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
色覚異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
包茎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
社会環境	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
運動不能	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.25.2- 6　軽度の有害事象（器官別大分類及び基本語別） - on-treatment 期間 -安全性解析対象集団

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	823				819				819				825			
Exposure time (year)	1488.3				1443.9				1508.0				1526.8			
Events	646	(78.5)	3099	208.2	633	(77.3)	3067	212.4	645	(78.8)	2904	192.6	640	(77.6)	2795	183.1
胃腸障害	336	(40.8)	830	55.8	323	(39.4)	866	60.0	225	(27.5)	444	29.4	226	(27.4)	400	26.2
下痢	114	(13.9)	185	12.4	108	(13.2)	154	10.7	66	(8.1)	106	7.0	59	(7.2)	69	4.5
悪心	109	(13.2)	170	11.4	119	(14.5)	186	12.9	46	(5.6)	56	3.7	56	(6.8)	77	5.0
嘔吐	57	(6.9)	78	5.2	70	(8.5)	97	6.7	29	(3.5)	32	2.1	24	(2.9)	24	1.6
便秘	38	(4.6)	40	2.7	57	(7.0)	66	4.6	21	(2.6)	26	1.7	27	(3.3)	28	1.8
消化不良	34	(4.1)	48	3.2	39	(4.8)	49	3.4	15	(1.8)	17	1.1	16	(1.9)	17	1.1
腹部不快感	30	(3.6)	58	3.9	30	(3.7)	72	5.0	16	(2.0)	25	1.7	12	(1.5)	18	1.2
腹痛	30	(3.6)	31	2.1	16	(2.0)	19	1.3	17	(2.1)	20	1.3	23	(2.8)	25	1.6
上腹部痛	19	(2.3)	19	1.3	25	(3.1)	30	2.1	16	(2.0)	18	1.2	14	(1.7)	22	1.4
腹部膨満	16	(1.9)	21	1.4	18	(2.2)	19	1.3	12	(1.5)	15	1.0	4	(0.5)	4	0.3
胃食道逆流性疾患	20	(2.4)	27	1.8	18	(2.2)	18	1.2	5	(0.6)	5	0.3	5	(0.6)	5	0.3
放屁	11	(1.3)	16	1.1	20	(2.4)	25	1.7	9	(1.1)	10	0.7	4	(0.5)	5	0.3
歯痛	11	(1.3)	13	0.9	5	(0.6)	7	0.5	8	(1.0)	13	0.9	9	(1.1)	12	0.8
胃炎	8	(1.0)	8	0.5	11	(1.3)	12	0.8	6	(0.7)	6	0.4	4	(0.5)	4	0.3
大腸ポリープ	8	(1.0)	8	0.5	7	(0.9)	9	0.6	8	(1.0)	8	0.5	5	(0.6)	7	0.5
痔核	6	(0.7)	6	0.4	8	(1.0)	8	0.6	7	(0.9)	7	0.5	5	(0.6)	5	0.3
憩室	7	(0.9)	7	0.5	3	(0.4)	3	0.2	7	(0.9)	7	0.5	4	(0.5)	4	0.3
おくび	9	(1.1)	10	0.7	11	(1.3)	11	0.8	0				0			
慢性胃炎	6	(0.7)	6	0.4	3	(0.4)	3	0.2	8	(1.0)	8	0.5	3	(0.4)	3	0.2
裂孔ヘルニア	3	(0.4)	3	0.2	5	(0.6)	5	0.3	1	(0.1)	1	0.1	6	(0.7)	6	0.4
腸憩室	6	(0.7)	6	0.4	2	(0.2)	2	0.1	4	(0.5)	4	0.3	2	(0.2)	3	0.2
過敏性腸症候群	5	(0.6)	5	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1	5	(0.6)	5	0.3
胃腸障害	2	(0.2)	2	0.1	5	(0.6)	5	0.3	1	(0.1)	1	0.1	3	(0.4)	4	0.3
口内乾燥	1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2	3	(0.4)	3	0.2

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	1642				1644				3286			
Exposure time (year)	2932.2				3034.8				5967.0			
Events	1279	(77.9)	6166	210.3	1285	(78.2)	5699	187.8	2564	(78.0)	11865	198.8
胃腸障害	659	(40.1)	1696	57.8	451	(27.4)	844	27.8	1110	(33.8)	2540	42.6
下痢	222	(13.5)	339	11.6	125	(7.6)	175	5.8	347	(10.6)	514	8.6
悪心	228	(13.9)	356	12.1	102	(6.2)	133	4.4	330	(10.0)	489	8.2
嘔吐	127	(7.7)	175	6.0	53	(3.2)	56	1.8	180	(5.5)	231	3.9
便秘	95	(5.8)	106	3.6	48	(2.9)	54	1.8	143	(4.4)	160	2.7
消化不良	73	(4.4)	97	3.3	31	(1.9)	34	1.1	104	(3.2)	131	2.2
腹部不快感	60	(3.7)	130	4.4	28	(1.7)	43	1.4	88	(2.7)	173	2.9
腹痛	46	(2.8)	50	1.7	40	(2.4)	45	1.5	86	(2.6)	95	1.6
上腹部痛	44	(2.7)	49	1.7	30	(1.8)	40	1.3	74	(2.3)	89	1.5
腹部膨満	34	(2.1)	40	1.4	16	(1.0)	19	0.6	50	(1.5)	59	1.0
胃食道逆流性疾患	38	(2.3)	45	1.5	10	(0.6)	10	0.3	48	(1.5)	55	0.9
放屁	31	(1.9)	41	1.4	13	(0.8)	15	0.5	44	(1.3)	56	0.9
歯痛	16	(1.0)	20	0.7	17	(1.0)	25	0.8	33	(1.0)	45	0.8
胃炎	19	(1.2)	20	0.7	10	(0.6)	10	0.3	29	(0.9)	30	0.5
大腸ポリープ	15	(0.9)	17	0.6	13	(0.8)	15	0.5	28	(0.9)	32	0.5
痔核	14	(0.9)	14	0.5	12	(0.7)	12	0.4	26	(0.8)	26	0.4
憩室	10	(0.6)	10	0.3	11	(0.7)	11	0.4	21	(0.6)	21	0.4
おくび	20	(1.2)	21	0.7	0				20	(0.6)	21	0.4
慢性胃炎	9	(0.5)	9	0.3	11	(0.7)	11	0.4	20	(0.6)	20	0.3
裂孔ヘルニア	8	(0.5)	8	0.3	7	(0.4)	7	0.2	15	(0.5)	15	0.3
腸憩室	8	(0.5)	8	0.3	6	(0.4)	7	0.2	14	(0.4)	15	0.3
過敏性腸症候群	6	(0.4)	6	0.2	6	(0.4)	6	0.2	12	(0.4)	12	0.2
胃腸障害	7	(0.4)	7	0.2	4	(0.2)	5	0.2	11	(0.3)	12	0.2
口内乾燥	4	(0.2)	4	0.1	6	(0.4)	6	0.2	10	(0.3)	10	0.2

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
嚥下障害	4	(0.5)	4	0.3	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
齲歯	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	5	(0.6)	5	0.3
びらん性胃炎	0				3	(0.4)	3	0.2	4	(0.5)	4	0.3	1	(0.1)	1	0.1
十二指腸炎	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
鼠径ヘルニア	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
大腸炎	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
胃ポリープ	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
下腹部痛	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
食中毒	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
直腸ポリープ	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
直腸出血	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
胃排出不全	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1
膵炎	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
膵嚢胞	4	(0.5)	4	0.3	0				1	(0.1)	1	0.1	0			
バレット食道	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
血便排泄	0				3	(0.4)	3	0.2	0				1	(0.1)	1	0.1
腹部ヘルニア	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
臍ヘルニア	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1	0			
胃十二指腸炎	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
小腸炎	1	(0.1)	1	0.1	1	(0.1)	2	0.1	1	(0.1)	1	0.1	0			
消化性潰瘍	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
心窩部不快感	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
軟便	3	(0.4)	3	0.2	0				0				0			
排便回数増加	0				0				3	(0.4)	3	0.2	0			
変色便	0				0				3	(0.4)	3	0.2	0			
裂肛	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
びらん性十二指腸炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
びらん性食道炎	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
アフタ性口内炎	0				0				2	(0.2)	2	0.1	0			
レッチング	2	(0.2)	2	0.1	0				0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
嚥下障害	6	(0.4)	6	0.2	3	(0.2)	3	0.1	9	(0.3)	9	0.2
齲歯	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2
びらん性胃炎	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
十二指腸炎	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
鼠径ヘルニア	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
大腸炎	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
胃ポリープ	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
下腹部痛	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
食中毒	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
直腸ポリープ	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
直腸出血	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
胃排出不全	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
膵炎	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
膵嚢胞	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
バレット食道	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
血便排泄	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
腹部ヘルニア	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
臍ヘルニア	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
胃十二指腸炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
小腸炎	2	(0.1)	3	0.1	1	(0.1)	1	<0.1	3	(0.1)	4	0.1
消化性潰瘍	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
心窩部不快感	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
軟便	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
排便回数増加	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
変色便	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
裂肛	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
びらん性十二指腸炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
びらん性食道炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
アフタ性口内炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
レッチング	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胃障害	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
胃潰瘍	0				0				2	(0.2)	2	0.1	0			
逆流性胃炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
口腔内潰瘍形成	0				0				1	(0.1)	1	0.1	1	(0.1)	2	0.1
硬便	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
歯の脱落	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
十二指腸ポリープ	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
十二指腸胃逆流	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
消化管運動障害	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
食道炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
食道静脈瘤	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
潰瘍性大腸炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
糖尿病性胃不全麻痺	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
便習慣変化	0				2	(0.2)	2	0.1	0				0			
慢性膵炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
嚥下痛	0				2	(0.2)	2	0.1	0				0			
キライディティ症候群	1	(0.1)	1	0.1	0				0				0			
セリアック病	0				1	(0.1)	1	0.1	0				0			
異常便	0				0				0				1	(0.1)	1	0.1
胃酸過多	0				0				0				1	(0.1)	1	0.1
胃十二指腸潰瘍	1	(0.1)	1	0.1	0				0				0			
胃腸音異常	1	(0.1)	1	0.1	0				0				0			
回腸潰瘍	1	(0.1)	1	0.1	0				0				0			
空気嚥下	0				1	(0.1)	1	0.1	0				0			
限局性腹腔内液貯留	0				0				1	(0.1)	1	0.1	0			
呼気臭	0				1	(0.1)	1	0.1	0				0			
口蓋障害	1	(0.1)	1	0.1	0				0				0			
口腔そう痒症	1	(0.1)	1	0.1	0				0				0			
口腔障害	0				0				0				1	(0.1)	1	0.1
口腔内出血	0				1	(0.1)	1	0.1	0				0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class / Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胃障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胃潰瘍	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
逆流性胃炎	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
口腔内潰瘍形成	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
硬便	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
歯の脱落	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
十二指腸ポリープ	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
十二指腸胃逆流	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
消化管運動障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
食道炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
食道静脈瘤	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
潰瘍性大腸炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
糖尿病性胃不全麻痺	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
便習慣変化	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
慢性膵炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
嚥下痛	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
キライディティ症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
セリアック病	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
異常便	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胃酸過多	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胃十二指腸潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胃腸音異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
回腸潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
空気嚥下	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
限局性腹腔内液貯留	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼気臭	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口蓋障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔そう痒症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口腔内出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
口腔内痛	0				0				1	(0.1)	1	0.1	0			
口唇腫脹	0				0				1	(0.1)	1	0.1	0			
口唇浮腫	1	(0.1)	3	0.2	0				0				0			
歯の障害	1	(0.1)	1	0.1	0				0				0			
歯周病	0				0				0				1	(0.1)	1	0.1
歯槽骨吸収	0				0				1	(0.1)	1	0.1	0			
歯肉腫脹	0				0				0				1	(0.1)	1	0.1
歯肉出血	0				1	(0.1)	1	0.1	0				0			
歯肉痛	0				1	(0.1)	1	0.1	0				0			
十二指腸潰瘍	0				0				1	(0.1)	1	0.1	0			
出血性びらん性胃炎	0				0				0				1	(0.1)	1	0.1
出血性大腸潰瘍	0				0				1	(0.1)	1	0.1	0			
消化管壁肥厚	0				0				0				1	(0.1)	1	0.1
消化器痛	0				0				0				1	(0.1)	1	0.1
上部消化管出血	0				0				0				1	(0.1)	1	0.1
食道運動障害	1	(0.1)	1	0.1	0				0				0			
食道狭窄	1	(0.1)	1	0.1	0				0				0			
食道憩室	0				0				1	(0.1)	1	0.1	0			
食道潰瘍	0				0				0				1	(0.1)	1	0.1
舌腫脹	0				0				1	(0.1)	1	0.1	0			
舌障害	0				0				1	(0.1)	1	0.1	0			
舌変色	0				1	(0.1)	1	0.1	0				0			
腸管ポリープ	0				0				1	(0.1)	1	0.1	0			
腸間膜脂肪織炎	1	(0.1)	1	0.1	0				0				0			
排便回数減少	0				1	(0.1)	1	0.1	0				0			
白色便	1	(0.1)	1	0.1	0				0				0			
肥厚性胃炎	0				0				1	(0.1)	1	0.1	0			
非感染性歯肉炎	0				0				0				1	(0.1)	1	0.1
腹部圧痛	0				0				1	(0.1)	1	0.1	0			
糞塊	0				1	(0.1)	1	0.1	0				0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
口腔内痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口唇腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口唇浮腫	1	(0.1)	3	0.1	0				1	(<0.1)	3	0.1
歯の障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
歯周病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯槽骨吸収	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯肉腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯肉出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
歯肉痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
十二指腸潰瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性びらん性胃炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性大腸潰瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
消化管壁肥厚	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
消化器痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
上部消化管出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
食道運動障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
食道狭窄	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
食道憩室	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
食道潰瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
舌腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
舌障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
舌変色	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腸管ポリープ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腸間膜脂肪織炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
排便回数減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
白色便	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肥厚性胃炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
非感染性歯肉炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腹部圧痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糞塊	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
変色歯	0				1	(0.1)	1	0.1	0				0			
埋伏歯	1	(0.1)	1	0.1	0				0				0			
門脈圧亢進性胃障害	0				1	(0.1)	1	0.1	0				0			
肛門そう痒症	0				1	(0.1)	1	0.1	0				0			
肛門肥大乳頭	0				0				1	(0.1)	1	0.1	0			
膵石灰化	1	(0.1)	1	0.1	0				0				0			
膵臓障害	1	(0.1)	1	0.1	0				0				0			
感染症および寄生虫症	264	(32.1)	448	30.1	240	(29.3)	404	28.0	274	(33.5)	462	30.6	262	(31.8)	448	29.3
鼻咽頭炎	55	(6.7)	69	4.6	45	(5.5)	56	3.9	61	(7.4)	77	5.1	56	(6.8)	73	4.8
尿路感染	54	(6.6)	72	4.8	36	(4.4)	42	2.9	45	(5.5)	62	4.1	46	(5.6)	53	3.5
上気道感染	35	(4.3)	38	2.6	29	(3.5)	32	2.2	38	(4.6)	45	3.0	40	(4.8)	53	3.5
インフルエンザ	29	(3.5)	37	2.5	30	(3.7)	37	2.6	29	(3.5)	30	2.0	30	(3.6)	41	2.7
気管支炎	18	(2.2)	22	1.5	14	(1.7)	14	1.0	24	(2.9)	26	1.7	28	(3.4)	35	2.3
副鼻腔炎	14	(1.7)	18	1.2	16	(2.0)	20	1.4	16	(2.0)	18	1.2	16	(1.9)	18	1.2
胃腸炎	11	(1.3)	12	0.8	16	(2.0)	16	1.1	12	(1.5)	12	0.8	11	(1.3)	11	0.7
肺炎	14	(1.7)	14	0.9	9	(1.1)	14	1.0	8	(1.0)	8	0.5	11	(1.3)	11	0.7
咽頭炎	10	(1.2)	10	0.7	10	(1.2)	13	0.9	6	(0.7)	6	0.4	10	(1.2)	10	0.7
蜂巣炎	8	(1.0)	8	0.5	9	(1.1)	10	0.7	7	(0.9)	7	0.5	9	(1.1)	11	0.7
膀胱炎	6	(0.7)	6	0.4	10	(1.2)	12	0.8	7	(0.9)	8	0.5	6	(0.7)	8	0.5
帯状疱疹	8	(1.0)	12	0.8	9	(1.1)	10	0.7	6	(0.7)	6	0.4	4	(0.5)	4	0.3
歯感染	10	(1.2)	13	0.9	9	(1.1)	9	0.6	4	(0.5)	5	0.3	3	(0.4)	3	0.2
爪真菌症	9	(1.1)	9	0.6	5	(0.6)	5	0.3	6	(0.7)	6	0.4	5	(0.6)	5	0.3
結膜炎	6	(0.7)	6	0.4	8	(1.0)	10	0.7	7	(0.9)	7	0.5	3	(0.4)	3	0.2
限局性感染	6	(0.7)	6	0.4	4	(0.5)	4	0.3	7	(0.9)	8	0.5	4	(0.5)	4	0.3
足部白癬	4	(0.5)	4	0.3	3	(0.4)	3	0.2	4	(0.5)	4	0.3	8	(1.0)	8	0.5
鼻炎	1	(0.1)	1	0.1	5	(0.6)	5	0.3	12	(1.5)	12	0.8	1	(0.1)	1	0.1
ウイルス性胃腸炎	5	(0.6)	5	0.3	6	(0.7)	6	0.4	2	(0.2)	2	0.1	5	(0.6)	5	0.3
ウイルス感染	3	(0.4)	3	0.2	7	(0.9)	7	0.5	5	(0.6)	8	0.5	2	(0.2)	2	0.1
真菌感染	2	(0.2)	2	0.1	2	(0.2)	3	0.2	6	(0.7)	6	0.4	5	(0.6)	5	0.3

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
変色歯	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
埋伏歯	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
門脈圧亢進性胃障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肛門そう痒症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肛門肥大乳頭	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膵石灰化	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵臓障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染症および寄生虫症	504	(30.7)	852	29.1	536	(32.6)	910	30.0	1040	(31.6)	1762	29.5
鼻咽頭炎	100	(6.1)	125	4.3	117	(7.1)	150	4.9	217	(6.6)	275	4.6
尿路感染	90	(5.5)	114	3.9	91	(5.5)	115	3.8	181	(5.5)	229	3.8
上気道感染	64	(3.9)	70	2.4	78	(4.7)	98	3.2	142	(4.3)	168	2.8
インフルエンザ	59	(3.6)	74	2.5	59	(3.6)	71	2.3	118	(3.6)	145	2.4
気管支炎	32	(1.9)	36	1.2	52	(3.2)	61	2.0	84	(2.6)	97	1.6
副鼻腔炎	30	(1.8)	38	1.3	32	(1.9)	36	1.2	62	(1.9)	74	1.2
胃腸炎	27	(1.6)	28	1.0	23	(1.4)	23	0.8	50	(1.5)	51	0.9
肺炎	23	(1.4)	28	1.0	19	(1.2)	19	0.6	42	(1.3)	47	0.8
咽頭炎	20	(1.2)	23	0.8	16	(1.0)	16	0.5	36	(1.1)	39	0.7
蜂巣炎	17	(1.0)	18	0.6	16	(1.0)	18	0.6	33	(1.0)	36	0.6
膀胱炎	16	(1.0)	18	0.6	13	(0.8)	16	0.5	29	(0.9)	34	0.6
帯状疱疹	17	(1.0)	22	0.8	10	(0.6)	10	0.3	27	(0.8)	32	0.5
歯感染	19	(1.2)	22	0.8	7	(0.4)	8	0.3	26	(0.8)	30	0.5
爪真菌症	14	(0.9)	14	0.5	11	(0.7)	11	0.4	25	(0.8)	25	0.4
結膜炎	14	(0.9)	16	0.5	10	(0.6)	10	0.3	24	(0.7)	26	0.4
限局性感染	10	(0.6)	10	0.3	11	(0.7)	12	0.4	21	(0.6)	22	0.4
足部白癬	7	(0.4)	7	0.2	12	(0.7)	12	0.4	19	(0.6)	19	0.3
鼻炎	6	(0.4)	6	0.2	13	(0.8)	13	0.4	19	(0.6)	19	0.3
ウイルス性胃腸炎	11	(0.7)	11	0.4	7	(0.4)	7	0.2	18	(0.5)	18	0.3
ウイルス感染	10	(0.6)	10	0.3	7	(0.4)	10	0.3	17	(0.5)	20	0.3
真菌感染	4	(0.2)	5	0.2	11	(0.7)	11	0.4	15	(0.5)	16	0.3

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
下気道感染	3	(0.4)	3	0.2	5	(0.6)	5	0.3	5	(0.6)	5	0.3	1	(0.1)	1	0.1
歯膿瘍	4	(0.5)	5	0.3	1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1
ヘリコバクター感染	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1
せつ	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2
感染性皮膚潰瘍	0				2	(0.2)	3	0.2	1	(0.1)	1	0.1	4	(0.5)	5	0.3
眼感染	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
喉頭炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2
ウイルス性上気道感染	0				4	(0.5)	4	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1
外耳炎	3	(0.4)	4	0.3	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
気道感染	1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1	0			
急性副鼻腔炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
口腔ヘルペス	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
皮膚感染	1	(0.1)	1	0.1	0				3	(0.4)	4	0.3	2	(0.2)	2	0.1
咽頭扁桃炎	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
口腔カンジダ症	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
歯肉炎	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
耳感染	0				0				2	(0.2)	2	0.1	3	(0.4)	3	0.2
創傷感染	2	(0.2)	3	0.2	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
中耳炎	2	(0.2)	4	0.3	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
肺感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
毛包炎	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
カンジダ感染	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0				0			
ヘリコバクター性胃炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
外陰膣真菌感染	0				0				2	(0.2)	2	0.1	2	(0.2)	3	0.2
憩室炎	2	(0.2)	2	0.1	0				0				2	(0.2)	2	0.1
精巣上体炎	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				0			
丹毒	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	0			
爪囲炎	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
膿瘍	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
皮膚真菌感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
下気道感染	8	(0.5)	8	0.3	6	(0.4)	6	0.2	14	(0.4)	14	0.2
歯膿瘍	5	(0.3)	6	0.2	5	(0.3)	5	0.2	10	(0.3)	11	0.2
ヘリコバクター感染	5	(0.3)	5	0.2	3	(0.2)	3	0.1	8	(0.2)	8	0.1
せつ	2	(0.1)	2	0.1	5	(0.3)	5	0.2	7	(0.2)	7	0.1
感染性皮膚潰瘍	2	(0.1)	3	0.1	5	(0.3)	6	0.2	7	(0.2)	9	0.2
眼感染	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
喉頭炎	2	(0.1)	2	0.1	5	(0.3)	5	0.2	7	(0.2)	7	0.1
ウイルス性上気道感染	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
外耳炎	5	(0.3)	6	0.2	1	(0.1)	1	<0.1	6	(0.2)	7	0.1
気道感染	5	(0.3)	5	0.2	1	(0.1)	1	<0.1	6	(0.2)	6	0.1
急性副鼻腔炎	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
口腔ヘルペス	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
皮膚感染	1	(0.1)	1	<0.1	5	(0.3)	6	0.2	6	(0.2)	7	0.1
咽頭扁桃炎	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
口腔カンジダ症	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
歯肉炎	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
耳感染	0				5	(0.3)	5	0.2	5	(0.2)	5	0.1
創傷感染	2	(0.1)	3	0.1	3	(0.2)	3	0.1	5	(0.2)	6	0.1
中耳炎	2	(0.1)	4	0.1	3	(0.2)	3	0.1	5	(0.2)	7	0.1
肺感染	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
毛包炎	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
カンジダ感染	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
ヘリコバクター性胃炎	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
外陰膣真菌感染	0				4	(0.2)	5	0.2	4	(0.1)	5	0.1
憩室炎	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
精巣上体炎	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
丹毒	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
爪囲炎	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
膿瘍	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
皮膚真菌感染	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ウイルス性気道感染	0				0				0				3	(0.4)	3	0.2
ウイルス性消化管感染	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
ダニ皮膚炎	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
レンサ球菌性咽頭炎	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
外陰部膣カンジダ症	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
急性中耳炎	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
赤痢	1	(0.1)	4	0.3	1	(0.1)	2	0.1	1	(0.1)	1	0.1	0			
唾液腺炎	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
体部白癬	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
単純ヘルペス	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
爪感染	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
敗血症	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
慢性腎盂腎炎	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
迷路炎	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
扁桃炎	0				0				3	(0.4)	3	0.2	0			
癜風	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
アデノウイルス結膜炎	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
ウイルス性気管支炎	1	(0.1)	1	0.1	0				1	(0.1)	2	0.1	0			
カンピロバクター感染	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
回虫症	0				2	(0.2)	2	0.1	0				0			
気管気管支炎	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
細菌性耳感染	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
細菌尿	0				0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
歯周炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
処置後感染	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
切開部位感染	2	(0.2)	2	0.1	0				0				0			
大腸菌性尿路感染	0				0				2	(0.2)	2	0.1	0			
尿路性敗血症	2	(0.2)	2	0.1	0				0				0			
麦粒腫	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
皮下組織膿瘍	2	(0.2)	2	0.1	0				0				0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ウイルス性気道感染	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
ウイルス性消化管感染	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
ダニ皮膚炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
レンサ球菌性咽頭炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
外陰部膣カンジダ症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
急性中耳炎	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
赤痢	2	(0.1)	6	0.2	1	(0.1)	1	<0.1	3	(0.1)	7	0.1
唾液腺炎	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
体部白癬	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
単純ヘルペス	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
爪感染	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
敗血症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
慢性腎盂腎炎	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
迷路炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
扁桃炎	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
癜風	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
アデノウイルス結膜炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
ウイルス性気管支炎	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
カンピロバクター感染	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
回虫症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
気管気管支炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
細菌性耳感染	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
細菌尿	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
歯周炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
処置後感染	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
切開部位感染	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
大腸菌性尿路感染	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
尿路性敗血症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
麦粒腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
皮下組織膿瘍	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腹壁膿瘍	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
慢性副鼻腔炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
無症候性細菌尿	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
膣感染	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
Ｂ型肝炎	0				0				0				1	(0.1)	1	0.1
Ｃ型肝炎	0				0				1	(0.1)	1	0.1	0			
インフルエンザ性肺炎	1	(0.1)	1	0.1	0				0				0			
ウイルス性胃炎	0				1	(0.1)	1	0.1	0				0			
ウイルス性鼻炎	0				0				1	(0.1)	1	0.1	0			
ウイルス性扁桃炎	0				0				1	(0.1)	1	0.1	0			
カテーテル留置部位膿瘍	1	(0.1)	1	0.1	0				0				0			
カンジダ尿	1	(0.1)	1	0.1	0				0				0			
クレブシエラ膀胱炎	0				0				0				1	(0.1)	1	0.1
トコジラミ寄生	0				0				1	(0.1)	1	0.1	0			
ブドウ球菌感染	1	(0.1)	1	0.1	0				0				0			
ブドウ球菌性菌血症	0				0				0				1	(0.1)	1	0.1
ブドウ球菌性尿路感染	0				0				0				1	(0.1)	1	0.1
ブドウ球菌皮膚感染	0				0				0				1	(0.1)	1	0.1
ヘルペス性皮膚炎	0				1	(0.1)	1	0.1	0				0			
ライノウイルス感染	0				0				0				1	(0.1)	1	0.1
医療機器関連感染	0				0				0				1	(0.1)	1	0.1
陰嚢膿瘍	1	(0.1)	1	0.1	0				0				0			
陰部ヘルペス	1	(0.1)	1	0.1	0				0				0			
外陰部膣炎	0				1	(0.1)	1	0.1	0				0			
感染性嚢腫	0				0				1	(0.1)	1	0.1	0			
感染性皮膚嚢腫	0				0				0				1	(0.1)	1	0.1
寄生虫性胃腸炎	0				1	(0.1)	1	0.1	0				0			
急性扁桃炎	0				0				0				1	(0.1)	1	0.1
菌血症	0				0				0				1	(0.1)	1	0.1
結核	0				0				0				1	(0.1)	1	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腹壁膿瘍	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
慢性副鼻腔炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
無症候性細菌尿	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
膣感染	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
Ｂ型肝炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
Ｃ型肝炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
インフルエンザ性肺炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ウイルス性胃炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ウイルス性鼻炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ウイルス性扁桃炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
カテーテル留置部位膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
カンジダ尿	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
クレブシエラ膀胱炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
トコジラミ寄生	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ブドウ球菌感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ブドウ球菌性菌血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ブドウ球菌性尿路感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ブドウ球菌皮膚感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ヘルペス性皮膚炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ライノウイルス感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
医療機器関連感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
陰嚢膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
陰部ヘルペス	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
外陰部膣炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
感染性嚢腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感染性皮膚嚢腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
寄生虫性胃腸炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
急性扁桃炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
菌血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結核	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
股部白癬	0				0				0				1	(0.1)	1	0.1
口腔感染	0				0				1	(0.1)	1	0.1	0			
口腔真菌感染	0				0				0				1	(0.1)	1	0.1
細菌性下痢	0				1	(0.1)	1	0.1	0				0			
細菌性眼感染	0				0				0				1	(0.1)	1	0.1
細菌性気道感染	0				0				0				1	(0.1)	1	0.1
細菌性結膜炎	0				0				0				1	(0.1)	1	0.1
細菌性上気道感染	0				1	(0.1)	1	0.1	0				0			
細菌性中耳炎	0				1	(0.1)	1	0.1	0				0			
細菌性爪床感染	0				0				1	(0.1)	1	0.1	0			
細菌性肺炎	0				0				0				1	(0.1)	1	0.1
細菌性副鼻腔炎	0				0				1	(0.1)	1	0.1	0			
四肢膿瘍	0				1	(0.1)	1	0.1	0				0			
脂腺感染	0				0				0				1	(0.1)	1	0.1
歯冠周囲炎	0				0				0				1	(0.1)	1	0.1
耳下腺炎	0				0				0				1	(0.1)	1	0.1
手白癬	1	(0.1)	1	0.1	0				0				0			
術後創感染	0				0				0				1	(0.1)	1	0.1
処置後蜂巣炎	0				1	(0.1)	1	0.1	0				0			
小腸内細菌過剰増殖	0				0				0				1	(0.1)	1	0.1
真菌性口腔咽頭炎	0				0				0				1	(0.1)	1	0.1
真菌性性器感染	0				1	(0.1)	1	0.1	0				0			
腎感染	1	(0.1)	1	0.1	0				0				0			
腎盂腎炎	1	(0.1)	1	0.1	0				0				0			
水痘	0				1	(0.1)	1	0.1	0				0			
性器カンジダ症	0				0				0				1	(0.1)	1	0.1
性器感染	0				0				1	(0.1)	1	0.1	0			
精巣炎	0				0				0				1	(0.1)	1	0.1
前庭神経炎	1	(0.1)	1	0.1	0				0				0			
腸球菌感染	0				0				1	(0.1)	1	0.1	0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
股部白癬	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口腔感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
口腔真菌感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性下痢	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
細菌性眼感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性気道感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性結膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性上気道感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
細菌性中耳炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
細菌性爪床感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性肺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
細菌性副鼻腔炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
四肢膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脂腺感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
歯冠周囲炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
耳下腺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
手白癬	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
術後創感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
処置後蜂巣炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
小腸内細菌過剰増殖	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
真菌性口腔咽頭炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
真菌性性器感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎盂腎炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
水痘	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
性器カンジダ症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
性器感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精巣炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
前庭神経炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腸球菌感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腸球菌性尿路感染	0				1	(0.1)	1	0.1	0				0			
頭部白癬	0				0				0				1	(0.1)	1	0.1
軟骨膜炎	0				0				1	(0.1)	1	0.1	0			
軟部組織感染	0				1	(0.1)	1	0.1	0				0			
尿道炎	0				1	(0.1)	1	0.1	0				0			
熱帯性潰瘍	0				0				1	(0.1)	1	0.1	0			
膿痂疹	0				0				1	(0.1)	1	0.1	0			
百日咳	0				0				1	(0.1)	1	0.1	0			
腹部膿瘍	0				0				1	(0.1)	1	0.1	0			
埋込み部位感染	0				0				1	(0.1)	1	0.1	0			
咬傷感染	1	(0.1)	1	0.1	0				0				0			
肛門膿瘍	1	(0.1)	1	0.1	0				0				0			
鼠径部膿瘍	0				0				1	(0.1)	1	0.1	0			
臨床検査	150	(18.2)	242	16.3	149	(18.2)	248	17.2	137	(16.7)	213	14.1	144	(17.5)	226	14.8
リパーゼ増加	65	(7.9)	72	4.8	64	(7.8)	78	5.4	44	(5.4)	49	3.2	49	(5.9)	59	3.9
アミラーゼ増加	20	(2.4)	21	1.4	38	(4.6)	41	2.8	20	(2.4)	23	1.5	18	(2.2)	22	1.4
血中クレアチニン増加	16	(1.9)	18	1.2	10	(1.2)	11	0.8	12	(1.5)	12	0.8	15	(1.8)	16	1.0
膵酵素増加	8	(1.0)	8	0.5	6	(0.7)	7	0.5	6	(0.7)	6	0.4	5	(0.6)	5	0.3
血中カリウム増加	4	(0.5)	4	0.3	7	(0.9)	7	0.5	4	(0.5)	4	0.3	8	(1.0)	10	0.7
ヘモグロビン減少	4	(0.5)	5	0.3	4	(0.5)	4	0.3	5	(0.6)	5	0.3	7	(0.8)	7	0.5
アスパラギン酸アミノトランスフェラーゼ増加	8	(1.0)	9	0.6	1	(0.1)	1	0.1	4	(0.5)	4	0.3	5	(0.6)	5	0.3
アラニンアミノトランスフェラーゼ増加	7	(0.9)	9	0.6	3	(0.4)	4	0.3	4	(0.5)	4	0.3	4	(0.5)	4	0.3
血中トリグリセリド増加	4	(0.5)	4	0.3	7	(0.9)	7	0.5	3	(0.4)	3	0.2	2	(0.2)	2	0.1
体重減少	3	(0.4)	3	0.2	7	(0.9)	7	0.5	4	(0.5)	4	0.3	2	(0.2)	2	0.1
血圧上昇	4	(0.5)	4	0.3	3	(0.4)	4	0.3	5	(0.6)	8	0.5	3	(0.4)	4	0.3
血中カルシトニン増加	3	(0.4)	3	0.2	4	(0.5)	4	0.3	6	(0.7)	6	0.4	2	(0.2)	2	0.1
血中カルシウム増加	4	(0.5)	4	0.3	2	(0.2)	3	0.2	5	(0.6)	7	0.5	3	(0.4)	3	0.2

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腸球菌性尿路感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頭部白癬	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
軟骨膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
軟部組織感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿道炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
熱帯性潰瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膿痂疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
百日咳	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腹部膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
埋込み部位感染	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
咬傷感染	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肛門膿瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼠径部膿瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
臨床検査	299	(18.2)	490	16.7	281	(17.1)	439	14.5	580	(17.7)	929	15.6
リパーゼ増加	129	(7.9)	150	5.1	93	(5.7)	108	3.6	222	(6.8)	258	4.3
アミラーゼ増加	58	(3.5)	62	2.1	38	(2.3)	45	1.5	96	(2.9)	107	1.8
血中クレアチニン増加	26	(1.6)	29	1.0	27	(1.6)	28	0.9	53	(1.6)	57	1.0
膵酵素増加	14	(0.9)	15	0.5	11	(0.7)	11	0.4	25	(0.8)	26	0.4
血中カリウム増加	11	(0.7)	11	0.4	12	(0.7)	14	0.5	23	(0.7)	25	0.4
ヘモグロビン減少	8	(0.5)	9	0.3	12	(0.7)	12	0.4	20	(0.6)	21	0.4
アスパラギン酸アミノトランスフェラーゼ増加	9	(0.5)	10	0.3	9	(0.5)	9	0.3	18	(0.5)	19	0.3
アラニンアミノトランスフェラーゼ増加	10	(0.6)	13	0.4	8	(0.5)	8	0.3	18	(0.5)	21	0.4
血中トリグリセリド増加	11	(0.7)	11	0.4	5	(0.3)	5	0.2	16	(0.5)	16	0.3
体重減少	10	(0.6)	10	0.3	6	(0.4)	6	0.2	16	(0.5)	16	0.3
血圧上昇	7	(0.4)	8	0.3	8	(0.5)	12	0.4	15	(0.5)	20	0.3
血中カルシトニン増加	7	(0.4)	7	0.2	8	(0.5)	8	0.3	15	(0.5)	15	0.3
血中カルシウム増加	6	(0.4)	7	0.2	8	(0.5)	10	0.3	14	(0.4)	17	0.3

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
体重増加	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	3	0.2	5	(0.6)	5	0.3
血中尿素増加	4	(0.5)	5	0.3	5	(0.6)	5	0.3	1	(0.1)	2	0.1	1	(0.1)	1	0.1
血中ブドウ糖増加	4	(0.5)	4	0.3	1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1
尿中アルブミン／クレアチニン比増加	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
遊離脂肪酸増加	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	4	(0.5)	4	0.3
ビタミンＤ減少	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
ヘマトクリット減少	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
血中カリウム減少	1	(0.1)	1	0.1	1	(0.1)	1	0.1	3	(0.4)	4	0.3	2	(0.2)	2	0.1
白血球数増加	0				4	(0.5)	4	0.3	3	(0.4)	3	0.2	0			
肝酵素上昇	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				4	(0.5)	4	0.3
血中アルカリホスファターゼ増加	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
心電図Ｔ波逆転	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				3	(0.4)	3	0.2
心拍数増加	2	(0.2)	2	0.1	0				4	(0.5)	4	0.3	0			
血小板数減少	1	(0.1)	1	0.1	0				0				4	(0.5)	4	0.3
血中コレステロール増加	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
血中ビリルビン増加	4	(0.5)	4	0.3	0				0				1	(0.1)	1	0.1
尿中ブドウ糖陽性	0				0				1	(0.1)	1	0.1	4	(0.5)	4	0.3
トロポニン増加	1	(0.1)	1	0.1	0				0				3	(0.4)	3	0.2
好中球数増加	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1	0			
心雑音	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
赤血球数減少	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
赤血球分布幅増加	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
前立腺特異性抗原増加	2	(0.2)	2	0.1	0				0				2	(0.2)	2	0.1
低比重リポ蛋白増加	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
つぎ足歩行検査異常	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
グリコヘモグロビン増加	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
ヘマトクリット増加	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
ヘモグロビン増加	3	(0.4)	3	0.2	0				0				0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
体重増加	5	(0.3)	5	0.2	7	(0.4)	8	0.3	12	(0.4)	13	0.2
血中尿素増加	9	(0.5)	10	0.3	2	(0.1)	3	0.1	11	(0.3)	13	0.2
血中ブドウ糖増加	5	(0.3)	5	0.2	5	(0.3)	5	0.2	10	(0.3)	10	0.2
尿中アルブミン／クレアチニン比増加	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2
遊離脂肪酸増加	2	(0.1)	2	0.1	6	(0.4)	6	0.2	8	(0.2)	8	0.1
ビタミンＤ減少	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
ヘマトクリット減少	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
血中カリウム減少	2	(0.1)	2	0.1	5	(0.3)	6	0.2	7	(0.2)	8	0.1
白血球数増加	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
肝酵素上昇	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
血中アルカリホスファターゼ増加	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
心電図Ｔ波逆転	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
心拍数増加	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
血小板数減少	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
血中コレステロール増加	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
血中ビリルビン増加	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
尿中ブドウ糖陽性	0				5	(0.3)	5	0.2	5	(0.2)	5	0.1
トロポニン増加	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
好中球数増加	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
心雑音	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
赤血球数減少	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
赤血球分布幅増加	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
前立腺特異性抗原増加	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
低比重リポ蛋白増加	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
つぎ足歩行検査異常	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
グリコヘモグロビン増加	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
ヘマトクリット増加	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
ヘモグロビン増加	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
リパーゼ異常	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
駆出率減少	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
血圧低下	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
血中インスリン増加	0				0				0				3	(0.4)	3	0.2
血中マグネシウム減少	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
血中尿酸増加	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
心電図異常ＱＲＳ群	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
心電図変化	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
体温上昇	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
単球数増加	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
尿検査異常	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
尿中アルブミン陽性	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
尿中ヘモグロビン陽性	0				1	(0.1)	1	0.1	2	(0.2)	3	0.2	0			
ＱＲＳ軸異常	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
トランスアミナーゼ上昇	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
血液学的検査異常	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
血小板数増加	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
血中クレアチン増加	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
血中テストステロン減少	2	(0.2)	2	0.1	0				0				0			
血中ナトリウム増加	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
血中ブドウ糖減少	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
血中プロインスリン増加	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
血中鉄減少	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
高比重リポ蛋白減少	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
糸球体濾過率減少	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
心カテーテル検査	0				2	(0.2)	2	0.1	0				0			
心筋虚血の心電図所見	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
心電図ＱＴ延長	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
心電図異常	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
心電図異常Ｔ波	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
リパーゼ異常	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
駆出率減少	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
血圧低下	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
血中インスリン増加	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
血中マグネシウム減少	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
血中尿酸増加	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
心電図異常ＱＲＳ群	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
心電図変化	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
体温上昇	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
単球数増加	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
尿検査異常	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
尿中アルブミン陽性	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
尿中ヘモグロビン陽性	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
ＱＲＳ軸異常	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
トランスアミナーゼ上昇	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
血液学的検査異常	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血小板数増加	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血中クレアチン増加	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
血中テストステロン減少	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
血中ナトリウム増加	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
血中ブドウ糖減少	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
血中プロインスリン増加	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血中鉄減少	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
高比重リポ蛋白減少	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
糸球体濾過率減少	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心カテーテル検査	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
心筋虚血の心電図所見	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心電図ＱＴ延長	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
心電図異常	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
心電図異常Ｔ波	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
赤血球数増加	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
尿中アルブミン	0				2	(0.2)	2	0.1	0				0			
尿中ヘモグロビン	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
白血球数減少	0				2	(0.2)	2	0.1	0				0			
便潜血陽性	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
Ｂ型肝炎コア抗体陽性	0				0				1	(0.1)	1	0.1	0			
ヘマトクリット異常	0				0				1	(0.1)	1	0.1	0			
ヘモグロビン異常	0				0				1	(0.1)	1	0.1	0			
ヘリコバクター検査陽性	1	(0.1)	1	0.1	0				0				0			
γ－グルタミルトランスフェラーゼ増加	0				0				1	(0.1)	1	0.1	0			
冠血管造影	1	(0.1)	1	0.1	0				0				0			
肝機能検査異常	0				0				0				1	(0.1)	1	0.1
肝酵素異常	0				0				0				1	(0.1)	1	0.1
肝超音波検査異常	1	(0.1)	1	0.1	0				0				0			
眼圧上昇	1	(0.1)	1	0.1	0				0				0			
眼底検査異常	1	(0.1)	1	0.1	0				0				0			
駆出率	1	(0.1)	1	0.1	0				0				0			
頚動脈雑音	0				0				0				1	(0.1)	1	0.1
結腸内視鏡検査	0				0				1	(0.1)	1	0.1	0			
血圧異常	0				0				1	(0.1)	1	0.1	0			
血液スミア試験異常	0				1	(0.1)	1	0.1	0				0			
血液検査異常	0				0				1	(0.1)	2	0.1	0			
血球数異常	0				0				0				1	(0.1)	1	0.1
血中アルカリホスファターゼ	0				0				1	(0.1)	1	0.1	0			
血中アルカリホスファターゼ異常	1	(0.1)	1	0.1	0				0				0			
血中エストロゲン増加	1	(0.1)	1	0.1	0				0				0			
血中カルシウム減少	0				1	(0.1)	1	0.1	0				0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
赤血球数増加	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
尿中アルブミン	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
尿中ヘモグロビン	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
白血球数減少	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
便潜血陽性	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
Ｂ型肝炎コア抗体陽性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ヘマトクリット異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ヘモグロビン異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ヘリコバクター検査陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
γ－グルタミルトランスフェラーゼ増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
冠血管造影	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝機能検査異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝酵素異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝超音波検査異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼圧上昇	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼底検査異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
駆出率	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頚動脈雑音	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結腸内視鏡検査	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血圧異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血液スミア試験異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血液検査異常	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
血球数異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中アルカリホスファターゼ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中アルカリホスファターゼ異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中エストロゲン増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中カルシウム減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
血中テストステロン増加	0				0				0				1	(0.1)	1	0.1
血中トリグリセリド異常	1	(0.1)	1	0.1	0				0				0			
血中ビリルビン異常	1	(0.1)	1	0.1	0				0				0			
血中ブドウ糖変動	0				0				0				1	(0.1)	1	0.1
血中甲状腺刺激ホルモン増加	1	(0.1)	1	0.1	0				0				0			
血中葉酸減少	0				0				0				1	(0.1)	1	0.1
呼吸数増加	1	(0.1)	1	0.1	0				0				0			
好中球数異常	0				0				1	(0.1)	1	0.1	0			
好中球数減少	0				1	(0.1)	1	0.1	0				0			
骨密度減少	1	(0.1)	1	0.1	0				0				0			
脂質異常	1	(0.1)	1	0.1	0				0				0			
心電図ＱＲＳ群延長	0				1	(0.1)	1	0.1	0				0			
心電図Ｑ波	0				0				0				1	(0.1)	1	0.1
心電図ＳＴ部分異常	0				0				0				1	(0.1)	1	0.1
心電図ＳＴ部分上昇	0				1	(0.1)	1	0.1	0				0			
心電図Ｔ波	0				0				1	(0.1)	1	0.1	0			
心電図Ｔ波振幅減少	0				0				0				1	(0.1)	1	0.1
心電図異常Ｑ波	0				1	(0.1)	1	0.1	0				0			
心拍数異常	1	(0.1)	1	0.1	0				0				0			
心拍数不整	0				1	(0.1)	1	0.1	0				0			
心房圧上昇	0				0				0				1	(0.1)	1	0.1
低比重リポ蛋白異常	0				0				1	(0.1)	1	0.1	0			
糖鎖抗原１２５増加	0				1	(0.1)	1	0.1	0				0			
糖鎖抗原１９－９増加	1	(0.1)	1	0.1	0				0				0			
尿蛋白	0				0				1	(0.1)	1	0.1	0			
尿中アルブミン／クレアチニン比異常	0				1	(0.1)	1	0.1	0				0			
尿中クレアチニン増加	1	(0.1)	1	0.1	0				0				0			
尿中亜硝酸塩陽性	0				1	(0.1)	1	0.1	0				0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
血中テストステロン増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中トリグリセリド異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中ビリルビン異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中ブドウ糖変動	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血中甲状腺刺激ホルモン増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血中葉酸減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼吸数増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
好中球数異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
好中球数減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨密度減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脂質異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心電図ＱＲＳ群延長	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心電図Ｑ波	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図ＳＴ部分異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図ＳＴ部分上昇	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心電図Ｔ波	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図Ｔ波振幅減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心電図異常Ｑ波	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心拍数異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心拍数不整	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心房圧上昇	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
低比重リポ蛋白異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
糖鎖抗原１２５増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖鎖抗原１９－９増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿蛋白	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿中アルブミン／クレアチニン比異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中クレアチニン増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中亜硝酸塩陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
尿中血	0				1	(0.1)	1	0.1	0				0			
尿中血陽性	1	(0.1)	1	0.1	0				0				0			
尿中白血球陽性	1	(0.1)	1	0.1	0				0				0			
肺活量測定異常	0				0				0				1	(0.1)	1	0.1
平均血小板容積増加	0				1	(0.1)	1	0.1	0				0			
平均赤血球ヘモグロビン減少	0				0				1	(0.1)	1	0.1	0			
平均赤血球容積減少	0				0				1	(0.1)	1	0.1	0			
平均赤血球容積増加	0				0				0				1	(0.1)	1	0.1
便潜血	0				0				0				1	(0.1)	1	0.1
遊離サイロキシン減少	1	(0.1)	1	0.1	0				0				0			
筋骨格系および結合組織障害	148	(18.0)	198	13.3	127	(15.5)	164	11.4	165	(20.1)	232	15.4	143	(17.3)	221	14.5
背部痛	33	(4.0)	33	2.2	27	(3.3)	31	2.1	28	(3.4)	30	2.0	21	(2.5)	22	1.4
関節痛	26	(3.2)	27	1.8	19	(2.3)	19	1.3	30	(3.7)	36	2.4	31	(3.8)	36	2.4
四肢痛	24	(2.9)	27	1.8	12	(1.5)	13	0.9	25	(3.1)	26	1.7	22	(2.7)	23	1.5
筋骨格痛	11	(1.3)	11	0.7	16	(2.0)	16	1.1	11	(1.3)	12	0.8	14	(1.7)	18	1.2
変形性関節症	18	(2.2)	18	1.2	8	(1.0)	10	0.7	10	(1.2)	12	0.8	16	(1.9)	19	1.2
筋痙縮	13	(1.6)	16	1.1	7	(0.9)	7	0.5	12	(1.5)	13	0.9	7	(0.8)	14	0.9
筋肉痛	4	(0.5)	4	0.3	6	(0.7)	6	0.4	12	(1.5)	14	0.9	12	(1.5)	13	0.9
筋骨格系胸痛	5	(0.6)	5	0.3	3	(0.4)	3	0.2	11	(1.3)	12	0.8	5	(0.6)	5	0.3
頚部痛	3	(0.4)	3	0.2	6	(0.7)	6	0.4	6	(0.7)	6	0.4	6	(0.7)	6	0.4
関節腫脹	2	(0.2)	2	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3	5	(0.6)	5	0.3
変形性脊椎症	1	(0.1)	1	0.1	2	(0.2)	2	0.1	8	(1.0)	8	0.5	2	(0.2)	2	0.1
骨減少症	1	(0.1)	1	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3	3	(0.4)	3	0.2
弾発指	2	(0.2)	2	0.1	4	(0.5)	5	0.3	3	(0.4)	4	0.3	2	(0.2)	2	0.1
関節炎	2	(0.2)	2	0.1	0				3	(0.4)	3	0.2	4	(0.5)	4	0.3
外骨腫	2	(0.2)	2	0.1	0				0				6	(0.7)	6	0.4
骨粗鬆症	0				4	(0.5)	4	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1
側腹部痛	6	(0.7)	6	0.4	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
尿中血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中血陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿中白血球陽性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺活量測定異常	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
平均血小板容積増加	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
平均赤血球ヘモグロビン減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
平均赤血球容積減少	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
平均赤血球容積増加	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
便潜血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
遊離サイロキシン減少	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
筋骨格系および結合組織障害	275	(16.7)	362	12.3	308	(18.7)	453	14.9	583	(17.7)	815	13.7
背部痛	60	(3.7)	64	2.2	49	(3.0)	52	1.7	109	(3.3)	116	1.9
関節痛	45	(2.7)	46	1.6	61	(3.7)	72	2.4	106	(3.2)	118	2.0
四肢痛	36	(2.2)	40	1.4	47	(2.9)	49	1.6	83	(2.5)	89	1.5
筋骨格痛	27	(1.6)	27	0.9	25	(1.5)	30	1.0	52	(1.6)	57	1.0
変形性関節症	26	(1.6)	28	1.0	26	(1.6)	31	1.0	52	(1.6)	59	1.0
筋痙縮	20	(1.2)	23	0.8	19	(1.2)	27	0.9	39	(1.2)	50	0.8
筋肉痛	10	(0.6)	10	0.3	24	(1.5)	27	0.9	34	(1.0)	37	0.6
筋骨格系胸痛	8	(0.5)	8	0.3	16	(1.0)	17	0.6	24	(0.7)	25	0.4
頚部痛	9	(0.5)	9	0.3	12	(0.7)	12	0.4	21	(0.6)	21	0.4
関節腫脹	5	(0.3)	5	0.2	9	(0.5)	9	0.3	14	(0.4)	14	0.2
変形性脊椎症	3	(0.2)	3	0.1	10	(0.6)	10	0.3	13	(0.4)	13	0.2
骨減少症	5	(0.3)	5	0.2	7	(0.4)	7	0.2	12	(0.4)	12	0.2
弾発指	6	(0.4)	7	0.2	5	(0.3)	6	0.2	11	(0.3)	13	0.2
関節炎	2	(0.1)	2	0.1	7	(0.4)	7	0.2	9	(0.3)	9	0.2
外骨腫	2	(0.1)	2	0.1	6	(0.4)	6	0.2	8	(0.2)	8	0.1
骨粗鬆症	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
側腹部痛	7	(0.4)	7	0.2	1	(0.1)	1	<0.1	8	(0.2)	8	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肩回旋筋腱板症候群	1	(0.1)	1	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1
足変形	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	2	(0.2)	2	0.1
腱炎	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
滑液包炎	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
筋骨格硬直	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
筋力低下	0				1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1
椎間板突出	3	(0.4)	3	0.2	0				3	(0.4)	4	0.3	0			
顎関節症候群	3	(0.4)	3	0.2	0				2	(0.2)	2	0.1	0			
滑液嚢腫	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
関節障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
筋炎	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
足底筋膜炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
関節可動域低下	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
関節周囲炎	0				0				0				4	(0.5)	4	0.3
四肢不快感	0				0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
側弯症	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
椎間板変性症	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
顎痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
痛風性関節炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
関節リウマチ	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
関節摩擦音	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
関節滲出液	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
筋萎縮	0				0				0				2	(0.2)	2	0.1
筋拘縮	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
筋骨格不快感	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
筋攣縮	0				0				2	(0.2)	2	0.1	0			
骨端症	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
骨痛	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
骨嚢腫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
脊柱管狭窄症	0				0				0				2	(0.2)	2	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肩回旋筋腱板症候群	2	(0.1)	2	0.1	5	(0.3)	5	0.2	7	(0.2)	7	0.1
足変形	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
腱炎	3	(0.2)	3	0.1	4	(0.2)	4	0.1	7	(0.2)	7	0.1
滑液包炎	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
筋骨格硬直	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
筋力低下	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
椎間板突出	3	(0.2)	3	0.1	3	(0.2)	4	0.1	6	(0.2)	7	0.1
顎関節症候群	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
滑液嚢腫	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
関節障害	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
筋炎	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
足底筋膜炎	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
関節可動域低下	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
関節周囲炎	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
四肢不快感	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
側弯症	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
椎間板変性症	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
顎痛	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
痛風性関節炎	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
関節リウマチ	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
関節摩擦音	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
関節滲出液	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
筋萎縮	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
筋拘縮	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
筋骨格不快感	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
筋攣縮	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
骨端症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
骨痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
骨嚢腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
脊柱管狭窄症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
尾骨痛	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
肋軟骨炎	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
シェーグレン症候群	0				1	(0.1)	1	0.1	0				0			
ピロリン酸カルシウム結晶性軟骨石灰化症	0				0				1	(0.1)	1	0.1	0			
ミオキミア	0				0				1	(0.1)	1	0.1	0			
顎骨嚢胞	0				1	(0.1)	1	0.1	0				0			
乾癬性関節症	0				1	(0.1)	1	0.1	0				0			
筋骨格障害	0				1	(0.1)	1	0.1	0				0			
筋肉疲労	0				0				1	(0.1)	1	0.1	0			
筋膜疼痛症候群	0				1	(0.1)	1	0.1	0				0			
腰部脊柱管狭窄症	0				0				1	(0.1)	1	0.1	0			
骨炎	0				0				1	(0.1)	1	0.1	0			
骨病変	0				1	(0.1)	1	0.1	0				0			
指変形	0				1	(0.1)	1	0.1	0				0			
斜頚	0				0				1	(0.1)	1	0.1	0			
出血性関節症	0				0				0				1	(0.1)	1	0.1
脊椎すべり症	0				0				0				1	(0.1)	1	0.1
脊椎炎	1	(0.1)	1	0.1	0				0				0			
脊椎骨棘	1	(0.1)	1	0.1	0				0				0			
脊椎痛	0				1	(0.1)	1	0.1	0				0			
仙腸骨炎	0				1	(0.1)	1	0.1	0				0			
線維筋痛	0				0				1	(0.1)	2	0.1	0			
足底腱膜線維腫症	0				0				0				1	(0.1)	1	0.1
多発性筋炎	1	(0.1)	1	0.1	0				0				0			
中足骨痛	1	(0.1)	1	0.1	0				0				0			
椎間関節症候群	0				0				1	(0.1)	1	0.1	0			
椎間板障害	0				0				0				1	(0.1)	1	0.1
椎間板線維輪断裂	1	(0.1)	1	0.1	0				0				0			
半月板変性	0				0				1	(0.1)	1	0.1	0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
尾骨痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肋軟骨炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
シェーグレン症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
ピロリン酸カルシウム結晶性軟骨石灰化症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ミオキミア	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
顎骨嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乾癬性関節症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
筋骨格障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
筋肉疲労	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋膜疼痛症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腰部脊柱管狭窄症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
骨炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
骨病変	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
指変形	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
斜頚	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
出血性関節症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脊椎すべり症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脊椎炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脊椎骨棘	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脊椎痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
仙腸骨炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
線維筋痛	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
足底腱膜線維腫症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
多発性筋炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
中足骨痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
椎間関節症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎間板障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
椎間板線維輪断裂	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
半月板変性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
膝蓋大腿関節痛症候群	0				0				0				1	(0.1)	1	0.1
膝関節変形	1	(0.1)	1	0.1	0				0				0			
腹直筋離開	0				1	(0.1)	1	0.1	0				0			
脛骨内側過労性症候群	1	(0.1)	1	0.1	0				0				0			
腱鞘炎	1	(0.1)	1	0.1	0				0				0			
腱付着部症	0				0				0				1	(0.1)	1	0.1
耳径部腫瘤	1	(0.1)	1	0.1	0				0				0			
神経系障害	130	(15.8)	181	12.2	122	(14.9)	166	11.5	136	(16.6)	214	14.2	133	(16.1)	201	13.2
頭痛	42	(5.1)	54	3.6	36	(4.4)	50	3.5	48	(5.9)	78	5.2	58	(7.0)	86	5.6
浮動性めまい	43	(5.2)	45	3.0	30	(3.7)	35	2.4	32	(3.9)	45	3.0	31	(3.8)	34	2.2
糖尿病性ニューロパチー	9	(1.1)	9	0.6	8	(1.0)	8	0.6	8	(1.0)	8	0.5	9	(1.1)	9	0.6
感覚鈍麻	8	(1.0)	10	0.7	7	(0.9)	7	0.5	7	(0.9)	7	0.5	4	(0.5)	4	0.3
錯感覚	8	(1.0)	8	0.5	4	(0.5)	4	0.3	3	(0.4)	3	0.2	6	(0.7)	6	0.4
坐骨神経痛	2	(0.2)	2	0.1	1	(0.1)	1	0.1	7	(0.9)	7	0.5	3	(0.4)	3	0.2
味覚異常	1	(0.1)	1	0.1	7	(0.9)	7	0.5	3	(0.4)	3	0.2	2	(0.2)	2	0.1
傾眠	3	(0.4)	3	0.2	4	(0.5)	5	0.3	2	(0.2)	3	0.2	3	(0.4)	4	0.3
手根管症候群	3	(0.4)	4	0.3	2	(0.2)	2	0.1	4	(0.5)	5	0.3	3	(0.4)	3	0.2
末梢性ニューロパチー	4	(0.5)	4	0.3	3	(0.4)	4	0.3	3	(0.4)	3	0.2	2	(0.2)	2	0.1
振戦	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	5	(0.6)	5	0.3
嗜眠	1	(0.1)	1	0.1	5	(0.6)	5	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1
失神	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
記憶障害	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
健忘	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
神経根障害	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
下肢静止不能症候群	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
頚動脈狭窄	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
失神寸前の状態	1	(0.1)	1	0.1	2	(0.2)	3	0.2	0				2	(0.2)	2	0.1
第７脳神経麻痺	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
一過性脳虚血発作	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
膝蓋大腿関節痛症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膝関節変形	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腹直筋離開	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脛骨内側過労性症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腱鞘炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腱付着部症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鼡径部腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経系障害	252	(15.3)	347	11.8	269	(16.4)	415	13.7	521	(15.9)	762	12.8
頭痛	78	(4.8)	104	3.5	106	(6.4)	164	5.4	184	(5.6)	268	4.5
浮動性めまい	73	(4.4)	80	2.7	63	(3.8)	79	2.6	136	(4.1)	159	2.7
糖尿病性ニューロパチー	17	(1.0)	17	0.6	17	(1.0)	17	0.6	34	(1.0)	34	0.6
感覚鈍麻	15	(0.9)	17	0.6	11	(0.7)	11	0.4	26	(0.8)	28	0.5
錯感覚	12	(0.7)	12	0.4	9	(0.5)	9	0.3	21	(0.6)	21	0.4
坐骨神経痛	3	(0.2)	3	0.1	10	(0.6)	10	0.3	13	(0.4)	13	0.2
味覚異常	8	(0.5)	8	0.3	5	(0.3)	5	0.2	13	(0.4)	13	0.2
傾眠	7	(0.4)	8	0.3	5	(0.3)	7	0.2	12	(0.4)	15	0.3
手根管症候群	5	(0.3)	6	0.2	7	(0.4)	8	0.3	12	(0.4)	14	0.2
末梢性ニューロパチー	7	(0.4)	8	0.3	5	(0.3)	5	0.2	12	(0.4)	13	0.2
振戦	4	(0.2)	4	0.1	7	(0.4)	7	0.2	11	(0.3)	11	0.2
嗜眠	6	(0.4)	6	0.2	2	(0.1)	2	0.1	8	(0.2)	8	0.1
失神	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
記憶障害	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
健忘	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
神経根障害	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
下肢静止不能症候群	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
頚動脈狭窄	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
失神寸前の状態	3	(0.2)	4	0.1	2	(0.1)	2	0.1	5	(0.2)	6	0.1
第７脳神経麻痺	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
一過性脳虚血発作	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
虚血性脳卒中	0				0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
灼熱感	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1	0			
振動覚低下	0				1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
慢性多発ニューロパチー	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1	0			
神経痛	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
脊髄症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
体位性めまい	0				1	(0.1)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
副鼻腔炎に伴う頭痛	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
平衡障害	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
片頭痛	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
アルツハイマー型認知症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
パーキンソン病	0				0				2	(0.2)	2	0.1	0			
感覚消失	0				2	(0.2)	2	0.1	0				0			
虚血性脳小血管疾患	0				0				2	(0.2)	2	0.1	0			
緊張性頭痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
頚動脈硬化症	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
腰髄神経根障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
神経圧迫	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
多発ニューロパチー	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
大脳萎縮	0				0				2	(0.2)	2	0.1	0			
椎骨脳底動脈不全	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
低血糖性意識消失	1	(0.1)	1	0.1	0				0				1	(0.1)	2	0.1
認知障害	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
脳室拡張	0				0				2	(0.2)	2	0.1	0			
味覚減退	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
老年認知症	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
くも膜嚢胞	0				0				0				1	(0.1)	1	0.1
ジスキネジア	0				0				0				1	(0.1)	1	0.1
ヘルペス後神経痛	0				0				1	(0.1)	1	0.1	0			
ラクナ梗塞	0				0				0				1	(0.1)	1	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
虚血性脳卒中	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
灼熱感	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
振動覚低下	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
慢性多発ニューロパチー	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
神経痛	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
脊髄症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
体位性めまい	1	(0.1)	2	0.1	2	(0.1)	2	0.1	3	(0.1)	4	0.1
副鼻腔炎に伴う頭痛	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
平衡障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
片頭痛	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
アルツハイマー型認知症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
パーキンソン病	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
感覚消失	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
虚血性脳小血管疾患	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
緊張性頭痛	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
頚動脈硬化症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腰髄神経根障害	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
神経圧迫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
多発ニューロパチー	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
大脳萎縮	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
椎骨脳底動脈不全	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
低血糖性意識消失	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
認知障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
脳室拡張	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
味覚減退	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
老年認知症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
くも膜嚢胞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ジスキネジア	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ヘルペス後神経痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ラクナ梗塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
意識消失	0				1	(0.1)	1	0.1	0				0			
意識変容状態	0				0				1	(0.1)	1	0.1	0			
異常感覚	0				0				0				1	(0.1)	1	0.1
運動失調	0				0				0				1	(0.1)	1	0.1
過眠症	0				0				1	(0.1)	1	0.1	0			
感覚障害	0				1	(0.1)	1	0.1	0				0			
蟻走感	0				0				0				1	(0.1)	1	0.1
協調運動異常	0				1	(0.1)	2	0.1	0				0			
頚髄神経根障害	0				1	(0.1)	1	0.1	0				0			
頚動脈疾患	0				0				0				1	(0.1)	1	0.1
頚動脈閉塞	0				0				0				1	(0.1)	1	0.1
腰仙部神経根炎	1	(0.1)	1	0.1	0				0				0			
坐骨神経ニューロパチー	0				0				1	(0.1)	1	0.1	0			
塞栓性脳卒中	0				0				0				1	(0.1)	1	0.1
視野欠損	0				0				1	(0.1)	1	0.1	0			
自律神経失調	0				0				1	(0.1)	1	0.1	0			
周期性四肢運動障害	1	(0.1)	1	0.1	0				0				0			
神経根圧迫	1	(0.1)	1	0.1	0				0				0			
睡眠時麻痺	0				0				0				1	(0.1)	1	0.1
脊髄髄膜嚢胞	0				0				1	(0.1)	1	0.1	0			
多発性硬化症	0				0				1	(0.1)	1	0.1	0			
代謝性脳症	0				0				1	(0.1)	1	0.1	0			
第４脳神経麻痺	0				0				1	(0.1)	1	0.1	0			
第６脳神経不全麻痺	1	(0.1)	1	0.1	0				0				0			
単ニューロパチー	0				0				0				1	(0.1)	1	0.1
認知症	0				0				0				1	(0.1)	1	0.1
脳虚血	0				0				1	(0.1)	1	0.1	0			
脳梗塞	0				0				1	(0.1)	1	0.1	0			
脳症	0				0				1	(0.1)	1	0.1	0			
反射減弱	0				0				0				1	(0.1)	1	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
意識消失	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
意識変容状態	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
異常感覚	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
運動失調	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
過眠症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
感覚障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
蟻走感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
協調運動異常	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
頚髄神経根障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
頚動脈疾患	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
頚動脈閉塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腰仙部神経根炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
坐骨神経ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
塞栓性脳卒中	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
視野欠損	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
自律神経失調	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
周期性四肢運動障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経根圧迫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
睡眠時麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脊髄髄膜嚢胞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
多発性硬化症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
代謝性脳症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
第４脳神経麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
第６脳神経不全麻痺	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
単ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
認知症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳虚血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳梗塞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
反射減弱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肘部管症候群	0				0				1	(0.1)	2	0.1	0			
不全片麻痺	0				0				1	(0.1)	1	0.1	0			
本態性振戦	0				1	(0.1)	1	0.1	0				0			
末梢性感覚ニューロパチー	0				0				0				1	(0.1)	1	0.1
末梢性感覚運動ニューロパチー	0				0				1	(0.1)	1	0.1	0			
末梢性麻痺	0				0				0				1	(0.1)	1	0.1
慢性炎症性脱髄性多発根ニューロパチー	1	(0.1)	1	0.1	0				0				0			
味覚消失	1	(0.1)	1	0.1	0				0				0			
肋間神経痛	0				1	(0.1)	1	0.1	0				0			
痙攣発作	0				1	(0.1)	1	0.1	0				0			
腓骨神経麻痺	0				0				0				1	(0.1)	1	0.1
代謝および栄養障害	152	(18.5)	196	13.2	130	(15.9)	169	11.7	134	(16.4)	181	12.0	109	(13.2)	148	9.7
食欲減退	62	(7.5)	67	4.5	58	(7.1)	71	4.9	15	(1.8)	17	1.1	5	(0.6)	5	0.3
脂質異常症	13	(1.6)	13	0.9	17	(2.1)	17	1.2	22	(2.7)	22	1.5	15	(1.8)	15	1.0
高カリウム血症	22	(2.7)	24	1.6	9	(1.1)	10	0.7	17	(2.1)	18	1.2	15	(1.8)	16	1.0
高トリグリセリド血症	12	(1.5)	13	0.9	5	(0.6)	5	0.3	7	(0.9)	9	0.6	16	(1.9)	17	1.1
高血糖	7	(0.9)	9	0.6	1	(0.1)	1	0.1	15	(1.8)	19	1.3	15	(1.8)	16	1.0
高カルシウム血症	11	(1.3)	12	0.8	8	(1.0)	8	0.6	6	(0.7)	6	0.4	9	(1.1)	11	0.7
低カリウム血症	6	(0.7)	6	0.4	9	(1.1)	10	0.7	13	(1.6)	13	0.9	5	(0.6)	7	0.5
コントロール不良の糖尿病	7	(0.9)	7	0.5	4	(0.5)	4	0.3	7	(0.9)	9	0.6	13	(1.6)	14	0.9
ビタミンＤ欠乏	8	(1.0)	8	0.5	7	(0.9)	7	0.5	8	(1.0)	8	0.5	7	(0.8)	7	0.5
糖尿病	3	(0.4)	3	0.2	5	(0.6)	5	0.3	11	(1.3)	11	0.7	8	(1.0)	9	0.6
痛風	8	(1.0)	9	0.6	5	(0.6)	5	0.3	4	(0.5)	6	0.4	6	(0.7)	6	0.4
食欲亢進	6	(0.7)	6	0.4	3	(0.4)	3	0.2	3	(0.4)	3	0.2	1	(0.1)	1	0.1
ビタミンＢ１２欠乏	2	(0.2)	2	0.1	5	(0.6)	5	0.3	3	(0.4)	3	0.2	2	(0.2)	2	0.1
高脂血症	2	(0.2)	2	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3	5	(0.6)	5	0.3
低ナトリウム血症	1	(0.1)	1	0.1	2	(0.2)	2	0.1	5	(0.6)	5	0.3	1	(0.1)	1	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肘部管症候群	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
不全片麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
本態性振戦	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
末梢性感覚ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢性感覚運動ニューロパチー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢性麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
慢性炎症性脱髄性多発根ニューロパチー	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
味覚消失	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肋間神経痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
痙攣発作	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腓骨神経麻痺	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
代謝および栄養障害	282	(17.2)	365	12.4	243	(14.8)	329	10.8	525	(16.0)	694	11.6
食欲減退	120	(7.3)	138	4.7	20	(1.2)	22	0.7	140	(4.3)	160	2.7
脂質異常症	30	(1.8)	30	1.0	37	(2.3)	37	1.2	67	(2.0)	67	1.1
高カリウム血症	31	(1.9)	34	1.2	32	(1.9)	34	1.1	63	(1.9)	68	1.1
高トリグリセリド血症	17	(1.0)	18	0.6	23	(1.4)	26	0.9	40	(1.2)	44	0.7
高血糖	8	(0.5)	10	0.3	30	(1.8)	35	1.2	38	(1.2)	45	0.8
高カルシウム血症	19	(1.2)	20	0.7	15	(0.9)	17	0.6	34	(1.0)	37	0.6
低カリウム血症	15	(0.9)	16	0.5	18	(1.1)	20	0.7	33	(1.0)	36	0.6
コントロール不良の糖尿病	11	(0.7)	11	0.4	20	(1.2)	23	0.8	31	(0.9)	34	0.6
ビタミンＤ欠乏	15	(0.9)	15	0.5	15	(0.9)	15	0.5	30	(0.9)	30	0.5
糖尿病	8	(0.5)	8	0.3	19	(1.2)	20	0.7	27	(0.8)	28	0.5
痛風	13	(0.8)	14	0.5	10	(0.6)	12	0.4	23	(0.7)	26	0.4
食欲亢進	9	(0.5)	9	0.3	4	(0.2)	4	0.1	13	(0.4)	13	0.2
ビタミンＢ１２欠乏	7	(0.4)	7	0.2	5	(0.3)	5	0.2	12	(0.4)	12	0.2
高脂血症	3	(0.2)	3	0.1	9	(0.5)	9	0.3	12	(0.4)	12	0.2
低ナトリウム血症	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
低マグネシウム血症	3	(0.4)	3	0.2	3	(0.4)	3	0.2	2	(0.2)	2	0.1	0			
高尿酸血症	2	(0.2)	3	0.2	1	(0.1)	1	0.1	4	(0.5)	4	0.3	0			
高コレステロール血症	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
脱水	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2
高アミラーゼ血症	2	(0.2)	3	0.2	0				2	(0.2)	2	0.1	0			
高ナトリウム血症	0				0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
低カルシウム血症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
低血糖症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
２型糖尿病	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
マグネシウム欠乏	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
高リパーゼ血症	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
水分過負荷	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
低リン酸血症	0				0				2	(0.2)	2	0.1	0			
電解質失調	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
肥満	0				2	(0.2)	2	0.1	0				0			
葉酸欠乏	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
アルコール不耐性	1	(0.1)	1	0.1	0				0				0			
カルシウム欠乏	0				0				1	(0.1)	1	0.1	0			
ビタミン欠乏症	0				0				0				1	(0.1)	1	0.1
ラクトース不耐性	0				1	(0.1)	1	0.1	0				0			
悪液質	0				1	(0.1)	1	0.1	0				0			
拒食	0				1	(0.1)	1	0.1	0				0			
血液量減少症	0				0				0				1	(0.1)	1	0.1
高カルシトニン血症	0				0				1	(0.1)	1	0.1	0			
高マグネシウム血症	0				1	(0.1)	1	0.1	0				0			
高リン酸塩血症	0				1	(0.1)	1	0.1	0				0			
体液貯留	0				0				0				1	(0.1)	1	0.1
代謝障害	0				0				1	(0.1)	1	0.1	0			
低アルブミン血症	0				0				0				1	(0.1)	1	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
低マグネシウム血症	6	(0.4)	6	0.2	2	(0.1)	2	0.1	8	(0.2)	8	0.1
高尿酸血症	3	(0.2)	4	0.1	4	(0.2)	4	0.1	7	(0.2)	8	0.1
高コレステロール血症	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
脱水	1	(0.1)	1	<0.1	4	(0.2)	4	0.1	5	(0.2)	5	0.1
高アミラーゼ血症	2	(0.1)	3	0.1	2	(0.1)	2	0.1	4	(0.1)	5	0.1
高ナトリウム血症	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
低カルシウム血症	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
低血糖症	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
２型糖尿病	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
マグネシウム欠乏	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
高リパーゼ血症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
水分過負荷	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
低リン酸血症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
電解質失調	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
肥満	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
葉酸欠乏	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
アルコール不耐性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
カルシウム欠乏	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ビタミン欠乏症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
ラクトース不耐性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
悪液質	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
拒食	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血液量減少症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高カルシトニン血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高マグネシウム血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高リン酸塩血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
体液貯留	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
代謝障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
低アルブミン血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
眼障害	110	(13.4)	139	9.3	112	(13.7)	155	10.7	94	(11.5)	123	8.2	101	(12.2)	136	8.9
白内障	36	(4.4)	38	2.6	34	(4.2)	37	2.6	24	(2.9)	25	1.7	31	(3.8)	32	2.1
糖尿病網膜症	21	(2.6)	22	1.5	33	(4.0)	39	2.7	22	(2.7)	22	1.5	29	(3.5)	32	2.1
網膜症	5	(0.6)	5	0.3	7	(0.9)	7	0.5	5	(0.6)	5	0.3	6	(0.7)	6	0.4
霧視	7	(0.9)	7	0.5	6	(0.7)	6	0.4	3	(0.4)	3	0.2	3	(0.4)	3	0.2
高血圧性網膜症	2	(0.2)	2	0.1	4	(0.5)	4	0.3	3	(0.4)	3	0.2	8	(1.0)	8	0.5
緑内障	5	(0.6)	5	0.3	4	(0.5)	4	0.3	3	(0.4)	3	0.2	5	(0.6)	5	0.3
黄斑浮腫	2	(0.2)	2	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3	2	(0.2)	2	0.1
眼乾燥	5	(0.6)	5	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
眼出血	2	(0.2)	2	0.1	1	(0.1)	1	0.1	4	(0.5)	5	0.3	3	(0.4)	4	0.3
老視	3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3
遠視	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	3	(0.4)	3	0.2
眼痛	2	(0.2)	2	0.1	4	(0.5)	4	0.3	1	(0.1)	1	0.1	0			
網膜出血	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3
乱視	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
黄斑変性	0				0				5	(0.6)	5	0.3	0			
結膜出血	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
視力障害	2	(0.2)	2	0.1	0				3	(0.4)	3	0.2	0			
視力低下	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
硝子体出血	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
黄斑症	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	0			
黄斑線維症	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	0			
核性白内障	2	(0.2)	3	0.2	0				2	(0.2)	2	0.1	0			
眼瞼下垂	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
近視	0				1	(0.1)	1	0.1	0				3	(0.4)	3	0.2
網膜血管瘤	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
網膜変性	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
加齢黄斑変性	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
眼そう痒症	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
眼刺激	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
眼障害	222	(13.5)	294	10.0	195	(11.9)	259	8.5	417	(12.7)	553	9.3
白内障	70	(4.3)	75	2.6	55	(3.3)	57	1.9	125	(3.8)	132	2.2
糖尿病網膜症	54	(3.3)	61	2.1	51	(3.1)	54	1.8	105	(3.2)	115	1.9
網膜症	12	(0.7)	12	0.4	11	(0.7)	11	0.4	23	(0.7)	23	0.4
霧視	13	(0.8)	13	0.4	6	(0.4)	6	0.2	19	(0.6)	19	0.3
高血圧性網膜症	6	(0.4)	6	0.2	11	(0.7)	11	0.4	17	(0.5)	17	0.3
緑内障	9	(0.5)	9	0.3	8	(0.5)	8	0.3	17	(0.5)	17	0.3
黄斑浮腫	5	(0.3)	5	0.2	6	(0.4)	6	0.2	11	(0.3)	11	0.2
眼乾燥	7	(0.4)	7	0.2	3	(0.2)	3	0.1	10	(0.3)	10	0.2
眼出血	3	(0.2)	3	0.1	7	(0.4)	9	0.3	10	(0.3)	12	0.2
老視	5	(0.3)	5	0.2	5	(0.3)	5	0.2	10	(0.3)	10	0.2
遠視	4	(0.2)	4	0.1	5	(0.3)	5	0.2	9	(0.3)	9	0.2
眼痛	6	(0.4)	6	0.2	1	(0.1)	1	<0.1	7	(0.2)	7	0.1
網膜出血	2	(0.1)	2	0.1	5	(0.3)	5	0.2	7	(0.2)	7	0.1
乱視	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
黄斑変性	0				5	(0.3)	5	0.2	5	(0.2)	5	0.1
結膜出血	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
視力障害	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
視力低下	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
硝子体出血	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
黄斑症	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
黄斑線維症	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
核性白内障	2	(0.1)	3	0.1	2	(0.1)	2	0.1	4	(0.1)	5	0.1
眼瞼下垂	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
近視	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
網膜血管瘤	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
網膜変性	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
加齢黄斑変性	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
眼そう痒症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
眼刺激	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
眼瞼炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
眼瞼浮腫	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
光視症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
硝子体剥離	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
皮質白内障	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
複視	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
網膜剥離	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
網脈絡膜症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
翼状片	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
流涙増加	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
開放隅角緑内障	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
眼の障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
屈折障害	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
硝子体浮遊物	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
新生血管加齢黄斑変性	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
糖尿病性網膜浮腫	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
虹彩炎	1	(0.1)	1	0.1	0				0				1	(0.1)	2	0.1
網膜障害	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
網膜静脈血栓症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
アレルギー性眼瞼炎	0				0				0				1	(0.1)	1	0.1
アレルギー性結膜炎	0				1	(0.1)	1	0.1	0				0			
マイボーム腺機能不全	0				1	(0.1)	1	0.1	0				0			
一過性黒内障	1	(0.1)	1	0.1	0				0				0			
黄斑円孔	0				0				1	(0.1)	1	0.1	0			
角膜リポイド環	0				0				0				1	(0.1)	1	0.1
角膜混濁	0				0				0				1	(0.1)	1	0.1
乾性加齢黄斑変性	0				1	(0.1)	1	0.1	0				0			
眼の変色	1	(0.1)	1	0.1	0				0				0			
眼球突出症	0				0				0				1	(0.1)	1	0.1
眼球浮腫	0				0				1	(0.1)	1	0.1	0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
眼瞼炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
眼瞼浮腫	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
光視症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
硝子体剥離	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
皮質白内障	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
複視	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
網膜剥離	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
網脈絡膜症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
翼状片	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
流涙増加	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
開放隅角緑内障	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
眼の障害	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
屈折障害	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
硝子体浮遊物	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
新生血管加齢黄斑変性	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
糖尿病性網膜浮腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
虹彩炎	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
網膜障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
網膜静脈血栓症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
アレルギー性眼瞼炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
アレルギー性結膜炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
マイボーム腺機能不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
一過性黒内障	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
黄斑円孔	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
角膜リポイド環	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
角膜混濁	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乾性加齢黄斑変性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼の変色	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼球突出症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼球浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
眼筋麻痺	1	(0.1)	1	0.1	0				0				0			
眼充血	0				1	(0.1)	1	0.1	0				0			
眼沈着物	0				1	(0.1)	1	0.1	0				0			
眼部不快感	0				0				0				1	(0.1)	1	0.1
眼瞼皮膚のたるみ	1	(0.1)	1	0.1	0				0				0			
眼瞼痙攣	0				1	(0.1)	1	0.1	0				0			
結膜刺激	0				0				0				1	(0.1)	1	0.1
結膜充血	1	(0.1)	1	0.1	0				0				0			
後天性涙道狭窄	1	(0.1)	1	0.1	0				0				0			
高眼圧症	0				0				1	(0.1)	1	0.1	0			
視神経乳頭浮腫	0				1	(0.1)	1	0.1	0				0			
斜視	0				0				1	(0.1)	1	0.1	0			
弱視	0				0				1	(0.1)	1	0.1	0			
硝子体混濁	1	(0.1)	1	0.1	0				0				0			
星状硝子体症	0				1	(0.1)	1	0.1	0				0			
前房出血	1	(0.1)	1	0.1	0				0				0			
増殖性網膜症	0				0				1	(0.1)	1	0.1	0			
調節障害	0				1	(0.1)	1	0.1	0				0			
糖尿病性白内障	0				1	(0.1)	1	0.1	0				0			
瞳孔障害	0				0				0				1	(0.1)	1	0.1
虹彩毛様体炎	0				0				1	(0.1)	1	0.1	0			
嚢下白内障	0				0				1	(0.1)	1	0.1	0			
嚢胞様黄斑浮腫	0				0				1	(0.1)	1	0.1	0			
閉塞隅角緑内障	0				1	(0.1)	2	0.1	0				0			
網膜血管障害	1	(0.1)	1	0.1	0				0				0			
網膜血管新生	0				1	(0.1)	1	0.1	0				0			
網膜色素上皮症	0				0				0				1	(0.1)	1	0.1
網膜裂孔	0				0				0				1	(0.1)	1	0.1
網膜滲出物	0				0				1	(0.1)	1	0.1	0			
網脈絡膜萎縮	0				0				0				1	(0.1)	1	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
眼筋麻痺	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼充血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼沈着物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼部不快感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼瞼皮膚のたるみ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼瞼痙攣	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
結膜刺激	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
結膜充血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
後天性涙道狭窄	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高眼圧症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
視神経乳頭浮腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
斜視	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
弱視	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
硝子体混濁	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
星状硝子体症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
前房出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
増殖性網膜症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
調節障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
糖尿病性白内障	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
瞳孔障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
虹彩毛様体炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
嚢下白内障	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
嚢胞様黄斑浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
閉塞隅角緑内障	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
網膜血管障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
網膜血管新生	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
網膜色素上皮症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
網膜裂孔	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
網膜滲出物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
網脈絡膜萎縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
落屑症候群	0				0				1	(0.1)	1	0.1	0			
涙液分泌低下	0				1	(0.1)	1	0.1	0				0			
涙器構造障害	0				0				1	(0.1)	1	0.1	0			
霰粒腫	1	(0.1)	1	0.1	0				0				0			
腎および尿路障害	86	(10.4)	99	6.7	77	(9.4)	89	6.2	107	(13.1)	149	9.9	117	(14.2)	154	10.1
ミクロアルブミン尿	20	(2.4)	20	1.3	19	(2.3)	20	1.4	29	(3.5)	33	2.2	32	(3.9)	33	2.2
腎嚢胞	14	(1.7)	14	0.9	12	(1.5)	13	0.9	16	(2.0)	17	1.1	16	(1.9)	17	1.1
蛋白尿	11	(1.3)	11	0.7	4	(0.5)	4	0.3	11	(1.3)	12	0.8	12	(1.5)	12	0.8
腎結石症	3	(0.4)	3	0.2	7	(0.9)	7	0.5	12	(1.5)	15	1.0	8	(1.0)	8	0.5
慢性腎臓病	4	(0.5)	4	0.3	4	(0.5)	4	0.3	7	(0.9)	9	0.6	10	(1.2)	10	0.7
糖尿病性腎症	4	(0.5)	4	0.3	5	(0.6)	5	0.3	6	(0.7)	6	0.4	5	(0.6)	5	0.3
腎症	2	(0.2)	2	0.1	2	(0.2)	2	0.1	7	(0.9)	7	0.5	8	(1.0)	8	0.5
血尿	2	(0.2)	2	0.1	2	(0.2)	2	0.1	4	(0.5)	4	0.3	10	(1.2)	10	0.7
急性腎不全	6	(0.7)	6	0.4	1	(0.1)	1	0.1	5	(0.6)	5	0.3	5	(0.6)	5	0.3
排尿困難	4	(0.5)	4	0.3	3	(0.4)	3	0.2	5	(0.6)	5	0.3	5	(0.6)	5	0.3
腎機能障害	7	(0.9)	7	0.5	3	(0.4)	3	0.2	3	(0.4)	3	0.2	1	(0.1)	1	0.1
尿失禁	3	(0.4)	3	0.2	5	(0.6)	5	0.3	3	(0.4)	3	0.2	3	(0.4)	3	0.2
糖尿	1	(0.1)	1	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3
白血球尿	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	4	(0.5)	4	0.3
尿異常	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
腎不全	5	(0.6)	5	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1
夜間頻尿	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1
頻尿	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
緊張性膀胱	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
アルブミン尿	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
腎仙痛	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
水腎症	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
膀胱憩室	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
ケトン尿	0				0				0				2	(0.2)	2	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
落屑症候群	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
涙液分泌低下	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
涙器構造障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
霰粒腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎および尿路障害	163	(9.9)	188	6.4	224	(13.6)	303	10.0	387	(11.8)	491	8.2
ミクロアルブミン尿	39	(2.4)	40	1.4	61	(3.7)	66	2.2	100	(3.0)	106	1.8
腎嚢胞	26	(1.6)	27	0.9	32	(1.9)	34	1.1	58	(1.8)	61	1.0
蛋白尿	15	(0.9)	15	0.5	23	(1.4)	24	0.8	38	(1.2)	39	0.7
腎結石症	10	(0.6)	10	0.3	20	(1.2)	23	0.8	30	(0.9)	33	0.6
慢性腎臓病	8	(0.5)	8	0.3	17	(1.0)	19	0.6	25	(0.8)	27	0.5
糖尿病性腎症	9	(0.5)	9	0.3	11	(0.7)	11	0.4	20	(0.6)	20	0.3
腎症	4	(0.2)	4	0.1	15	(0.9)	15	0.5	19	(0.6)	19	0.3
血尿	4	(0.2)	4	0.1	14	(0.9)	14	0.5	18	(0.5)	18	0.3
急性腎不全	7	(0.4)	7	0.2	10	(0.6)	10	0.3	17	(0.5)	17	0.3
排尿困難	7	(0.4)	7	0.2	10	(0.6)	10	0.3	17	(0.5)	17	0.3
腎機能障害	10	(0.6)	10	0.3	4	(0.2)	4	0.1	14	(0.4)	14	0.2
尿失禁	8	(0.5)	8	0.3	6	(0.4)	6	0.2	14	(0.4)	14	0.2
糖尿	2	(0.1)	2	0.1	8	(0.5)	8	0.3	10	(0.3)	10	0.2
白血球尿	3	(0.2)	3	0.1	7	(0.4)	7	0.2	10	(0.3)	10	0.2
尿異常	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2
腎不全	6	(0.4)	6	0.2	2	(0.1)	3	0.1	8	(0.2)	9	0.2
夜間頻尿	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
頻尿	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
緊張性膀胱	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
アルブミン尿	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
腎仙痛	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
水腎症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
膀胱憩室	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
ケトン尿	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腎硬化症	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
腎腫瘤	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
腎盂腎杯拡張症	0				0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
多尿	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
尿管結石	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
尿閉	0				0				0				2	(0.2)	2	0.1
尿路結石	0				0				0				2	(0.2)	2	0.1
腹圧性尿失禁	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
慢性糸球体腎炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
ネフローゼ症候群	1	(0.1)	1	0.1	0				0				0			
下部尿路症状	0				0				1	(0.1)	1	0.1	0			
気尿症	0				0				0				1	(0.1)	1	0.1
鹿角状結石	0				1	(0.1)	1	0.1	0				0			
失禁	1	(0.1)	1	0.1	0				0				0			
腎下垂症	0				0				1	(0.1)	1	0.1	0			
腎拡張症	0				0				0				1	(0.1)	1	0.1
腎脂肪腫症	0				1	(0.1)	1	0.1	0				0			
腎臓痛	1	(0.1)	1	0.1	0				0				0			
腎損傷	0				0				0				1	(0.1)	1	0.1
切迫性尿失禁	0				1	(0.1)	1	0.1	0				0			
着色尿	0				1	(0.1)	1	0.1	0				0			
尿道狭窄	0				0				0				1	(0.1)	1	0.1
尿路障害	0				0				1	(0.1)	1	0.1	0			
無尿	0				0				0				1	(0.1)	1	0.1
膀胱結石	1	(0.1)	1	0.1	0				0				0			
膀胱痛	0				0				1	(0.1)	1	0.1	0			
呼吸器、胸郭および縦隔障害	88	(10.7)	107	7.2	70	(8.5)	87	6.0	99	(12.1)	132	8.8	108	(13.1)	147	9.6
咳嗽	24	(2.9)	27	1.8	14	(1.7)	14	1.0	28	(3.4)	28	1.9	33	(4.0)	34	2.2
呼吸困難	9	(1.1)	10	0.7	11	(1.3)	13	0.9	10	(1.2)	10	0.7	19	(2.3)	19	1.2

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
腎硬化症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腎腫瘤	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
腎盂腎杯拡張症	0				2	(0.1)	3	0.1	2	(0.1)	3	0.1
多尿	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
尿管結石	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
尿閉	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
尿路結石	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
腹圧性尿失禁	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
慢性糸球体腎炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
ネフローゼ症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
下部尿路症状	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
気尿症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鹿角状結石	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
失禁	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎下垂症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎拡張症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎脂肪腫症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎臓痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腎損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
切迫性尿失禁	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
着色尿	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
尿道狭窄	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
尿路障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
無尿	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膀胱結石	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膀胱痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
呼吸器、胸郭および縦隔障害	158	(9.6)	194	6.6	207	(12.6)	279	9.2	365	(11.1)	473	7.9
咳嗽	38	(2.3)	41	1.4	61	(3.7)	62	2.0	99	(3.0)	103	1.7
呼吸困難	20	(1.2)	23	0.8	29	(1.8)	29	1.0	49	(1.5)	52	0.9

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
口腔咽頭痛	5	(0.6)	5	0.3	5	(0.6)	6	0.4	9	(1.1)	9	0.6	11	(1.3)	13	0.9
肺腫瘤	7	(0.9)	7	0.5	3	(0.4)	3	0.2	7	(0.9)	7	0.5	5	(0.6)	5	0.3
慢性閉塞性肺疾患	2	(0.2)	3	0.2	3	(0.4)	3	0.2	7	(0.9)	9	0.6	7	(0.8)	7	0.5
アレルギー性鼻炎	3	(0.4)	3	0.2	3	(0.4)	3	0.2	6	(0.7)	6	0.4	4	(0.5)	8	0.5
鼻閉	3	(0.4)	6	0.4	2	(0.2)	2	0.1	5	(0.6)	5	0.3	4	(0.5)	4	0.3
睡眠時無呼吸症候群	2	(0.2)	2	0.1	0				3	(0.4)	3	0.2	8	(1.0)	8	0.5
鼻漏	5	(0.6)	5	0.3	1	(0.1)	1	0.1	5	(0.6)	6	0.4	2	(0.2)	2	0.1
鼻出血	3	(0.4)	4	0.3	1	(0.1)	1	0.1	4	(0.5)	9	0.6	3	(0.4)	3	0.2
無気肺	3	(0.4)	3	0.2	0				5	(0.6)	5	0.3	3	(0.4)	4	0.3
労作性呼吸困難	0				4	(0.5)	4	0.3	5	(0.6)	5	0.3	2	(0.2)	2	0.1
しゃっくり	4	(0.5)	5	0.3	5	(0.6)	5	0.3	0				1	(0.1)	1	0.1
喘息	2	(0.2)	2	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2	2	(0.2)	3	0.2
副鼻腔うっ血	1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
呼吸障害	1	(0.1)	2	0.1	0				4	(0.5)	4	0.3	2	(0.2)	2	0.1
慢性気管支炎	2	(0.2)	2	0.1	3	(0.4)	3	0.2	0				2	(0.2)	2	0.1
上気道うっ血	0				2	(0.2)	3	0.2	0				3	(0.4)	5	0.3
くしゃみ	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
気道うっ血	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
湿性咳嗽	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
肺水腫	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
咽喉刺激感	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
胸水	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
上気道咳症候群	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
肺気腫	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
肺高血圧症	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
発声障害	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
咽喉乾燥	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
気胸	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
急性肺水腫	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
肺うっ血	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
口腔咽頭痛	10	(0.6)	11	0.4	20	(1.2)	22	0.7	30	(0.9)	33	0.6
肺腫瘤	10	(0.6)	10	0.3	12	(0.7)	12	0.4	22	(0.7)	22	0.4
慢性閉塞性肺疾患	5	(0.3)	6	0.2	14	(0.9)	16	0.5	19	(0.6)	22	0.4
アレルギー性鼻炎	6	(0.4)	6	0.2	10	(0.6)	14	0.5	16	(0.5)	20	0.3
鼻閉	5	(0.3)	8	0.3	9	(0.5)	9	0.3	14	(0.4)	17	0.3
睡眠時無呼吸症候群	2	(0.1)	2	0.1	11	(0.7)	11	0.4	13	(0.4)	13	0.2
鼻漏	6	(0.4)	6	0.2	7	(0.4)	8	0.3	13	(0.4)	14	0.2
鼻出血	4	(0.2)	5	0.2	7	(0.4)	12	0.4	11	(0.3)	17	0.3
無気肺	3	(0.2)	3	0.1	8	(0.5)	9	0.3	11	(0.3)	12	0.2
労作性呼吸困難	4	(0.2)	4	0.1	7	(0.4)	7	0.2	11	(0.3)	11	0.2
しゃっくり	9	(0.5)	10	0.3	1	(0.1)	1	<0.1	10	(0.3)	11	0.2
喘息	5	(0.3)	5	0.2	5	(0.3)	6	0.2	10	(0.3)	11	0.2
副鼻腔うっ血	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
呼吸障害	1	(0.1)	2	0.1	6	(0.4)	6	0.2	7	(0.2)	8	0.1
慢性気管支炎	5	(0.3)	5	0.2	2	(0.1)	2	0.1	7	(0.2)	7	0.1
上気道うっ血	2	(0.1)	3	0.1	3	(0.2)	5	0.2	5	(0.2)	8	0.1
くしゃみ	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
気道うっ血	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
湿性咳嗽	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
肺水腫	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
咽喉刺激感	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
胸水	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
上気道咳症候群	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
肺気腫	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
肺高血圧症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
発声障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
咽喉乾燥	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
気胸	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
急性肺水腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肺うっ血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肺塞栓症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
肺障害	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
肺肉芽腫	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
鼻茸	0				0				0				2	(0.2)	2	0.1
副鼻腔障害	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
いびき	1	(0.1)	1	0.1	0				0				0			
カタル	1	(0.1)	1	0.1	0				0				0			
間質性肺疾患	0				0				0				1	(0.1)	1	0.1
気管支拡張症	0				0				0				1	(0.1)	1	0.1
気管支反応性亢進	0				0				0				1	(0.1)	1	0.1
気管支壁肥厚	0				0				0				1	(0.1)	1	0.1
気管支痙攣	0				0				1	(0.1)	2	0.1	0			
逆流性喉頭炎	0				1	(0.1)	1	0.1	0				0			
胸膜炎	0				0				0				1	(0.1)	1	0.1
胸膜線維症	0				1	(0.1)	1	0.1	0				0			
胸膜痛	1	(0.1)	1	0.1	0				0				0			
誤嚥性肺炎	0				0				0				1	(0.1)	1	0.1
拘束性肺疾患	1	(0.1)	1	0.1	0				0				0			
徐呼吸	1	(0.1)	1	0.1	0				0				0			
声帯の炎症	0				0				0				1	(0.1)	1	0.1
声帯障害	0				0				1	(0.1)	1	0.1	0			
息詰まり	1	(0.1)	1	0.1	0				0				0			
低酸素症	0				1	(0.1)	1	0.1	0				0			
肺浸潤	0				0				1	(0.1)	1	0.1	0			
肺線維症	0				0				0				1	(0.1)	1	0.1
肺動脈性肺高血圧症	0				0				1	(0.1)	1	0.1	0			
鼻そう痒症	1	(0.1)	1	0.1	0				0				0			
鼻の炎症	0				1	(0.1)	1	0.1	0				0			
鼻乾燥	0				0				1	(0.1)	1	0.1	0			
鼻甲介肥大	0				0				0				1	(0.1)	1	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
肺塞栓症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
肺障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肺肉芽腫	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
鼻茸	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
副鼻腔障害	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
いびき	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
カタル	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
間質性肺疾患	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
気管支拡張症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
気管支反応性亢進	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
気管支壁肥厚	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
気管支痙攣	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
逆流性喉頭炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胸膜炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胸膜線維症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胸膜痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
誤嚥性肺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
拘束性肺疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
徐呼吸	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
声帯の炎症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
声帯障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
息詰まり	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
低酸素症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺浸潤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺線維症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺動脈性肺高血圧症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鼻そう痒症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻の炎症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻乾燥	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鼻甲介肥大	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
鼻中隔弯曲	1	(0.1)	1	0.1	0				0				0			
鼻浮腫	0				1	(0.1)	2	0.1	0				0			
副鼻腔分泌過多	0				1	(0.1)	1	0.1	0				0			
喘息クリーゼ	0				0				0				1	(0.1)	1	0.1
喘鳴	1	(0.1)	1	0.1	0				0				0			
一般・全身障害および投与部位の状態	81	(9.8)	102	6.9	97	(11.8)	123	8.5	93	(11.4)	118	7.8	99	(12.0)	117	7.7
疲労	19	(2.3)	20	1.3	27	(3.3)	31	2.1	9	(1.1)	9	0.6	16	(1.9)	16	1.0
末梢性浮腫	12	(1.5)	12	0.8	7	(0.9)	7	0.5	21	(2.6)	24	1.6	19	(2.3)	20	1.3
無力症	13	(1.6)	13	0.9	19	(2.3)	21	1.5	6	(0.7)	6	0.4	11	(1.3)	11	0.7
発熱	5	(0.6)	5	0.3	4	(0.5)	4	0.3	10	(1.2)	11	0.7	9	(1.1)	9	0.6
非心臓性胸痛	8	(1.0)	8	0.5	7	(0.9)	7	0.5	8	(1.0)	8	0.5	3	(0.4)	3	0.2
末梢腫脹	8	(1.0)	10	0.7	2	(0.2)	2	0.1	11	(1.3)	15	1.0	4	(0.5)	4	0.3
胸痛	2	(0.2)	2	0.1	6	(0.7)	9	0.6	5	(0.6)	5	0.3	9	(1.1)	9	0.6
胸部不快感	3	(0.4)	4	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1	10	(1.2)	10	0.7
疼痛	1	(0.1)	1	0.1	5	(0.6)	5	0.3	8	(1.0)	10	0.7	3	(0.4)	4	0.3
注射部位内出血	1	(0.1)	1	0.1	3	(0.4)	3	0.2	6	(0.7)	7	0.5	4	(0.5)	4	0.3
悪寒	4	(0.5)	4	0.3	1	(0.1)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	4	0.3
倦怠感	3	(0.4)	3	0.2	2	(0.2)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
インフルエンザ様疾患	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1	2	(0.2)	2	0.1
早期満腹	2	(0.2)	2	0.1	2	(0.2)	2	0.1	0				0			
注射部位出血	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
熱感	0				3	(0.4)	3	0.2	1	(0.1)	1	0.1	0			
嚢胞	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
ポリープ	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
注射部位反応	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	2	0.1	0			
注射部位疼痛	1	(0.1)	1	0.1	0				0				2	(0.2)	2	0.1
浮腫	1	(0.1)	1	0.1	0				1	(0.1)	2	0.1	1	(0.1)	1	0.1
歩行障害	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
鼻中隔弯曲	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻浮腫	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
副鼻腔分泌過多	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
喘息クリーゼ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
喘鳴	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
一般・全身障害および投与部位の状態	178	(10.8)	225	7.7	192	(11.7)	235	7.7	370	(11.3)	460	7.7
疲労	46	(2.8)	51	1.7	25	(1.5)	25	0.8	71	(2.2)	76	1.3
末梢性浮腫	19	(1.2)	19	0.6	40	(2.4)	44	1.4	59	(1.8)	63	1.1
無力症	32	(1.9)	34	1.2	17	(1.0)	17	0.6	49	(1.5)	51	0.9
発熱	9	(0.5)	9	0.3	19	(1.2)	20	0.7	28	(0.9)	29	0.5
非心臓性胸痛	15	(0.9)	15	0.5	11	(0.7)	11	0.4	26	(0.8)	26	0.4
末梢腫脹	10	(0.6)	12	0.4	15	(0.9)	19	0.6	25	(0.8)	31	0.5
胸痛	8	(0.5)	11	0.4	14	(0.9)	14	0.5	22	(0.7)	25	0.4
胸部不快感	7	(0.4)	8	0.3	12	(0.7)	12	0.4	19	(0.6)	20	0.3
疼痛	6	(0.4)	6	0.2	11	(0.7)	14	0.5	17	(0.5)	20	0.3
注射部位内出血	4	(0.2)	4	0.1	10	(0.6)	11	0.4	14	(0.4)	15	0.3
悪寒	5	(0.3)	6	0.2	4	(0.2)	5	0.2	9	(0.3)	11	0.2
倦怠感	5	(0.3)	6	0.2	2	(0.1)	2	0.1	7	(0.2)	8	0.1
インフルエンザ様疾患	3	(0.2)	3	0.1	3	(0.2)	4	0.1	6	(0.2)	7	0.1
早期満腹	4	(0.2)	4	0.1	0				4	(0.1)	4	0.1
注射部位出血	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
熱感	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
嚢胞	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
ポリープ	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
注射部位反応	2	(0.1)	2	0.1	1	(0.1)	2	0.1	3	(0.1)	4	0.1
注射部位疼痛	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
浮腫	1	(0.1)	1	<0.1	2	(0.1)	3	0.1	3	(0.1)	4	0.1
歩行障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
圧痛	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
医薬品副作用	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
炎症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
化生	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
空腹	0				0				2	(0.2)	2	0.1	0			
口渇	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
石灰沈着症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
全身性浮腫	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
注射部位血腫	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
注射部位腫瘤	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
不快感	0				2	(0.2)	2	0.1	0				0			
ヘルニア	0				1	(0.1)	1	0.1	0				0			
医療機器機能不良	0				1	(0.1)	1	0.1	0				0			
局所腫脹	0				0				1	(0.1)	1	0.1	0			
血管穿刺部位内出血	0				0				0				1	(0.1)	1	0.1
限局性浮腫	0				0				0				1	(0.1)	1	0.1
硬結	1	(0.1)	1	0.1	0				0				0			
腫瘤	0				1	(0.1)	1	0.1	0				0			
重力性浮腫	0				0				0				1	(0.1)	1	0.1
小結節	0				0				0				1	(0.1)	1	0.1
線維症	1	(0.1)	1	0.1	0				0				0			
注射部位萎縮	0				0				1	(0.1)	1	0.1	0			
注射部位結節	0				0				0				1	(0.1)	1	0.1
注射部位硬結	1	(0.1)	1	0.1	0				0				0			
注射部位熱感	0				0				1	(0.1)	1	0.1	0			
注射部位不快感	0				1	(0.1)	2	0.1	0				0			
注射部位変色	1	(0.1)	1	0.1	0				0				0			
捻髪音	0				0				0				1	(0.1)	1	0.1
粘膜過形成	0				0				0				1	(0.1)	1	0.1
微石症	0				0				1	(0.1)	1	0.1	0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
圧痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
医薬品副作用	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
炎症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
化生	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
空腹	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
口渇	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
石灰沈着症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
全身性浮腫	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
注射部位血腫	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
注射部位腫瘤	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
不快感	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
ヘルニア	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
医療機器機能不良	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
局所腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管穿刺部位内出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
限局性浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
硬結	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
重力性浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
小結節	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
線維症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
注射部位萎縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
注射部位結節	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
注射部位硬結	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
注射部位熱感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
注射部位不快感	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
注射部位変色	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
捻髪音	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
粘膜過形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
微石症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
薬物特異体質反応	0				1	(0.1)	1	0.1	0				0			
薬物不耐性	0				0				1	(0.1)	1	0.1	0			
冷感	0				0				0				1	(0.1)	1	0.1
傷害、中毒および処置合併症	67	(8.1)	79	5.3	75	(9.2)	92	6.4	107	(13.1)	130	8.6	83	(10.1)	103	6.7
転倒	10	(1.2)	11	0.7	9	(1.1)	12	0.8	9	(1.1)	11	0.7	17	(2.1)	22	1.4
挫傷	3	(0.4)	3	0.2	7	(0.9)	7	0.5	17	(2.1)	18	1.2	7	(0.8)	7	0.5
創傷	8	(1.0)	9	0.6	8	(1.0)	8	0.6	9	(1.1)	9	0.6	3	(0.4)	4	0.3
四肢損傷	7	(0.9)	8	0.5	2	(0.2)	2	0.1	9	(1.1)	9	0.6	6	(0.7)	6	0.4
靱帯捻挫	1	(0.1)	1	0.1	7	(0.9)	7	0.5	7	(0.9)	8	0.5	5	(0.6)	5	0.3
偶発的過量投与	2	(0.2)	2	0.1	2	(0.2)	2	0.1	5	(0.6)	6	0.4	9	(1.1)	13	0.9
皮膚擦過傷	2	(0.2)	2	0.1	3	(0.4)	4	0.3	9	(1.1)	10	0.7	2	(0.2)	2	0.1
肉離れ	6	(0.7)	6	0.4	3	(0.4)	3	0.2	4	(0.5)	5	0.3	1	(0.1)	1	0.1
節足動物咬傷	1	(0.1)	1	0.1	4	(0.5)	4	0.3	5	(0.6)	5	0.3	3	(0.4)	3	0.2
裂傷	4	(0.5)	4	0.3	3	(0.4)	3	0.2	3	(0.4)	4	0.3	2	(0.2)	2	0.1
熱傷	5	(0.6)	5	0.3	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
過量投与	0				5	(0.6)	6	0.4	0				4	(0.5)	4	0.3
交通事故	4	(0.5)	5	0.3	3	(0.4)	3	0.2	2	(0.2)	2	0.1	0			
歯牙破折	4	(0.5)	5	0.3	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
関節損傷	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
足骨折	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	2	(0.2)	2	0.1
不適切な投与計画での薬剤の投与	0				3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1
処置による疼痛	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2	0			
動物咬傷	0				2	(0.2)	2	0.1	3	(0.4)	3	0.2	0			
術後貧血	1	(0.1)	1	0.1	0				3	(0.4)	3	0.2	0			
体内異物	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
頭部損傷	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
誤薬投与	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
上顆炎	0				0				1	(0.1)	1	0.1	2	(0.2)	2	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
薬物特異体質反応	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
薬物不耐性	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
冷感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
傷害、中毒および処置合併症	142	(8.6)	171	5.8	190	(11.6)	233	7.7	332	(10.1)	404	6.8
転倒	19	(1.2)	23	0.8	26	(1.6)	33	1.1	45	(1.4)	56	0.9
挫傷	10	(0.6)	10	0.3	24	(1.5)	25	0.8	34	(1.0)	35	0.6
創傷	16	(1.0)	17	0.6	12	(0.7)	13	0.4	28	(0.9)	30	0.5
四肢損傷	9	(0.5)	10	0.3	15	(0.9)	15	0.5	24	(0.7)	25	0.4
靱帯捻挫	8	(0.5)	8	0.3	12	(0.7)	13	0.4	20	(0.6)	21	0.4
偶発的過量投与	4	(0.2)	4	0.1	14	(0.9)	19	0.6	18	(0.5)	23	0.4
皮膚擦過傷	5	(0.3)	6	0.2	11	(0.7)	12	0.4	16	(0.5)	18	0.3
肉離れ	9	(0.5)	9	0.3	5	(0.3)	6	0.2	14	(0.4)	15	0.3
節足動物咬傷	5	(0.3)	5	0.2	8	(0.5)	8	0.3	13	(0.4)	13	0.2
裂傷	7	(0.4)	7	0.2	5	(0.3)	6	0.2	12	(0.4)	13	0.2
熱傷	7	(0.4)	7	0.2	3	(0.2)	3	0.1	10	(0.3)	10	0.2
過量投与	5	(0.3)	6	0.2	4	(0.2)	4	0.1	9	(0.3)	10	0.2
交通事故	7	(0.4)	8	0.3	2	(0.1)	2	0.1	9	(0.3)	10	0.2
歯牙破折	5	(0.3)	6	0.2	2	(0.1)	2	0.1	7	(0.2)	8	0.1
関節損傷	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
足骨折	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
不適切な投与計画での薬剤の投与	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
処置による疼痛	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
動物咬傷	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
術後貧血	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
体内異物	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
頭部損傷	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
誤薬投与	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
上顆炎	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ワクチン接種合併症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
関節脱臼	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
眼挫傷	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
胸部損傷	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
手骨折	0				2	(0.2)	2	0.1	0				0			
手首関節骨折	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
処置後甲状腺機能低下症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
処置後出血	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
上腕骨骨折	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
創部炎症	0				0				0				2	(0.2)	2	0.1
損傷	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
凍瘡	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
軟部組織損傷	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
皮膚損傷	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
肋骨骨折	0				0				0				2	(0.2)	2	0.1
橈骨骨折	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
移植血管合併症	0				0				1	(0.1)	1	0.1	0			
引っかき傷	0				0				0				1	(0.1)	1	0.1
栄養補給チューブ合併症	0				1	(0.1)	1	0.1	0				0			
下肢骨折	1	(0.1)	1	0.1	0				0				0			
外陰腟損傷	1	(0.1)	1	0.1	0				0				0			
外傷性血腫	0				0				0				1	(0.1)	1	0.1
外傷性潰瘍	1	(0.1)	1	0.1	0				0				0			
角膜損傷	0				0				1	(0.1)	1	0.1	0			
眼外傷	0				0				1	(0.1)	1	0.1	0			
筋断裂	0				1	(0.1)	1	0.1	0				0			
肩甲骨骨折	0				0				0				1	(0.1)	1	0.1
誤った投与期間	0				1	(0.1)	1	0.1	0				0			
誤った投与経路	0				1	(0.1)	1	0.1	0				0			
口腔内損傷	0				1	(0.1)	1	0.1	0				0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
ワクチン接種合併症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
関節脱臼	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
眼挫傷	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
胸部損傷	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
手骨折	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
手首関節骨折	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
処置後甲状腺機能低下症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
処置後出血	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
上腕骨骨折	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
創部炎症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
損傷	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
凍瘡	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
軟部組織損傷	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
皮膚損傷	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
肋骨骨折	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
橈骨骨折	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
移植血管合併症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
引っかき傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
栄養補給チューブ合併症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
下肢骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
外陰腟損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
外傷性血腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外傷性潰瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
角膜損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼外傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
筋断裂	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肩甲骨骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
誤った投与期間	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
誤った投与経路	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口腔内損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
口唇損傷	0				0				1	(0.1)	1	0.1	0			
腰椎骨折	0				1	(0.1)	1	0.1	0				0			
骨格損傷	1	(0.1)	1	0.1	0				0				0			
事故	0				0				1	(0.1)	1	0.1	0			
術後創合併症	0				0				0				1	(0.1)	1	0.1
処置による悪心	0				0				1	(0.1)	1	0.1	0			
処置後浮腫	0				0				1	(0.1)	1	0.1	0			
心臓処置合併症	0				0				0				1	(0.1)	1	0.1
節足動物刺傷	0				1	(0.1)	1	0.1	0				0			
創傷出血	0				0				1	(0.1)	1	0.1	0			
第１度熱傷	0				0				0				1	(0.1)	1	0.1
中毒	1	(0.1)	1	0.1	0				0				0			
爪損傷	0				0				1	(0.1)	1	0.1	0			
凍傷	0				0				1	(0.1)	1	0.1	0			
投薬過誤	0				1	(0.1)	1	0.1	0				0			
熱射病	0				0				0				1	(0.1)	1	0.1
脳振盪	1	(0.1)	1	0.1	0				0				0			
背部損傷	0				1	(0.1)	1	0.1	0				0			
白内障手術合併症	0				0				0				1	(0.1)	1	0.1
半月板損傷	1	(0.1)	1	0.1	0				0				0			
薬剤誤投与	1	(0.1)	1	0.1	0				0				0			
漿液腫	0				0				1	(0.1)	1	0.1	0			
腓骨骨折	0				0				1	(0.1)	1	0.1	0			
腱断裂	0				1	(0.1)	1	0.1	0				0			
靭帯断裂	0				0				1	(0.1)	1	0.1	0			
皮膚および皮下組織障害	63	(7.7)	81	5.4	71	(8.7)	100	6.9	70	(8.5)	91	6.0	86	(10.4)	104	6.8
発疹	7	(0.9)	8	0.5	9	(1.1)	9	0.6	8	(1.0)	8	0.5	13	(1.6)	14	0.9
そう痒症	11	(1.3)	13	0.9	10	(1.2)	14	1.0	7	(0.9)	7	0.5	8	(1.0)	8	0.5
皮膚潰瘍	7	(0.9)	7	0.5	5	(0.6)	5	0.3	7	(0.9)	10	0.7	7	(0.8)	7	0.5

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
口唇損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腰椎骨折	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
骨格損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
事故	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
術後創合併症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
処置による悪心	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
処置後浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心臓処置合併症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
節足動物刺傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
創傷出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
第１度熱傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
中毒	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
爪損傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
凍傷	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
投薬過誤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
熱射病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脳振盪	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
背部損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
白内障手術合併症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
半月板損傷	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
薬剤誤投与	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
漿液腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腓骨骨折	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腱断裂	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
靭帯断裂	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚および皮下組織障害	134	(8.2)	181	6.2	156	(9.5)	195	6.4	290	(8.8)	376	6.3
発疹	16	(1.0)	17	0.6	21	(1.3)	22	0.7	37	(1.1)	39	0.7
そう痒症	21	(1.3)	27	0.9	15	(0.9)	15	0.5	36	(1.1)	42	0.7
皮膚潰瘍	12	(0.7)	12	0.4	14	(0.9)	17	0.6	26	(0.8)	29	0.5

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
湿疹	1	(0.1)	1	0.1	3	(0.4)	3	0.2	8	(1.0)	9	0.6	3	(0.4)	4	0.3
蕁麻疹	4	(0.5)	4	0.3	4	(0.5)	4	0.3	1	(0.1)	1	0.1	4	(0.5)	4	0.3
日光角化症	2	(0.2)	2	0.1	5	(0.6)	8	0.6	1	(0.1)	1	0.1	4	(0.5)	4	0.3
皮膚炎	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	5	(0.6)	5	0.3
糖尿病性足病変	3	(0.4)	3	0.2	3	(0.4)	3	0.2	3	(0.4)	3	0.2	2	(0.2)	2	0.1
皮膚乾燥	0				5	(0.6)	5	0.3	2	(0.2)	2	0.1	4	(0.5)	4	0.3
紅斑	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2
多汗症	3	(0.4)	3	0.2	4	(0.5)	4	0.3	0				2	(0.2)	2	0.1
皮膚病変	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	5	(0.6)	5	0.3
間擦疹	2	(0.2)	2	0.1	3	(0.4)	4	0.3	1	(0.1)	1	0.1	2	(0.2)	2	0.1
接触性皮膚炎	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	4	(0.5)	4	0.3
皮膚嚢腫	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2
過角化	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	3	(0.4)	3	0.2
水疱	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
斑状出血	2	(0.2)	2	0.1	0				4	(0.5)	4	0.3	0			
嵌入爪	0				4	(0.5)	4	0.3	0				1	(0.1)	1	0.1
褥瘡性潰瘍	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
ざ瘡	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	0			
紅斑性皮疹	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	0			
脂漏性皮膚炎	3	(0.4)	3	0.2	1	(0.1)	2	0.1	0				0			
寝汗	3	(0.4)	4	0.3	1	(0.1)	1	0.1	0				0			
脱毛症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
アトピー性皮膚炎	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
アレルギー性皮膚炎	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
全身性そう痒症	0				0				3	(0.4)	3	0.2	0			
爪の障害	2	(0.2)	2	0.1	0				1	(0.1)	1	0.1	0			
皮膚腫瘤	0				0				2	(0.2)	2	0.1	1	(0.1)	1	0.1
皮膚剥脱	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
うっ滞性皮膚炎	0				0				2	(0.2)	2	0.1	0			
そう痒性皮疹	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
湿疹	4	(0.2)	4	0.1	11	(0.7)	13	0.4	15	(0.5)	17	0.3
蕁麻疹	8	(0.5)	8	0.3	5	(0.3)	5	0.2	13	(0.4)	13	0.2
日光角化症	7	(0.4)	10	0.3	5	(0.3)	5	0.2	12	(0.4)	15	0.3
皮膚炎	5	(0.3)	5	0.2	7	(0.4)	7	0.2	12	(0.4)	12	0.2
糖尿病性足病変	6	(0.4)	6	0.2	5	(0.3)	5	0.2	11	(0.3)	11	0.2
皮膚乾燥	5	(0.3)	5	0.2	6	(0.4)	6	0.2	11	(0.3)	11	0.2
紅斑	4	(0.2)	4	0.1	5	(0.3)	5	0.2	9	(0.3)	9	0.2
多汗症	7	(0.4)	7	0.2	2	(0.1)	2	0.1	9	(0.3)	9	0.2
皮膚病変	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2
間擦疹	5	(0.3)	6	0.2	3	(0.2)	3	0.1	8	(0.2)	9	0.2
接触性皮膚炎	2	(0.1)	2	0.1	6	(0.4)	6	0.2	8	(0.2)	8	0.1
皮膚嚢腫	2	(0.1)	2	0.1	5	(0.3)	5	0.2	7	(0.2)	7	0.1
過角化	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
水疱	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
斑状出血	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
嵌入爪	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
褥瘡性潰瘍	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
ざ瘡	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
紅斑性皮疹	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
脂漏性皮膚炎	4	(0.2)	5	0.2	0				4	(0.1)	5	0.1
寝汗	4	(0.2)	5	0.2	0				4	(0.1)	5	0.1
脱毛症	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
アトピー性皮膚炎	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
アレルギー性皮膚炎	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
全身性そう痒症	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
爪の障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
皮膚腫瘤	0				3	(0.2)	3	0.1	3	(0.1)	3	0.1
皮膚剥脱	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
うっ滞性皮膚炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
そう痒性皮疹	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
乾癬	1	(0.1)	2	0.1	0				0				1	(0.1)	1	0.1
汗疹	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
顔面腫脹	1	(0.1)	2	0.1	1	(0.1)	1	0.1	0				0			
丘疹	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
血管浮腫	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
血性水疱	0				2	(0.2)	2	0.1	0				0			
脂肪肥大症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
水疱性皮膚炎	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
全身性皮疹	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
糖尿病性潰瘍	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
日光黒子	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
皮脂欠乏性湿疹	1	(0.1)	1	0.1	0				0				1	(0.1)	2	0.1
皮膚障害	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
皮膚弛緩症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
びまん性脱毛症	0				0				0				1	(0.1)	1	0.1
乾皮症	0				1	(0.1)	1	0.1	0				0			
環状肉芽腫	0				1	(0.1)	1	0.1	0				0			
丘疹性皮疹	0				1	(0.1)	1	0.1	0				0			
血管周囲細胞浸潤性皮膚炎	0				0				1	(0.1)	1	0.1	0			
後天性リポジストロフィー	0				0				1	(0.1)	1	0.1	0			
光線過敏性反応	0				0				1	(0.1)	2	0.1	0			
紫斑	0				1	(0.1)	1	0.1	0				0			
脂漏	0				0				1	(0.1)	1	0.1	0			
手掌・足底発赤知覚不全症候群	0				1	(0.1)	1	0.1	0				0			
酒さ	1	(0.1)	1	0.1	0				0				0			
掌蹠角皮症	0				1	(0.1)	1	0.1	0				0			
神経皮膚炎	0				0				0				1	(0.1)	1	0.1
爪変色	0				0				0				1	(0.1)	1	0.1
点状出血	0				1	(0.1)	1	0.1	0				0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
乾癬	1	(0.1)	2	0.1	1	(0.1)	1	<0.1	2	(0.1)	3	0.1
汗疹	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
顔面腫脹	2	(0.1)	3	0.1	0				2	(0.1)	3	0.1
丘疹	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血管浮腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血性水疱	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
脂肪肥大症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
水疱性皮膚炎	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
全身性皮疹	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
糖尿病性潰瘍	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
日光黒子	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
皮脂欠乏性湿疹	1	(0.1)	1	<0.1	1	(0.1)	2	0.1	2	(0.1)	3	0.1
皮膚障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
皮膚弛緩症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
びまん性脱毛症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乾皮症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
環状肉芽腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
丘疹性皮疹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管周囲細胞浸潤性皮膚炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
後天性リポジストロフィー	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
光線過敏性反応	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
紫斑	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
脂漏	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
手掌・足底発赤知覚不全症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
酒さ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
掌蹠角皮症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経皮膚炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
爪変色	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
点状出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
内方発育毛	0				0				0				1	(0.1)	1	0.1
斑状皮疹	0				0				0				1	(0.1)	1	0.1
皮下気腫	0				0				0				1	(0.1)	1	0.1
皮膚アミロイドーシス	0				0				1	(0.1)	1	0.1	0			
皮膚亀裂	0				0				1	(0.1)	1	0.1	0			
皮膚筋炎	1	(0.1)	3	0.2	0				0				0			
皮膚刺激	0				1	(0.1)	1	0.1	0				0			
皮膚灼熱感	0				0				1	(0.1)	1	0.1	0			
皮膚反応	0				0				1	(0.1)	1	0.1	0			
皮膚変色	0				0				0				1	(0.1)	1	0.1
薬疹	0				0				0				1	(0.1)	2	0.1
扁平苔癬	0				0				0				1	(0.1)	1	0.1
痂皮	0				1	(0.1)	1	0.1	0				0			
痒疹	0				0				0				1	(0.1)	1	0.1
心臓障害	65	(7.9)	86	5.8	58	(7.1)	87	6.0	74	(9.0)	101	6.7	65	(7.9)	82	5.4
心房細動	9	(1.1)	9	0.6	8	(1.0)	9	0.6	11	(1.3)	13	0.9	10	(1.2)	12	0.8
狭心症	3	(0.4)	3	0.2	6	(0.7)	6	0.4	11	(1.3)	12	0.8	9	(1.1)	11	0.7
心室性期外収縮	6	(0.7)	7	0.5	5	(0.6)	5	0.3	3	(0.4)	3	0.2	6	(0.7)	6	0.4
右脚ブロック	6	(0.7)	6	0.4	5	(0.6)	5	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1
動悸	5	(0.6)	5	0.3	5	(0.6)	6	0.4	5	(0.6)	6	0.4	0			
第一度房室ブロック	4	(0.5)	4	0.3	3	(0.4)	3	0.2	2	(0.2)	2	0.1	5	(0.6)	5	0.3
僧帽弁閉鎖不全症	4	(0.5)	4	0.3	3	(0.4)	3	0.2	3	(0.4)	3	0.2	2	(0.2)	2	0.1
冠動脈疾患	3	(0.4)	3	0.2	4	(0.5)	4	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1
左室肥大	0				4	(0.5)	4	0.3	3	(0.4)	3	0.2	4	(0.5)	4	0.3
左室機能不全	3	(0.4)	3	0.2	1	(0.1)	1	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1
頻脈	2	(0.2)	3	0.2	3	(0.4)	3	0.2	4	(0.5)	4	0.3	1	(0.1)	1	0.1
左脚ブロック	2	(0.2)	2	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	2	(0.2)	2	0.1
徐脈	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
うっ血性心不全	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
内方発育毛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
斑状皮疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮下気腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚アミロイドーシス	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚亀裂	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚筋炎	1	(0.1)	3	0.1	0				1	(<0.1)	3	0.1
皮膚刺激	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮膚灼熱感	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚反応	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
皮膚変色	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
薬疹	0				1	(0.1)	2	0.1	1	(<0.1)	2	<0.1
扁平苔癬	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
痂皮	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
痒疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心臓障害	123	(7.5)	173	5.9	139	(8.5)	183	6.0	262	(8.0)	356	6.0
心房細動	17	(1.0)	18	0.6	21	(1.3)	25	0.8	38	(1.2)	43	0.7
狭心症	9	(0.5)	9	0.3	20	(1.2)	23	0.8	29	(0.9)	32	0.5
心室性期外収縮	11	(0.7)	12	0.4	9	(0.5)	9	0.3	20	(0.6)	21	0.4
右脚ブロック	11	(0.7)	11	0.4	6	(0.4)	6	0.2	17	(0.5)	17	0.3
動悸	10	(0.6)	11	0.4	5	(0.3)	6	0.2	15	(0.5)	17	0.3
第一度房室ブロック	7	(0.4)	7	0.2	7	(0.4)	7	0.2	14	(0.4)	14	0.2
僧帽弁閉鎖不全症	7	(0.4)	7	0.2	5	(0.3)	5	0.2	12	(0.4)	12	0.2
冠動脈疾患	7	(0.4)	7	0.2	4	(0.2)	4	0.1	11	(0.3)	11	0.2
左室肥大	4	(0.2)	4	0.1	7	(0.4)	7	0.2	11	(0.3)	11	0.2
左室機能不全	4	(0.2)	4	0.1	6	(0.4)	6	0.2	10	(0.3)	10	0.2
頻脈	5	(0.3)	6	0.2	5	(0.3)	5	0.2	10	(0.3)	11	0.2
左脚ブロック	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
徐脈	3	(0.2)	3	0.1	6	(0.4)	6	0.2	9	(0.3)	9	0.2
うっ血性心不全	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
上室性期外収縮	1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2	1	(0.1)	1	0.1
心不全	3	(0.4)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1
不安定狭心症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1
三尖弁閉鎖不全症	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1	1	(0.1)	1	0.1
大動脈弁閉鎖不全症	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0				3	(0.4)	3	0.2
心筋虚血	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
洞性徐脈	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	4	(0.5)	4	0.3
不整脈	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
洞性頻脈	3	(0.4)	3	0.2	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
心拡大	3	(0.4)	3	0.2	0				0				1	(0.1)	1	0.1
心筋梗塞	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
心室内伝導障害	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
心房粗動	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
拡張機能障害	0				2	(0.2)	2	0.1	1	(0.1)	1	0.1	0			
左房拡張	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
洞結節機能不全	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
右房拡張	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
冠動脈狭窄	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
急性心筋梗塞	0				0				2	(0.2)	2	0.1	0			
結節性不整脈	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
心筋症	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
肺動脈弁閉鎖不全症	0				2	(0.2)	2	0.1	0				0			
慢性心不全	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
右室不全	1	(0.1)	1	0.1	0				0				0			
期外収縮	0				0				0				1	(0.1)	1	0.1
急性冠動脈症候群	1	(0.1)	1	0.1	0				0				0			
高血圧性心筋症	0				0				1	(0.1)	1	0.1	0			
高血圧性心疾患	1	(0.1)	1	0.1	0				0				0			
左室不全	1	(0.1)	1	0.1	0				0				0			
収縮機能障害	0				0				1	(0.1)	1	0.1	0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
上室性期外収縮	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
心不全	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
不安定狭心症	2	(0.1)	2	0.1	6	(0.4)	6	0.2	8	(0.2)	8	0.1
三尖弁閉鎖不全症	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
大動脈弁閉鎖不全症	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
心筋虚血	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
洞性徐脈	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
不整脈	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
洞性頻脈	3	(0.2)	3	0.1	2	(0.1)	2	0.1	5	(0.2)	5	0.1
心拡大	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
心筋梗塞	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
心室内伝導障害	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
心房粗動	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
拡張機能障害	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
左房拡張	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
洞結節機能不全	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
右房拡張	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
冠動脈狭窄	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
急性心筋梗塞	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
結節性不整脈	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
心筋症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
肺動脈弁閉鎖不全症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
慢性心不全	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
右室不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
期外収縮	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性冠動脈症候群	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高血圧性心筋症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
高血圧性心疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
左室不全	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
収縮機能障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
上室性頻脈性不整脈	0				0				0				1	(0.1)	1	0.1
心筋線維症	0				1	(0.1)	1	0.1	0				0			
心室拡張	0				0				1	(0.1)	1	0.1	0			
心室性頻脈	0				0				1	(0.1)	1	0.1	0			
心室性頻脈性不整脈	0				0				0				1	(0.1)	1	0.1
心室性不整脈	0				0				0				1	(0.1)	1	0.1
心室肥大	0				1	(0.1)	1	0.1	0				0			
心室壁運動低下	0				0				1	(0.1)	1	0.1	0			
心粗動	0				1	(0.1)	1	0.1	0				0			
心臓弁膜疾患	0				1	(0.1)	1	0.1	0				0			
心肥大	0				0				1	(0.1)	1	0.1	0			
心房拡張	1	(0.1)	1	0.1	0				0				0			
心房頻脈	0				0				1	(0.1)	1	0.1	0			
僧帽弁疾患	0				1	(0.1)	1	0.1	0				0			
僧帽弁石灰化	0				0				1	(0.1)	1	0.1	0			
大動脈弁狭窄	1	(0.1)	1	0.1	0				0				0			
大動脈弁硬化症	0				0				1	(0.1)	1	0.1	0			
第二度房室ブロック	0				0				0				1	(0.1)	1	0.1
伝導障害	0				1	(0.1)	1	0.1	0				0			
洞性不整脈	0				0				1	(0.1)	1	0.1	0			
発作性頻脈	0				0				0				1	(0.1)	1	0.1
房室ブロック	1	(0.1)	1	0.1	0				0				0			
無症候性心筋梗塞	0				1	(0.1)	1	0.1	0				0			
両側性脚ブロック	1	(0.1)	1	0.1	0				0				0			
血管障害	52	(6.3)	56	3.8	55	(6.7)	64	4.4	56	(6.8)	67	4.4	52	(6.3)	62	4.1
高血圧	18	(2.2)	18	1.2	19	(2.3)	21	1.5	25	(3.1)	27	1.8	21	(2.5)	23	1.5
低血圧	8	(1.0)	8	0.5	8	(1.0)	8	0.6	10	(1.2)	12	0.8	8	(1.0)	8	0.5
起立性低血圧	3	(0.4)	3	0.2	4	(0.5)	4	0.3	3	(0.4)	3	0.2	1	(0.1)	1	0.1
大動脈硬化症	2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	3	0.2

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
上室性頻脈性不整脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心筋線維症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心室拡張	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心室性頻脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心室性頻脈性不整脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心室性不整脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心室肥大	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心室壁運動低下	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心粗動	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心臓弁膜疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心肥大	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心房拡張	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
心房頻脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
僧帽弁疾患	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
僧帽弁石灰化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大動脈弁狭窄	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大動脈弁硬化症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
第二度房室ブロック	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
伝導障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
洞性不整脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
発作性頻脈	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
房室ブロック	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
無症候性心筋梗塞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
両側性脚ブロック	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管障害	107	(6.5)	120	4.1	108	(6.6)	129	4.3	215	(6.5)	249	4.2
高血圧	37	(2.3)	39	1.3	46	(2.8)	50	1.6	83	(2.5)	89	1.5
低血圧	16	(1.0)	16	0.5	18	(1.1)	20	0.7	34	(1.0)	36	0.6
起立性低血圧	7	(0.4)	7	0.2	4	(0.2)	4	0.1	11	(0.3)	11	0.2
大動脈硬化症	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
末梢動脈閉塞性疾患	1	(0.1)	1	0.1	4	(0.5)	4	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1
高血圧クリーゼ	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
血腫	3	(0.4)	3	0.2	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0			
大動脈瘤	0				4	(0.5)	4	0.3	0				3	(0.4)	3	0.2
静脈瘤	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2	0			
末梢血管障害	2	(0.2)	2	0.1	0				0				3	(0.4)	3	0.2
深部静脈血栓症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
末梢静脈疾患	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
ほてり	0				2	(0.2)	2	0.1	0				1	(0.1)	1	0.1
動脈硬化症	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
表在性血栓性静脈炎	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				0			
間欠性跛行	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
血管石灰化	0				0				0				2	(0.2)	2	0.1
血行不全	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
血栓性静脈炎	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
大動脈狭窄	2	(0.2)	2	0.1	0				0				0			
大動脈障害	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
潮紅	0				1	(0.1)	3	0.2	0				1	(0.1)	1	0.1
糖尿病性血管障害	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
動脈閉塞性疾患	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
末梢冷感	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
コントロール不良の血圧	0				0				1	(0.1)	1	0.1	0			
リンパうっ滞	0				0				0				1	(0.1)	1	0.1
リンパ浮腫	0				0				1	(0.1)	1	0.1	0			
起立性高血圧	0				1	(0.1)	1	0.1	0				0			
血管拡張	0				0				0				1	(0.1)	1	0.1
血管障害	1	(0.1)	1	0.1	0				0				0			
紅痛症	1	(0.1)	1	0.1	0				0				0			
高血圧性血管障害	0				0				1	(0.1)	1	0.1	0			
四肢静脈血栓症	0				0				0				1	(0.1)	1	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
末梢動脈閉塞性疾患	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
高血圧クリーゼ	3	(0.2)	3	0.1	5	(0.3)	5	0.2	8	(0.2)	8	0.1
血腫	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
大動脈瘤	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
静脈瘤	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
末梢血管障害	2	(0.1)	2	0.1	3	(0.2)	3	0.1	5	(0.2)	5	0.1
深部静脈血栓症	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
末梢静脈疾患	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
ほてり	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
動脈硬化症	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
表在性血栓性静脈炎	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
間欠性跛行	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血管石灰化	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
血行不全	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
血栓性静脈炎	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
大動脈狭窄	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
大動脈障害	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
潮紅	1	(0.1)	3	0.1	1	(0.1)	1	<0.1	2	(0.1)	4	0.1
糖尿病性血管障害	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
動脈閉塞性疾患	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
末梢冷感	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
コントロール不良の血圧	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
リンパうっ滞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
リンパ浮腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
起立性高血圧	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血管拡張	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
紅痛症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高血圧性血管障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
四肢静脈血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
静脈炎	0				0				0				1	(0.1)	1	0.1
静脈血栓症	0				1	(0.1)	1	0.1	0				0			
蒼白	0				1	(0.1)	1	0.1	0				0			
大動脈拡張	0				0				0				1	(0.1)	1	0.1
大動脈血栓症	0				0				0				1	(0.1)	1	0.1
低潅流	0				0				1	(0.1)	1	0.1	0			
動脈瘤	0				0				1	(0.1)	1	0.1	0			
微小血管症	0				0				0				1	(0.1)	1	0.1
帽状腱膜下血腫	0				0				1	(0.1)	1	0.1	0			
本態性高血圧症	0				0				1	(0.1)	1	0.1	0			
末梢動脈血栓症	1	(0.1)	1	0.1	0				0				0			
末梢動脈瘤	0				1	(0.1)	1	0.1	0				0			
毛細血管脆弱	0				0				1	(0.1)	1	0.1	0			
腕頭動脈硬化症	0				1	(0.1)	1	0.1	0				0			
血液およびリンパ系障害	38	(4.6)	46	3.1	31	(3.8)	33	2.3	40	(4.9)	49	3.2	53	(6.4)	60	3.9
貧血	24	(2.9)	27	1.8	18	(2.2)	19	1.3	26	(3.2)	28	1.9	35	(4.2)	39	2.6
鉄欠乏性貧血	3	(0.4)	3	0.2	4	(0.5)	4	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1
血小板減少症	1	(0.1)	1	0.1	0				6	(0.7)	6	0.4	2	(0.2)	2	0.1
リンパ節症	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
白血球増加症	3	(0.4)	3	0.2	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
血小板増加症	2	(0.2)	2	0.1	1	(0.1)	1	0.1	0				1	(0.1)	2	0.1
好酸球増加症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
縦隔リンパ節腫脹	2	(0.2)	2	0.1	0				0				1	(0.1)	1	0.1
小赤血球症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
正色素性正球性貧血	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
赤血球増加症	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1	0			
リンパ球減少症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
小球性貧血	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
白血球減少症	0				0				2	(0.2)	2	0.1	0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
静脈炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
静脈血栓症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
蒼白	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大動脈拡張	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大動脈血栓症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
低潅流	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
動脈瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
微小血管症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
帽状腱膜下血腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
本態性高血圧症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈血栓症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
末梢動脈瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
毛細血管脆弱	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腕頭動脈硬化症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
血液およびリンパ系障害	69	(4.2)	79	2.7	93	(5.7)	109	3.6	162	(4.9)	188	3.2
貧血	42	(2.6)	46	1.6	61	(3.7)	67	2.2	103	(3.1)	113	1.9
鉄欠乏性貧血	7	(0.4)	7	0.2	4	(0.2)	4	0.1	11	(0.3)	11	0.2
血小板減少症	1	(0.1)	1	<0.1	8	(0.5)	8	0.3	9	(0.3)	9	0.2
リンパ節症	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
白血球増加症	4	(0.2)	4	0.1	1	(0.1)	1	<0.1	5	(0.2)	5	0.1
血小板増加症	3	(0.2)	3	0.1	1	(0.1)	2	0.1	4	(0.1)	5	0.1
好酸球増加症	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
縦隔リンパ節腫脹	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
小赤血球症	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
正色素性正球性貧血	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1
赤血球増加症	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
リンパ球減少症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
小球性貧血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
白血球減少症	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脾臓石灰化	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
リンパ節炎	0				0				0				1	(0.1)	1	0.1
悪性貧血	0				0				0				1	(0.1)	1	0.1
巨赤芽球性貧血	1	(0.1)	1	0.1	0				0				0			
好中球増加症	0				0				0				1	(0.1)	1	0.1
腎性貧血	0				1	(0.1)	1	0.1	0				0			
大球性貧血	0				0				1	(0.1)	1	0.1	0			
大赤血球症	0				0				0				1	(0.1)	1	0.1
単クローン性Ｂ細胞リンパ球増加症	1	(0.1)	1	0.1	0				0				0			
単球増加症	0				0				0				1	(0.1)	1	0.1
播種性血管内凝固	0				0				0				1	(0.1)	1	0.1
肺門リンパ節腫脹	1	(0.1)	1	0.1	0				0				0			
免疫性血小板減少性紫斑病	0				0				1	(0.1)	1	0.1	0			
脾腫	0				0				1	(0.1)	1	0.1	0			
脾臓障害	0				0				1	(0.1)	1	0.1	0			
脾肉芽腫	1	(0.1)	1	0.1	0				0				0			
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	38	(4.6)	43	2.9	48	(5.9)	58	4.0	32	(3.9)	38	2.5	29	(3.5)	36	2.4
甲状腺新生物	5	(0.6)	6	0.4	5	(0.6)	5	0.3	7	(0.9)	7	0.5	6	(0.7)	6	0.4
大腸腺腫	3	(0.4)	3	0.2	8	(1.0)	8	0.6	8	(1.0)	9	0.6	4	(0.5)	5	0.3
基底細胞癌	5	(0.6)	5	0.3	7	(0.9)	14	1.0	3	(0.4)	3	0.2	5	(0.6)	6	0.4
甲状腺の良性新生物	2	(0.2)	2	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2	1	(0.1)	1	0.1
皮膚乳頭腫	2	(0.2)	2	0.1	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1
脂肪腫	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1
子宮平滑筋腫	2	(0.2)	2	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
脂漏性角化症	0				2	(0.2)	2	0.1	0				2	(0.2)	2	0.1
眼の母斑	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
脾臓石灰化	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
リンパ節炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
悪性貧血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
巨赤芽球性貧血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
好中球増加症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
腎性貧血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
大球性貧血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大赤血球症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
単クローン性Ｂ細胞リンパ球増加症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
単球増加症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
播種性血管内凝固	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肺門リンパ節腫脹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
免疫性血小板減少性紫斑病	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脾腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脾臓障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
脾肉芽腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	86	(5.2)	101	3.4	61	(3.7)	74	2.4	147	(4.5)	175	2.9
甲状腺新生物	10	(0.6)	11	0.4	13	(0.8)	13	0.4	23	(0.7)	24	0.4
大腸腺腫	11	(0.7)	11	0.4	12	(0.7)	14	0.5	23	(0.7)	25	0.4
基底細胞癌	12	(0.7)	19	0.6	8	(0.5)	9	0.3	20	(0.6)	28	0.5
甲状腺の良性新生物	5	(0.3)	5	0.2	4	(0.2)	4	0.1	9	(0.3)	9	0.2
皮膚乳頭腫	5	(0.3)	5	0.2	2	(0.1)	2	0.1	7	(0.2)	7	0.1
脂肪腫	2	(0.1)	2	0.1	4	(0.2)	4	0.1	6	(0.2)	6	0.1
子宮平滑筋腫	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
脂漏性角化症	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
眼の母斑	2	(0.1)	2	0.1	1	(0.1)	1	<0.1	3	(0.1)	3	0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
前立腺癌	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
皮膚有棘細胞癌	2	(0.2)	3	0.2	1	(0.1)	1	0.1	0				0			
良性副甲状腺腫瘍	1	(0.1)	1	0.1	2	(0.2)	2	0.1	0				0			
アクロコルドン	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
ボーエン病	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
肝臓血管腫	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
血管筋脂肪腫	2	(0.2)	2	0.1	0				0				0			
骨血管腫	0				0				2	(0.2)	2	0.1	0			
単クローン性免疫グロブリン血症	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
皮膚の新生物	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
副腎の良性新生物	2	(0.2)	2	0.1	0				0				0			
慢性リンパ性白血病	0				2	(0.2)	2	0.1	0				0			
メラノサイト性母斑	1	(0.1)	1	0.1	0				0				0			
リンパ節の良性新生物	1	(0.1)	1	0.1	0				0				0			
外陰部癌第０期	0				1	(0.1)	1	0.1	0				0			
肝新生物	1	(0.1)	1	0.1	0				0				0			
眼瞼乳頭腫	0				0				1	(0.1)	1	0.1	0			
血管腫	0				1	(0.1)	1	0.1	0				0			
口唇の悪性新生物、病期不明	1	(0.1)	1	0.1	0				0				0			
甲状腺腺腫	0				0				1	(0.1)	1	0.1	0			
再発前立腺癌	0				0				0				1	(0.1)	1	0.1
子宮内膜腺癌	0				0				1	(0.1)	1	0.1	0			
十二指腸の良性新生物	1	(0.1)	1	0.1	0				0				0			
消化管粘膜下腫瘍	1	(0.1)	1	0.1	0				0				0			
線維腫	0				1	(0.1)	1	0.1	0				0			
前立腺新生物	1	(0.1)	1	0.1	0				0				0			
前立腺腺腫	0				0				0				1	(0.1)	1	0.1
直腸腺腫	0				1	(0.1)	1	0.1	0				0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
前立腺癌	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
皮膚有棘細胞癌	3	(0.2)	4	0.1	0				3	(0.1)	4	0.1
良性副甲状腺腫瘍	3	(0.2)	3	0.1	0				3	(0.1)	3	0.1
アクロコルドン	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
ボーエン病	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
肝臓血管腫	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
血管筋脂肪腫	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
骨血管腫	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
単クローン性免疫グロブリン血症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
皮膚の新生物	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
副腎の良性新生物	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
慢性リンパ性白血病	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
メラノサイト性母斑	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
リンパ節の良性新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
外陰部癌第０期	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
眼瞼乳頭腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血管腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
口唇の悪性新生物、病期不明	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
甲状腺腺腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
再発前立腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮内膜腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
十二指腸の良性新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管粘膜下腫瘍	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
線維腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
前立腺新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
前立腺腺腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
直腸腺腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
乳癌	1	(0.1)	1	0.1	0				0				0			
乳腺線維腺腫	0				1	(0.1)	1	0.1	0				0			
乳頭様甲状腺癌	0				0				1	(0.1)	1	0.1	0			
乳房の上皮内癌	0				1	(0.1)	1	0.1	0				0			
肺新生物	0				1	(0.1)	1	0.1	0				0			
肺扁平上皮癌	0				0				0				1	(0.1)	1	0.1
副腎新生物	0				0				1	(0.1)	1	0.1	0			
副腎腺腫	1	(0.1)	1	0.1	0				0				0			
平滑筋腫	0				0				0				1	(0.1)	1	0.1
本態性血小板血症	1	(0.1)	1	0.1	0				0				0			
卵巣良性腫瘍	0				0				0				1	(0.1)	1	0.1
良性新生物	0				0				0				1	(0.1)	1	0.1
良性髄膜腫	0				1	(0.1)	1	0.1	0				0			
良性腺腫	0				1	(0.1)	1	0.1	0				0			
涙管の良性新生物	1	(0.1)	1	0.1	0				0				0			
扁平上皮癌	0				1	(0.1)	1	0.1	0				0			
棘細胞腫	0				0				1	(0.1)	1	0.1	0			
膀胱移行上皮癌	0				0				0				1	(0.1)	1	0.1
膀胱新生物	0				0				1	(0.1)	1	0.1	0			
膀胱乳頭腫	0				1	(0.1)	1	0.1	0				0			
膵管内乳頭粘液性腫瘍	0				0				0				1	(0.1)	1	0.1
肝胆道系障害	30	(3.6)	34	2.3	26	(3.2)	33	2.3	37	(4.5)	45	3.0	26	(3.2)	34	2.2
脂肪肝	12	(1.5)	12	0.8	15	(1.8)	16	1.1	17	(2.1)	17	1.1	13	(1.6)	13	0.9
胆石症	14	(1.7)	14	0.9	8	(1.0)	8	0.6	13	(1.6)	13	0.9	8	(1.0)	8	0.5
胆嚢ポリープ	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	3	(0.4)	3	0.2
肝嚢胞	3	(0.4)	3	0.2	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
慢性胆嚢炎	0				1	(0.1)	1	0.1	3	(0.4)	3	0.2	2	(0.2)	2	0.1
肝腫大	0				0				3	(0.4)	3	0.2	1	(0.1)	1	0.1
肝脾腫大	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
乳癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳腺線維腺腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳頭様甲状腺癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳房の上皮内癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肺扁平上皮癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副腎新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副腎腺腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
平滑筋腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
本態性血小板血症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
卵巣良性腫瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
良性髄膜腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
良性腺腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
涙管の良性新生物	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
扁平上皮癌	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
棘細胞腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膀胱移行上皮癌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膀胱新生物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膀胱乳頭腫	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膵管内乳頭粘液性腫瘍	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝胆道系障害	56	(3.4)	67	2.3	63	(3.8)	79	2.6	119	(3.6)	146	2.4
脂肪肝	27	(1.6)	28	1.0	30	(1.8)	30	1.0	57	(1.7)	58	1.0
胆石症	22	(1.3)	22	0.8	21	(1.3)	21	0.7	43	(1.3)	43	0.7
胆嚢ポリープ	1	(0.1)	1	<0.1	6	(0.4)	6	0.2	7	(0.2)	7	0.1
肝嚢胞	4	(0.2)	4	0.1	2	(0.1)	2	0.1	6	(0.2)	6	0.1
慢性胆嚢炎	1	(0.1)	1	<0.1	5	(0.3)	5	0.2	6	(0.2)	6	0.1
肝腫大	0				4	(0.2)	4	0.1	4	(0.1)	4	0.1
肝脾腫大	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胆道仙痛	0				0				1	(0.1)	1	0.1	1	(0.1)	1	0.1
オッディ括約筋機能不全	0				0				0				1	(0.1)	1	0.1
肝機能異常	1	(0.1)	1	0.1	0				0				0			
肝硬変	0				1	(0.1)	1	0.1	0				0			
肝腫瘤	0				0				1	(0.1)	1	0.1	0			
肝障害	1	(0.1)	1	0.1	0				0				0			
肝臓痛	0				0				0				1	(0.1)	1	0.1
急性胆嚢炎	1	(0.1)	1	0.1	0				0				0			
高ビリルビン血症	0				0				1	(0.1)	1	0.1	0			
自己免疫性肝炎	1	(0.1)	1	0.1	0				0				0			
胆管拡張	0				0				0				1	(0.1)	1	0.1
胆管結石	0				1	(0.1)	1	0.1	0				0			
胆汁うっ滞	0				0				0				1	(0.1)	1	0.1
胆汁うっ滞性黄疸	0				1	(0.1)	1	0.1	0				0			
胆道障害	0				1	(0.1)	1	0.1	0				0			
胆嚢コレステリン沈着症	0				0				1	(0.1)	1	0.1	0			
胆嚢炎	0				0				1	(0.1)	1	0.1	0			
胆嚢痛	0				1	(0.1)	1	0.1	0				0			
薬物性肝障害	0				0				0				1	(0.1)	1	0.1
精神障害	37	(4.5)	41	2.8	37	(4.5)	40	2.8	31	(3.8)	31	2.1	27	(3.3)	31	2.0
不眠症	9	(1.1)	10	0.7	14	(1.7)	14	1.0	12	(1.5)	12	0.8	4	(0.5)	4	0.3
うつ病	14	(1.7)	15	1.0	9	(1.1)	9	0.6	8	(1.0)	8	0.5	7	(0.8)	7	0.5
不安	11	(1.3)	11	0.7	6	(0.7)	6	0.4	6	(0.7)	6	0.4	10	(1.2)	10	0.7
睡眠障害	0				1	(0.1)	1	0.1	0				2	(0.2)	2	0.1
ストレス	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
パニック発作	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
異常な夢	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
気分変化	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
譫妄	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
胆道仙痛	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
オッディ括約筋機能不全	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝機能異常	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝硬変	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝腫瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
肝障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
肝臓痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
急性胆嚢炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
高ビリルビン血症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
自己免疫性肝炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆管拡張	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆管結石	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆汁うっ滞	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆汁うっ滞性黄疸	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆道障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
胆嚢コレステリン沈着症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆嚢炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
胆嚢痛	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
薬物性肝障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精神障害	74	(4.5)	81	2.8	58	(3.5)	62	2.0	132	(4.0)	143	2.4
不眠症	23	(1.4)	24	0.8	16	(1.0)	16	0.5	39	(1.2)	40	0.7
うつ病	23	(1.4)	24	0.8	15	(0.9)	15	0.5	38	(1.2)	39	0.7
不安	17	(1.0)	17	0.6	16	(1.0)	16	0.5	33	(1.0)	33	0.6
睡眠障害	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
ストレス	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
パニック発作	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
異常な夢	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
気分変化	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
譫妄	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
リビドー減退	0				0				1	(0.1)	1	0.1	0			
易刺激性	1	(0.1)	1	0.1	0				0				0			
気分変調性障害	1	(0.1)	1	0.1	0				0				0			
気力低下	1	(0.1)	1	0.1	0				0				0			
激越	0				0				0				1	(0.1)	1	0.1
錯乱状態	0				0				1	(0.1)	1	0.1	0			
食物嫌悪	0				0				1	(0.1)	1	0.1	0			
神経過敏	0				1	(0.1)	1	0.1	0				0			
神経性過食症	0				0				0				1	(0.1)	1	0.1
身体表現性障害	0				0				0				1	(0.1)	1	0.1
睡眠時驚愕	0				1	(0.1)	1	0.1	0				0			
精神状態変化	0				0				1	(0.1)	1	0.1	0			
大うつ病	1	(0.1)	1	0.1	0				0				0			
怒り	0				0				0				1	(0.1)	1	0.1
不安障害	1	(0.1)	1	0.1	0				0				0			
無感情	0				1	(0.1)	1	0.1	0				0			
抑うつ症状	0				1	(0.1)	1	0.1	0				0			
落ち着きのなさ	0				1	(0.1)	1	0.1	0				0			
生殖系および乳房障害	23	(2.8)	23	1.5	23	(2.8)	25	1.7	19	(2.3)	22	1.5	25	(3.0)	26	1.7
良性前立腺肥大症	10	(1.2)	10	0.7	6	(0.7)	6	0.4	2	(0.2)	2	0.1	8	(1.0)	8	0.5
前立腺腫大	2	(0.2)	2	0.1	4	(0.5)	4	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1
勃起不全	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	3	(0.4)	3	0.2
女性化乳房	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	2	(0.2)	2	0.1
前立腺炎	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1	1	(0.1)	1	0.1
亀頭包皮炎	0				1	(0.1)	1	0.1	2	(0.2)	4	0.3	0			
骨盤痛	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
子宮内膜増殖症	0				2	(0.2)	2	0.1	0				0			
前立腺石灰化	0				0				0				2	(0.2)	2	0.1
乳房痛	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
リビドー減退	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
易刺激性	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
気分変調性障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
気力低下	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
激越	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
錯乱状態	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
食物嫌悪	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
神経過敏	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
神経性過食症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
身体表現性障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
睡眠時驚愕	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
精神状態変化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
大うつ病	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
怒り	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
不安障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
無感情	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
抑うつ症状	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
落ち着きのなさ	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
生殖系および乳房障害	46	(2.8)	48	1.6	44	(2.7)	48	1.6	90	(2.7)	96	1.6
良性前立腺肥大症	16	(1.0)	16	0.5	10	(0.6)	10	0.3	26	(0.8)	26	0.4
前立腺腫大	6	(0.4)	6	0.2	6	(0.4)	6	0.2	12	(0.4)	12	0.2
勃起不全	4	(0.2)	4	0.1	4	(0.2)	4	0.1	8	(0.2)	8	0.1
女性化乳房	1	(0.1)	1	<0.1	3	(0.2)	3	0.1	4	(0.1)	4	0.1
前立腺炎	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
亀頭包皮炎	1	(0.1)	1	<0.1	2	(0.1)	4	0.1	3	(0.1)	5	0.1
骨盤痛	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
子宮内膜増殖症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
前立腺石灰化	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
乳房痛	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
閉経後出血	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
萎縮性外陰腟炎	0				0				0				1	(0.1)	1	0.1
陰茎腫脹	0				0				0				1	(0.1)	1	0.1
陰部そう痒症	0				0				1	(0.1)	1	0.1	0			
外陰部障害	1	(0.1)	1	0.1	0				0				0			
外陰腟乾燥	1	(0.1)	1	0.1	0				0				0			
外陰腟腫脹	0				0				1	(0.1)	1	0.1	0			
外陰腟痛	0				0				1	(0.1)	1	0.1	0			
血精液症	0				0				0				1	(0.1)	1	0.1
子宮ポリープ	0				0				1	(0.1)	1	0.1	0			
子宮頚管ポリープ	0				1	(0.1)	2	0.1	0				0			
性器発疹	0				0				1	(0.1)	1	0.1	0			
精巣腫脹	0				1	(0.1)	1	0.1	0				0			
精巣腫瘤	0				1	(0.1)	1	0.1	0				0			
精巣嚢胞	1	(0.1)	1	0.1	0				0				0			
前立腺障害	0				0				0				1	(0.1)	1	0.1
乳汁漏出症	0				0				0				1	(0.1)	1	0.1
乳房圧痛	0				0				1	(0.1)	1	0.1	0			
乳房過形成	0				1	(0.1)	1	0.1	0				0			
乳房腫瘤	0				1	(0.1)	1	0.1	0				0			
乳房石灰化	0				0				0				1	(0.1)	1	0.1
乳房線維化	1	(0.1)	1	0.1	0				0				0			
不正子宮出血	0				1	(0.1)	1	0.1	0				0			
卵巣腫大	0				0				0				1	(0.1)	1	0.1
卵巣嚢胞	0				1	(0.1)	1	0.1	0				0			
腟出血	0				0				0				1	(0.1)	1	0.1
腟分泌物	0				0				1	(0.1)	1	0.1	0			
耳および迷路障害	28	(3.4)	31	2.1	17	(2.1)	18	1.2	20	(2.4)	21	1.4	14	(1.7)	17	1.1
回転性めまい	11	(1.3)	12	0.8	7	(0.9)	7	0.5	5	(0.6)	5	0.3	8	(1.0)	9	0.6

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
閉経後出血	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
萎縮性外陰腟炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
陰茎腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
陰部そう痒症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外陰部障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
外陰腟乾燥	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
外陰腟腫脹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外陰腟痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
血精液症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮ポリープ	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
子宮頚管ポリープ	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
性器発疹	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
精巣腫脹	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
精巣腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
精巣嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
前立腺障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳汁漏出症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳房圧痛	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳房過形成	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳房腫瘤	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
乳房石灰化	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
乳房線維化	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
不正子宮出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
卵巣腫大	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
卵巣嚢胞	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
膣出血	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膣分泌物	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
耳および迷路障害	45	(2.7)	49	1.7	34	(2.1)	38	1.3	79	(2.4)	87	1.5
回転性めまい	18	(1.1)	19	0.6	13	(0.8)	14	0.5	31	(0.9)	33	0.6

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
耳垢栓塞	7	(0.9)	7	0.5	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
耳痛	3	(0.4)	3	0.2	1	(0.1)	1	0.1	4	(0.5)	4	0.3	1	(0.1)	2	0.1
耳鳴	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	3	0.2
頭位性回転性めまい	2	(0.2)	2	0.1	2	(0.2)	2	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1
耳不快感	1	(0.1)	1	0.1	0				2	(0.2)	2	0.1	0			
耳閉	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
耳漏	0				1	(0.1)	1	0.1	1	(0.1)	1	0.1	0			
聴力低下	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
両耳難聴	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
感音性難聴	0				0				0				1	(0.1)	1	0.1
耳の障害	0				0				1	(0.1)	1	0.1	0			
耳出血	0				1	(0.1)	1	0.1	0				0			
中耳の炎症	1	(0.1)	1	0.1	0				0				0			
中耳滲出液	0				0				1	(0.1)	1	0.1	0			
難聴	0				0				1	(0.1)	1	0.1	0			
外科および内科処置	7	(0.9)	10	0.7	20	(2.4)	22	1.5	20	(2.4)	28	1.9	15	(1.8)	18	1.2
白内障手術	3	(0.4)	4	0.3	5	(0.6)	6	0.4	7	(0.9)	11	0.7	5	(0.6)	7	0.5
抜歯	2	(0.2)	2	0.1	3	(0.4)	3	0.2	5	(0.6)	8	0.5	3	(0.4)	3	0.2
冠動脈ステント挿入	0				3	(0.4)	3	0.2	0				1	(0.1)	1	0.1
冠動脈血行再建	0				2	(0.2)	2	0.1	2	(0.2)	2	0.1	0			
歯内療法	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
動静脈瘻手術	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
末梢血行再建	0				0				0				2	(0.2)	2	0.1
末梢動脈ステント挿入	0				1	(0.1)	1	0.1	0				1	(0.1)	1	0.1
冠動脈形成	0				0				1	(0.1)	1	0.1	0			
眼レーザー手術	0				0				1	(0.1)	1	0.1	0			
眼内レンズ挿入	0				1	(0.1)	2	0.1	0				0			
口腔手術	1	(0.1)	1	0.1	0				0				0			
消化管拡張術	0				0				1	(0.1)	1	0.1	0			

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Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
耳垢栓塞	8	(0.5)	8	0.3	3	(0.2)	3	0.1	11	(0.3)	11	0.2
耳痛	4	(0.2)	4	0.1	5	(0.3)	6	0.2	9	(0.3)	10	0.2
耳鳴	4	(0.2)	4	0.1	4	(0.2)	5	0.2	8	(0.2)	9	0.2
頭位性回転性めまい	4	(0.2)	4	0.1	3	(0.2)	3	0.1	7	(0.2)	7	0.1
耳不快感	1	(0.1)	1	<0.1	2	(0.1)	2	0.1	3	(0.1)	3	0.1
耳閉	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
耳漏	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
聴力低下	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
両耳難聴	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
感音性難聴	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
耳の障害	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
耳出血	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
中耳の炎症	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
中耳滲出液	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
難聴	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
外科および内科処置	27	(1.6)	32	1.1	35	(2.1)	46	1.5	62	(1.9)	78	1.3
白内障手術	8	(0.5)	10	0.3	12	(0.7)	18	0.6	20	(0.6)	28	0.5
抜歯	5	(0.3)	5	0.2	8	(0.5)	11	0.4	13	(0.4)	16	0.3
冠動脈ステント挿入	3	(0.2)	3	0.1	1	(0.1)	1	<0.1	4	(0.1)	4	0.1
冠動脈血行再建	2	(0.1)	2	0.1	2	(0.1)	2	0.1	4	(0.1)	4	0.1
歯内療法	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
動静脈瘻手術	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
末梢血行再建	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
末梢動脈ステント挿入	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
冠動脈形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼レーザー手術	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
眼内レンズ挿入	1	(0.1)	2	0.1	0				1	(<0.1)	2	<0.1
口腔手術	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
消化管拡張術	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1

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System organ class Preferred term	Sema 0.5 mg				Sema 1.0 mg				Placebo 0.5 mg				Placebo 1.0 mg			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心臓ペースメーカー挿入	0				0				0				1	(0.1)	1	0.1
心房中隔欠損修復	0				0				1	(0.1)	1	0.1	0			
水瘤手術	0				1	(0.1)	1	0.1	0				0			
性転換ホルモン療法	0				1	(0.1)	1	0.1	0				0			
入院	1	(0.1)	1	0.1	0				0				0			
鼻ポリープ切除	0				0				0				1	(0.1)	1	0.1
鼻手術	0				0				1	(0.1)	1	0.1	0			
膝関節形成	0				0				1	(0.1)	1	0.1	0			
末梢動脈バイパス	0				0				1	(0.1)	1	0.1	0			
末梢動脈形成	0				0				0				1	(0.1)	1	0.1
網膜レーザー凝固	0				1	(0.1)	1	0.1	0				0			
翼状片手術	1	(0.1)	1	0.1	0				0				0			
内分泌障害	15	(1.8)	16	1.1	15	(1.8)	16	1.1	7	(0.9)	8	0.5	14	(1.7)	14	0.9
甲状腺機能低下症	8	(1.0)	8	0.5	4	(0.5)	4	0.3	2	(0.2)	2	0.1	7	(0.8)	7	0.5
甲状腺腫	4	(0.5)	4	0.3	4	(0.5)	4	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1
甲状腺機能亢進症	0				2	(0.2)	3	0.2	0				1	(0.1)	1	0.1
甲状腺嚢腫	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
性腺機能低下	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
続発性副甲状腺機能亢進症	1	(0.1)	1	0.1	0				1	(0.1)	1	0.1	0			
男性性腺機能低下	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
原発性副甲状腺機能亢進症	0				0				0				1	(0.1)	1	0.1
抗利尿ホルモン不適合分泌	0				0				1	(0.1)	1	0.1	0			
甲状腺炎	0				1	(0.1)	1	0.1	0				0			
甲状腺障害	0				1	(0.1)	1	0.1	0				0			
自己免疫性甲状腺炎	0				0				1	(0.1)	1	0.1	0			
副甲状腺機能亢進症	0				0				0				1	(0.1)	1	0.1
副腎機能亢進症	0				0				0				1	(0.1)	1	0.1
副腎腫瘤	0				0				1	(0.1)	1	0.1	0			
副腎障害	0				1	(0.1)	1	0.1	0				0			

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System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
心臓ペースメーカー挿入	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心房中隔欠損修復	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
水瘤手術	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
性転換ホルモン療法	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
入院	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
鼻ポリープ切除	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
鼻手術	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
膝関節形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈バイパス	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
末梢動脈形成	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
網膜レーザー凝固	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
翼状片手術	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
内分泌障害	30	(1.8)	32	1.1	21	(1.3)	22	0.7	51	(1.6)	54	0.9
甲状腺機能低下症	12	(0.7)	12	0.4	9	(0.5)	9	0.3	21	(0.6)	21	0.4
甲状腺腫	8	(0.5)	8	0.3	4	(0.2)	4	0.1	12	(0.4)	12	0.2
甲状腺機能亢進症	2	(0.1)	3	0.1	1	(0.1)	1	<0.1	3	(0.1)	4	0.1
甲状腺嚢腫	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
性腺機能低下	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
続発性副甲状腺機能亢進症	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
男性性腺機能低下	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
原発性副甲状腺機能亢進症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
抗利尿ホルモン不適合分泌	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
甲状腺炎	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
甲状腺障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
自己免疫性甲状腺炎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副甲状腺機能亢進症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副腎機能亢進症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副腎腫瘤	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
副腎障害	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

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System organ class Preferred term	Sema 0.5 mg N	(%)	E	R	Sema 1.0 mg N	(%)	E	R	Placebo 0.5 mg N	(%)	E	R	Placebo 1.0 mg N	(%)	E	R
免疫系障害	8	(1.0)	8	0.5	8	(1.0)	8	0.6	3	(0.4)	3	0.2	4	(0.5)	4	0.3
季節性アレルギー	5	(0.6)	5	0.3	5	(0.6)	5	0.3	2	(0.2)	2	0.1	2	(0.2)	2	0.1
薬物過敏症	1	(0.1)	1	0.1	2	(0.2)	2	0.1	1	(0.1)	1	0.1	2	(0.2)	2	0.1
過敏症	1	(0.1)	1	0.1	1	(0.1)	1	0.1	0				0			
節足動物咬傷アレルギー	1	(0.1)	1	0.1	0				0				0			
先天性、家族性および遺伝性障害	2	(0.2)	2	0.1	0				2	(0.2)	2	0.1	5	(0.6)	5	0.3
陰嚢水瘤	0				0				0				2	(0.2)	2	0.1
過長結腸	0				0				0				1	(0.1)	1	0.1
心室中隔欠損症	0				0				1	(0.1)	1	0.1	0			
心房中隔欠損症	0				0				1	(0.1)	1	0.1	0			
動静脈奇形	1	(0.1)	1	0.1	0				0				0			
皮様嚢腫	0				0				0				1	(0.1)	1	0.1
融合腎	0				0				0				1	(0.1)	1	0.1
臍奇形	1	(0.1)	1	0.1	0				0				0			
社会環境	1	(0.1)	1	0.1	0				0				1	(0.1)	1	0.1
歯科補てつ物使用者	0				0				0				1	(0.1)	1	0.1
食事療法非遵守	1	(0.1)	1	0.1	0				0				0			

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

Mild adverse events by system organ class and preferred term - summary - on-treatment - safety analysis set

System organ class Preferred term	Sema				Placebo				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
免疫系障害	16	(1.0)	16	0.5	7	(0.4)	7	0.2	23	(0.7)	23	0.4
季節性アレルギー	10	(0.6)	10	0.3	4	(0.2)	4	0.1	14	(0.4)	14	0.2
薬物過敏症	3	(0.2)	3	0.1	3	(0.2)	3	0.1	6	(0.2)	6	0.1
過敏症	2	(0.1)	2	0.1	0				2	(0.1)	2	<0.1
節足動物咬傷アレルギー	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
先天性、家族性および遺伝性障害	2	(0.1)	2	0.1	7	(0.4)	7	0.2	9	(0.3)	9	0.2
陰嚢水瘤	0				2	(0.1)	2	0.1	2	(0.1)	2	<0.1
過長結腸	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心室中隔欠損症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
心房中隔欠損症	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
動静脈奇形	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
皮様嚢腫	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
融合腎	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
臍奇形	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1
社会環境	1	(0.1)	1	<0.1	1	(0.1)	1	<0.1	2	(0.1)	2	<0.1
歯科補てつ物使用者	0				1	(0.1)	1	<0.1	1	(<0.1)	1	<0.1
食事療法非遵守	1	(0.1)	1	<0.1	0				1	(<0.1)	1	<0.1

MedDRA version 18.0. The 'on-treatment' summary of adverse events comprises events with onset on or after the day of first dose and until the subject's end-of-treatment, defined as the end-of-treatment follow-up visit scheduled 5 weeks after date of last dose, date of last dose plus 42 days or end of the subject's in-trial period, whichever comes first. Exposure time is calculated as the duration of this time span. Table is sorted in descending order by class and/or term based on the total percentage of subjects experiencing at least one event. Abbreviations: E: number of events, N: Number of subjects experiencing at least one event, R: event rate per 100 years of exposure, seq.: sequelae, %: percentage of subjects experiencing at least one event.

表 2.7.6.25.2-7　転記「死亡」の有害事象一覧 - in-trial 期間 – すべての無作為割り付け症例

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
103007 Sema 0.5 mg Sema 0.5 mg M/71/29.0	一般・全身障害および投与部位の状態/ 死亡/ Indetermined Cause Death	17DEC2014/ Fatal	472	Y	1	3	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
106005 Placebo 0.5 mg Placebo 0.5 mg F/69/27.0	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 胆嚢腺癌/ Adenocarcinoma And Well-Differentiated Infiltrating Gallbladder	17JUN2014/ Fatal	343	Y	60	4	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
122002 Sema 1.0 mg Sema 1.0 mg M/55/37.3	呼吸器、胸郭および縦隔障害/ 急性肺水腫/ Acute Pulmonary Edema	09NOV2014/ Fatal	496	Y	1	3	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
122007 Placebo 0.5 mg Placebo 0.5 mg M/77/29.0	心臓障害/ 急性心不全/ Acute Heart Failure	30JUL2015/ Fatal	751	N	1	7	Y/ Severe	Y	Unlikely/ Not Applicable	N
122020 Sema 0.5 mg Sema 0.5 mg M/69/29.2	心臓障害/ うっ血性心不全/ Worsening Congestive Heart Failure	23AUG2014/ Fatal	349	Y	1	7	Y/ Severe	Y	Unlikely/ Dose Not Changed	N

MedDRA version 18.0 ,
Age (years), M: Male,F: Female, BMI: Body mass index (kg/m^2).
Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
122031 Sema 0.5 mg Sema 0.5 mg F/65/38.7	心臓障害/ 心不全/ Decompensated Heart Failure	10AUG2015/ Fatal	628	Y	5	10	Y/ Severe	Y	Unlikely/ Not Applicable	N
122034 Placebo 0.5 mg Placebo 0.5 mg M/77/35.8	一般・全身障害および投与部位の状態/ 死亡/ Death	01MAR2014/ Fatal	96	Y	1	1	Y/ Severe	Y	Nk/ Dose Not Changed	N
123019 Sema 1.0 mg Sema 1.0 mg M/63/35.6	心臓障害/ 心原性ショック/ Irreversible Cardiogenic Shock	27SEP2015/ Fatal	761	Y	1	6	Y/ Severe	Y	Unlikely/ Not Applicable	N
123024 Placebo 0.5 mg Placebo 0.5 mg M/63/29.5	心臓障害/ 心原性ショック/ Irreversible Cardiogenic Shock	06JUN2015/ Fatal	640	Y	1	1	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
124013 Placebo 1.0 mg Placebo 1.0 mg M/69/32.4	心臓障害/ 完全房室ブロック/ Complete A-V Block	23JUN2015/ Fatal	644	Y	4	2	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
125019 Placebo 1.0 mg Placebo 1.0 mg M/53/34.1	感染症および寄生虫症/ 敗血症/ Sepsis	18JUL2014/ Fatal	262	Y	35	5	Y/ Severe	Y	Unlikely/ Not Applicable	N

MedDRA version 18.0 ,
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Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
127038 Placebo 1.0 mg Placebo 1.0 mg F/69/29.4	心臓障害/ 心筋梗塞/ Myocardial Infarction	21MAR2014/ Fatal	164	Y	5	4	Y/ Moderate	Y	Unlikely/ Dose Not Changed	N
127045 Placebo 0.5 mg Placebo 0.5 mg M/64/29.8	神経系障害/ 虚血性脳卒中/ Ischemic Stroke	15SEP2014/ Fatal	307	N	39	2	Y/ Severe	Y	Unlikely/ Not Applicable	N
141015 Sema 1.0 mg Sema 1.0 mg M/71/21.1	心臓障害/ 肺動脈弁狭窄/ Pulmonary Stenosis	01MAR2014/ Fatal	143	N	386	6	Y/ Severe	Y	Unlikely/ Not Applicable	N
	呼吸器、胸郭および縦隔障害/ 慢性閉塞性肺疾患/ Chronic Obstructive Airways Disease (End Stage)	21MAR2015/ Fatal	528	N	1	5	Y/ Severe	Y	Unlikely/ Not Applicable	N
	心臓障害/ 心筋虚血/ Ischaemic Heart Disease	21MAR2015/ Fatal	528	N	1	7	Y/ Severe	Y	Unlikely/ Not Applicable	N
148002 Placebo 0.5 mg Placebo 0.5 mg F/58/29.2	心臓障害/ うっ血性心不全/ Congestive Cardiac Failure	15DEC2013/ Fatal	69	Y	1	2	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
165004 Placebo 0.5 mg Placebo 0.5 mg F/67/23.5	神経系障害/ 出血性卒中/ Hemorrhagic Stroke	06MAY2014/ Fatal	152	N	7	3	Y/ Severe	Y	Unlikely/ Not Applicable	N

MedDRA version 18.0 ,
Age (years), M: Male,F: Female, BMI: Body mass index (kg/m^2).
Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
165004 Placebo 0.5 mg Placebo 0.5 mg F/67/23.5	感染症および寄生虫症/ 敗血症性ショック/ Septic Shock	11MAY2014/ Fatal	157	N	2	2	Y/ Severe	Y	Unlikely/ Not Applicable	N
169001 Sema 1.0 mg Sema 1.0 mg M/74/34.0	心臓障害/ 心筋梗塞/ Myocardial Infarction	21OCT2015/ Fatal	686	Y	1	4	Y/ Severe	Y	Possible/ Dose Not Changed	N
169005 Placebo 0.5 mg Placebo 0.5 mg M/65/32.8	胃腸障害/ 上部消化管出血/ Upper Gastrointestinal Haemorrhage	15MAY2014/ Fatal	163	Y	4	4	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	血管障害/ 出血性ショック/ Hemorrhagic Shock	18MAY2014/ Fatal	166	Y	1	5	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
202016 Placebo 0.5 mg Placebo 0.5 mg M/68/27.8	一般・全身障害および投与部位の状態/ 突然死/ Sudden Death	20MAR2015/ Fatal	468	Y	1	12	Y/ Severe	Y	Unlikely/ Not Applicable	N
203003 Placebo 0.5 mg Placebo 0.5 mg M/55/28.0	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 遠隔転移を伴う膵癌/ Pancreatic Adenocarcinoma Metastatic	13OCT2014/ Fatal	513	Y	282	17	Y/ Severe	Y	Possible/ Drug Withdrawn	N

MedDRA version 18.0 ,
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Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
205027 Placebo 1.0 mg M/72/38.2	腎および尿路障害/ 急性腎不全/ Acute On Chronic Renal Failure	22DEC2014/ Fatal	404	N	4	1	Y/ Severe	Y	/	
215008 Sema 0.5 mg Sema 0.5 mg F/65/29.3	代謝および栄養障害/ 乳酸アシドーシス/ Severe Lactate Acidosis	28DEC2014/ Fatal	516	N	2	10	Y/ Severe	Y	Unlikely/ Not Applicable	N
216006 Sema 1.0 mg Sema 1.0 mg F/61/24.8	一般・全身障害および投与部位の状態/ 死亡/ Death	28NOV2014/ Fatal	509	Y	1	6	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
226023 Sema 0.5 mg Sema 0.5 mg F/61/20.2	心臓障害/ 急性心筋梗塞/ Acute Myocardial Infarction	30JUL2015/ Fatal	638	Y	1	11	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
227015 Sema 1.0 mg Sema 1.0 mg F/71/33.4	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 遠隔転移を伴う甲状腺癌/ Metastatic Thyroid Papillary Adenocarcinoma	13AUG2015/ Fatal	661	N	1	17	Y/ Severe	Y	Unlikely/ Not Applicable	N
229001 Placebo 0.5 mg Placebo 0.5 mg F/51/25.7	呼吸器、胸郭および縦隔障害/ 喉頭狭窄/ Laryngeal Stenosis	28APR2015/ Fatal	636	Y	2	2	Y/ Severe	Y	Unlikely/ Dose Not Changed	N

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Age (years), M: Male,F: Female, BMI: Body mass index (kg/m^2).
Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
229017 Sema 0.5 mg Sema 0.5 mg M/64/30.8	心臓障害/ 急性心筋梗塞/ Acute Myocardial Infarction	30JUN2015/ Fatal	622	Y	1	7	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
229024 Placebo 1.0 mg Placebo 1.0 mg F/57/21.3	感染症および寄生虫症/ 胃腸炎/ Acute Gastroenteritis	16JAN2015/ Fatal	431	Y	17	3	Y/ Severe	Y	Unlikely/ Not Applicable	N
	感染症および寄生虫症/ 敗血症性ショック/ Septic Shock	31JAN2015/ Fatal	446	Y	2	2	Y/ Severe	Y	Unlikely/ Not Applicable	N
233001 Placebo 1.0 mg Placebo 1.0 mg M/65/27.6	心臓障害/ 急性心筋梗塞/ Acute Miocardial Infarction	15MAR2014/ Fatal	223	Y	1	4	Y/ Severe	Y	Unlikely/ Not Applicable	N
	感染症および寄生虫症/ 敗血症性ショック/ Septic Shock	15MAR2014/ Fatal	223	Y	1	3	Y/ Severe	Y	Unlikely/ Not Applicable	N
233014 Placebo 1.0 mg Placebo 1.0 mg M/64/27.3	感染症および寄生虫症/ 敗血症性ショック/ Septic Shock	01JUL2015/ Fatal	630	Y	1	14	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
251015 Sema 1.0 mg Sema 1.0 mg F/58/28.2	心臓障害/ 心不全/ Heart Failure. Dysfunction Of The Mitral Valve Prosthesis.	14MAY2014/ Fatal	189	Y	34	10	Y/ Severe	Y	Possible/ Drug Withdrawn	N

MedDRA version 18.0 ,
Age (years), M: Male,F: Female, BMI: Body mass index (kg/m^2).
Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
258024 Placebo 1.0 mg Placebo 1.0 mg M/61/33.3	心臓障害/ 心筋虚血/ Acute Myocardial Ischemia	16FEB2015/ Fatal	453	Y	7	18	Y/ Severe	Y	Unlikely/ Not Applicable	N
	心臓障害/ 心室細動/ Ventricular Fibrillation	22FEB2015/ Fatal	459	Y	1	20	Y/ Severe	Y	Unlikely/ Not Applicable	N
259001 Sema 1.0 mg Sema 1.0 mg F/71/38.1	一般・全身障害および投与部位の状態/ 死亡/ Death	18MAY2015/ Fatal	750	Y	1	13	Y/ Severe	Y	Unlikely/ Not Applicable	N
259009 Placebo 0.5 mg Placebo 0.5 mg F/63/37.5	心臓障害/ 急性心不全/ Acute Heart Failure	07FEB2015/ Fatal	578	Y	1	5	Y/ Severe	Y	Unlikely/ Not Applicable	N
259022 Placebo 0.5 mg Placebo 0.5 mg F/69/32.8	一般・全身障害および投与部位の状態/ 死亡/ Death Due To Unknown Cause	16JUN2014/ Fatal	243	Y	1	3	Y/ Severe	Y	Unlikely/ Not Applicable	N
260017 Placebo 1.0 mg Placebo 1.0 mg M/63/29.1	心臓障害/ 心筋梗塞/ Myocardial Infarction	14JAN2014/ Fatal	106	Y	1	1	Y/ Severe	Y	Possible/ Not Applicable	N

MedDRA version 18.0 ,
Age (years), M: Male,F: Female, BMI: Body mass index (kg/m^2).
Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
260018 Sema 0.5 mg Sema 0.5 mg M/66/39.1	呼吸器、胸郭および縦隔障害/ 肺水腫/ Pulmonary Edema	29MAY2015/ Fatal	576	Y	1	3	Y/ Severe	Y	Unlikely/ Not Applicable	N
262014 Sema 1.0 mg Sema 1.0 mg M/65/31.7	神経系障害/ 虚血性脳卒中/ Repeated Ischemic Stroke	22JUN2014/ Fatal	286	Y	5	6	Y/ Severe	Y	Unlikely/ Not Applicable	N
262035 Sema 1.0 mg Sema 1.0 mg F/54/38.1	神経系障害/ 虚血性脳卒中/ Acute Ischemic Stroke.	21MAR2014/ Fatal	150	Y	3	1	Y/ Severe	Y	Possible/ Dose Not Changed	N
262039 Sema 0.5 mg Sema 0.5 mg F/63/32.1	心臓障害/ 急性心不全/ Acute Cardiovascular Failure	11OCT2015/ Fatal	721	Y	1	2	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
284013 Placebo 0.5 mg Placebo 0.5 mg M/68/34.1	呼吸器、胸郭および縦隔障害/ 急性呼吸不全/ Acute Respiratory Failure	02DEC2014/ Fatal	484	Y	92	20	Y/ Severe	Y	Unlikely/ Drug Interrupted	N
	感染症および寄生虫症/ 敗血症性ショック/ Septic Shock	02DEC2014/ Fatal	484	Y	92	19	Y/ Severe	Y	Unlikely/ Drug Interrupted	N
	腎および尿路障害/ 慢性腎臓病/ Chronic Kindey Disease,stage4-5 Worsening	10DEC2014/ Fatal	492	Y	84	21	Y/ Severe	Y	Unlikely/ Not Applicable	N

MedDRA version 18.0 ,
Age (years), M: Male,F: Female, BMI: Body mass index (kg/m^2).
Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
284015 Placebo 1.0 mg Placebo 1.0 mg M/58/25.1	心臓障害/ 心原性ショック/ Cardiogenic Shock	07MAR2015/ Fatal	562	Y	1	4	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
303001 Sema 0.5 mg Sema 0.5 mg F/64/30.9	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 肝転移/ Suspected Liver Metastasis	11FEB2015/ Fatal	618	Y	74	7	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	腎および尿路障害/ 急性腎不全/ Acute Kidney Insufficiency	19APR2015/ Fatal	685	Y	7	9	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	感染症および寄生虫症/ 蜂巣炎/ Cellulitis Left Leg	19APR2015/ Fatal	685	Y	7	8	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	感染症および寄生虫症/ 敗血症/ Severe Sepsis	19APR2015/ Fatal	685	Y	7	10	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	代謝および栄養障害/ アシドーシス/ Severe Acidosis	19APR2015/ Fatal	685	Y	7	11	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
321002 Sema 0.5 mg Sema 0.5 mg M/62/37.6	一般・全身障害および投与部位の状態/ 心突然死/ Cardiac-Dependent Sudden Death	02SEP2013/ Fatal	98	Y	1	4	Y/ Severe	Y	Unlikely/ Not Applicable	N

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Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
325014 Placebo 0.5 mg Placebo 0.5 mg F/65/44.2	心臓障害/ 心筋梗塞/ Myocardial Infarction	24DEC2013/ Fatal	40	Y	1	2	Y/ Severe	Y	Unlikely/ Not Applicable	N
326007 Sema 0.5 mg Sema 0.5 mg M/72/31.5	一般・全身障害および投与部位の状態/ 死亡/ Death From Natural Causes	22DEC2013/ Fatal	73	Y	1	2	Y/ Severe	Y	Unlikely/ Not Applicable	N
326009 Placebo 1.0 mg Placebo 1.0 mg M/70/28.1	感染症および寄生虫症/ 脾臓膿瘍/ Splenic Abscess	05DEC2014/ Fatal	393	Y	60	3	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	神経系障害/ 脳虚血/ Ischemic Cerebrovascular Disease	18DEC2014/ Fatal	406	Y	47	4	Y/ Severe	Y	Unlikely/ Not Applicable	N
326010 Placebo 0.5 mg Placebo 0.5 mg M/57/22.0	一般・全身障害および投与部位の状態/ 死亡/ Unknown Cause Of Death	15JUL2015/ Fatal	595	N	1	7	Y/ Severe	Y	Unlikely/ Not Applicable	N
327021 Placebo 0.5 mg Placebo 0.5 mg M/67/30.8	一般・全身障害および投与部位の状態/ 多臓器不全/ Multiple Organ Failure	28NOV2015/ Fatal	752	Y	21	6	Y/ Severe	Y	Unlikely/ Not Applicable	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
329002 Sema 0.5 mg Sema 0.5 mg M/60/33.6	一般・全身障害および投与部位の状態/ 突然死/ Sudden Death	26FEB2014/ Fatal	232	Y	1	3	Y/ Severe	Y	Possible/ Dose Not Changed	N
329007 Sema 0.5 mg Sema 0.5 mg M/83/27.3	心臓障害/ 急性心筋梗塞/ Suddenly Myocardial Infarction	19MAR2015/ Fatal	542	Y	1	32	Y/ Severe	Y	Possible/ Dose Not Changed	N
329009 Sema 0.5 mg Sema 0.5 mg M/69/30.0	心臓障害/ 急性冠動脈症候群/ Acute Coronary Syndrome	02NOV2013/ Fatal	23	Y	4	4	Y/ Severe	Y	Possible/ Dose Not Changed	N
401002 Placebo 0.5 mg Placebo 0.5 mg M/79/28.9	心臓障害/ 心肺不全/ Acute Cardiopulmonary Insufficiency	02MAR2014/ Fatal	363	Y	1	6	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
403007 Placebo 0.5 mg Placebo 0.5 mg M/58/42.9	心臓障害/ 急性心不全/ Acute Heart Failure	09JUN2014/ Fatal	455	Y	3	11	Y/ Severe	Y	Unlikely/ Not Applicable	N
	腎および尿路障害/ 急性腎不全/ Acute Renal Failure	09JUN2014/ Fatal	455	Y	3	10	Y/ Severe	Y	Unlikely/ Not Applicable	N
404016 Sema 0.5 mg Sema 0.5 mg M/53/38.5	神経系障害/ 出血性卒中/ Hemorrhagic Stroke	05JUL2013/ Fatal	100	Y	1	2	Y/ Severe	Y	Unlikely/ Dose Not Changed	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
404022 Sema 1.0 mg Sema 1.0 mg M/63/33.4	感染症および寄生虫症/ 蜂巣炎/ Phlegmon Of The Left Leg And Foot.	14JAN2014/ Fatal	243	Y	92	3	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	感染症および寄生虫症/ ブドウ球菌性敗血症/ Staphylococcal Sepsis	04APR2014/ Fatal	323	Y	12	4	Y/ Severe	Y	Unlikely/ Unknown	N
	心臓障害/ 心血管不全/ Acute Cardiovascular Insufficiency	09APR2014/ Fatal	328	Y	7	5	Y/ Severe	Y	Unlikely/ Unknown	N
	呼吸器、胸郭および縦隔障害/ 呼吸不全/ Respiratory Insufficiency	09APR2014/ Fatal	328	Y	7	6	Y/ Severe	Y	Unlikely/ Unknown	N
405012 Placebo 1.0 mg Placebo 1.0 mg F/74/38.3	心臓障害/ 急性左室不全/ Acute Left Ventricular Failure	05DEC2013/ Fatal	65	Y	4	2	Y/ Severe	Y	Unlikely/ Not Applicable	N
	感染症および寄生虫症/ 肺炎/ Bilateral Pneumonia	07DEC2013/ Fatal	67	Y	2	7	Y/ Severe	Y	Unlikely/ Not Applicable	N
	呼吸器、胸郭および縦隔障害/ 肺高血圧症/ Pulmonary Hypertension	08DEC2013/ Fatal	68	Y	1	4	Y/ Severe	N	Unlikely/ Not Applicable	N
	心臓障害/ 右室不全/ Right Ventricular Heart Failure	08DEC2013/ Fatal	68	Y	1	8	Y/ Severe	Y	Unlikely/ Not Applicable	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
405012 Placebo 1.0 mg Placebo 1.0 mg F/74/38.3	心臓障害/ 心室無収縮/ Ventricular Asystole	08DEC2013/ Fatal	68	Y	1	5	Y/ Severe	Y	Unlikely/ Not Applicable	N
444009 Sema 1.0 mg Sema 1.0 mg M/63/28.9	感染症および寄生虫症/ 肺炎/ Poststenotic Pneumonia	09APR2015/ Fatal	583	Y	150	4	Y/ Moderate	Y	Unlikely/ Dose Not Changed	N
	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 肺腺癌第４期/ Lung Adenocarcinoma Stage Iv	23APR2015/ Fatal	597	Y	136	2	Y/ Severe	Y	Unlikely/ Drug Withdrawn	N
462009 Placebo 1.0 mg Placebo 1.0 mg M/79/31.5	胃腸障害/ 胃腸虚血/ Gut Ischemia	08FEB2015/ Fatal	580	Y	17	3	Y/ Severe	Y	Unlikely/ Drug Withdrawn	N
	胃腸障害/ 腸出血/ Intestinal Hemorrhage	24FEB2015/ Fatal	596	Y	1	4	Y/ Severe	Y	Unlikely/ Not Applicable	N
462011 Sema 1.0 mg Sema 1.0 mg M/76/32.7	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 小細胞肺癌/ Small-Cell Lung Cancer	13AUG2014/ Fatal	393	Y	42	2	Y/ Severe	Y	Unlikely/ Dose Not Changed	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
462011 Sema 1.0 mg Sema 1.0 mg M/76/32.7	呼吸器、胸郭および縦隔障害/ 慢性閉塞性肺疾患/ Chronic Obstructive Pulmonary Disease (Copd)	28AUG2014/ Fatal	408	Y	27	3	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
463001 Sema 0.5 mg Sema 0.5 mg F/84/32.9	心臓障害/ 完全房室ブロック/ Atrioventicular Block Iii Degree	05FEB2014/ Fatal	290	Y	2	4	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	心臓障害/ 洞性徐脈/ Sinus Bradicardia (38 Bpm)	05FEB2014/ Fatal	290	Y	2	2	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	心臓障害/ 心停止/ Cardiac Arrest	06FEB2014/ Fatal	291	Y	1	5	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
481018 Placebo 1.0 mg Placebo 1.0 mg F/72/25.1	心臓障害/ 心停止/ Carrdiac Arrest	05MAY2015/ Fatal	707	N	1	18	Y/ Severe	Y	Unlikely/ Not Applicable	N
481022 Placebo 1.0 mg Placebo 1.0 mg M/65/31.9	心臓障害/ 心不全/ Worsening Of Heart Failure	31OCT2014/ Fatal	509	Y	1	8	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
482014 Placebo 1.0 mg Placebo 1.0 mg F/66/43.1	呼吸器、胸郭および縦隔障害/ 肺塞栓症/ Pulmonary Embolism.	17JUL2015/ Fatal	676	Y	1	5	Y/ Severe	Y	Unlikely/ Dose Not Changed	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
484012 Placebo 1.0 mg Placebo 1.0 mg M/60/31.8	心臓障害/ 急性心筋梗塞/ Acute Myocardial Infarction	17MAR2014/ Fatal	153	N	1	2	Y/ Severe	Y	Unlikely/ Not Applicable	N
485017 Sema 0.5 mg Sema 0.5 mg F/66/34.0	胃腸障害/ 胃腸出血/ Acute Gastrointestinal Bleeding	22JAN2014/ Fatal	72	Y	1	1	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
505007 Sema 1.0 mg Sema 1.0 mg M/79/35.1	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 腎細胞癌/ Renal Cell Carcinoma	13FEB2014/ Fatal	248	Y	330	24	Y/ Severe	Y	Unlikely/ Drug Withdrawn	N
506010 Sema 0.5 mg Sema 0.5 mg F/64/25.8	神経系障害/ 血管性パーキンソニズム/ Vascular Parkinsonism (Chronic)	27JAN2014/ Fatal	225	Y	208	5	Y/ Severe	Y	Unlikely/ Drug Withdrawn	N
521020 Sema 0.5 mg Sema 0.5 mg M/63/33.9	心臓障害/ 大動脈弁疾患/ Aortic Valve Disease	22NOV2013/ Fatal	72	Y	1	3	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	心臓障害/ 心不全/ Sudden Death At Home-Heart Failure	22NOV2013/ Fatal	72	Y	1	2	Y/ Severe	Y	Unlikely/ Dose Not Changed	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
524013 Sema 1.0 mg Sema 1.0 mg F/72/42.7	心臓障害/ 心筋梗塞/ Myocardial Infarction	22APR2015/ Fatal	632	Y	1	16	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
525024 Sema 1.0 mg Sema 1.0 mg M/74/36.8	感染症および寄生虫症/ 肺炎/ Death Due To Pneumonia.	04FEB2014/ Fatal	118	N	9	10	Y/ Severe	Y	Unlikely/ Not Applicable	N
526044 Sema 1.0 mg Sema 1.0 mg M/86/30.3	感染症および寄生虫症/ 肺炎/ Pneumonia Which Led To Patient's Death	27MAY2014/ Fatal	184	Y	17	6	Y/ Severe	Y	Unlikely/ Not Applicable	N
528005 Placebo 1.0 mg Placebo 1.0 mg M/77/29.1	神経系障害/ 脳血管発作/ Cerebrovascular Accident Leading To Death	27OCT2015/ Fatal	777	N	7	14	Y/ Severe	Y	Unlikely/ Not Applicable	N
552030 Sema 1.0 mg Sema 1.0 mg M/69/28.0	神経系障害/ 脳梗塞/ Cerebral Infarction	05NOV2015/ Fatal	723	N	52	7	Y/ Moderate	Y	Unlikely/ Not Applicable	N
559004 Sema 1.0 mg Sema 1.0 mg M/75/28.9	一般・全身障害および投与部位の状態/ 死亡/ Death	02DEC2014/ Fatal	545	N	1	4	Y/ Severe	Y	Unlikely/ Not Applicable	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
560009 Placebo 1.0 mg Placebo 1.0 mg M/70/38.2	一般・全身障害および投与部位の状態/ 多臓器不全/ Multi-Organ Failure	19NOV2015/ Fatal	743	N	1	30	Y/ Severe	Y	Unlikely/ Not Applicable	N
	心臓障害/ 心筋梗塞/ Myocardial Infarction	19NOV2015/ Fatal	743	N	1	25	Y/ Severe	Y	Unlikely/ Not Applicable	N
562005 Placebo 0.5 mg Placebo 0.5 mg F/72/24.7	心臓障害/ 第一度房室ブロック/ 1st Degree Av Block	20OCT2013/ Fatal	31	Y	4	15	Y/ Moderate	Y	Possible/ Dose Not Changed	N
	腎および尿路障害/ 急性腎不全/ Acute Renal Failure	20OCT2013/ Fatal	31	Y	4	17	Y/ Severe	Y	Possible/ Dose Not Changed	N
	心臓障害/ 徐脈/ Bradycardia	20OCT2013/ Fatal	31	Y	4	14	Y/ Severe	Y	Possible/ Dose Not Changed	N
	免疫系障害/ アナフィラキシーショック/ Anaphylactic Shock	20OCT2013/ Fatal	31	Y	4	18	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	傷害、中毒および処置合併症/ 各種物質毒性/ Beta Blocker Toxicity	20OCT2013/ Fatal	31	Y	4	30	Y/ Severe	Y	Possible/ Dose Not Changed	N
	傷害、中毒および処置合併症/ 各種物質毒性/ Digitoxicity	20OCT2013/ Fatal	31	Y	4	10	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	代謝および栄養障害/ 高カリウム血症/ Hyperkalemia	20OCT2013/ Fatal	31	Y	4	23	Y/ Severe	Y	Possible/ Dose Not Changed	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
562005 Placebo 0.5 mg Placebo 0.5 mg F/72/24.7	血管障害/ 低血圧/ Hypotension	20OCT2013/ Fatal	31	Y	4	16	Y/ Severe	Y	Possible/ Dose Not Changed	N
	感染症および寄生虫症/ 敗血症/ Septicemia	20OCT2013/ Fatal	31	Y	4	24	Y/ Moderate	Y	Unlikely/ Dose Not Changed	N
	心臓障害/ 心原性ショック/ Cardiogenic Shock	22OCT2013/ Fatal	33	Y	2	22	Y/ Severe	Y	Possible/ Dose Not Changed	N
562006 Placebo 0.5 mg Placebo 0.5 mg M/77/30.6	感染症および寄生虫症/ 肺炎/ Pneumonia	22AUG2014/ Fatal	332	N	21	9	Y/ Severe	Y	Unlikely/ Not Applicable	N
	感染症および寄生虫症/ 尿路性敗血症/ Urosepsis	22AUG2014/ Fatal	332	N	21	15	Y/ Severe	Y	Unlikely/ Not Applicable	N
562007 Placebo 1.0 mg Placebo 1.0 mg M/58/29.1	心臓障害/ うっ血性心不全/ Worsening Congestive Heart Failure	13AUG2015/ Fatal	668	N	70	51	Y/ Severe	Y	Unlikely/ Not Applicable	N
563005 Sema 0.5 mg Sema 0.5 mg F/59/39.1	感染症および寄生虫症/ 腹部敗血症/ Abdominal Septic Infection	13APR2015/ Fatal	509	N	8	49	Y/ Severe	Y	Unlikely/ Not Applicable	N
	感染症および寄生虫症/ 腹膜炎/ Peritonitis On Stomach Dehiscence	13APR2015/ Fatal	509	N	8	37	Y/ Severe	Y	Unlikely/ Not Applicable	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
563005 Sema 0.5 mg Sema 0.5 mg F/59/39.1	腎および尿路障害/ 無尿/ Renal Oligoanuric Inssuficiency	13APR2015/ Fatal	509	N	8	34	Y/ Severe	Y	Unlikely/ Not Applicable	N
	肝胆道系障害/ 虚血性肝炎/ Liver Shock	20APR2015/ Fatal	516	N	1	33	Y/ Severe	Y	Unlikely/ Not Applicable	N
	感染症および寄生虫症/ 敗血症性脳症/ Septic Encephalopathy	20APR2015/ Fatal	516	N	1	48	Y/ Severe	Y	Unlikely/ Not Applicable	N
563010 Sema 1.0 mg Sema 1.0 mg M/63/29.9	呼吸器、胸郭および縦隔障害/ 誤嚥性肺炎/ Third Pneumonia By Aspiration	07JUN2015/ Fatal	559	Y	5	15	Y/ Severe	Y	Unlikely/ Not Applicable	N
564011 Sema 0.5 mg Sema 0.5 mg M/60/36.4	心臓障害/ 急性心筋梗塞/ Acute Non St Elevation Myocardial Infarction	30NOV2015/ Fatal	728	N	13	14	Y/ Severe	Y	Unlikely/ Not Applicable	N
	心臓障害/ 心停止/ Cardiac Arrest	12DEC2015/ Fatal	740	N	1	32	Y/ Severe	Y	Unlikely/ Not Applicable	N
601007 Placebo 1.0 mg Placebo 1.0 mg M/50/42.3	心臓障害/ 心室性頻脈/ Ventricular Tachycardia	14OCT2013/ Fatal	76	Y	4	2	Y/ Severe	Y	Unlikely/ Not Applicable	N
	心臓障害/ 心室細動/ Ventricular Fibrillation	17OCT2013/ Fatal	79	Y	1	3	Y/ Severe	Y	Unlikely/ Not Applicable	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
604006 Placebo 0.5 mg Placebo 0.5 mg M/64/23.1	心臓障害/ 心停止/ Cardiac Arrest	22DEC2013/ Fatal	263	Y	1	2	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
604015 Sema 0.5 mg Sema 0.5 mg F/71/46.9	腎および尿路障害/ 急性腎不全/ Acute Renal Failure	25MAR2014/ Fatal	324	Y	28	11	Y/ Moderate	Y	Unlikely/ Dose Not Changed	N
	皮膚および皮下組織障害/ 褥瘡性潰瘍/ Decubitus Ulcer	25MAR2014/ Fatal	324	Y	28	16	Y/ Severe	Y	Unlikely/ Drug Withdrawn	N
	感染症および寄生虫症/ ブドウ球菌感染/ Methicillin-Resistant Staphyloccocus Aureus	25MAR2014/ Fatal	324	Y	28	15	Y/ Moderate	Y	Unlikely/ Dose Not Changed	N
	感染症および寄生虫症/ 腸球菌感染/ Sepsis Urinary Tract Infection: Vre	25MAR2014/ Fatal	324	Y	28	10	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	呼吸器、胸郭および縦隔障害/ 呼吸不全/ Respiratory Failure	08APR2014/ Fatal	338	Y	14	17	Y/ Severe	Y	Unlikely/ Not Applicable	N
	神経系障害/ 代謝性脳症/ Toxic Metabolic Encephalopathy	13APR2014/ Fatal	343	Y	9	19	Y/ Severe	Y	Unlikely/ Not Applicable	N

MedDRA version 18.0 ,
Age (years), M: Male,F: Female, BMI: Body mass index (kg/m^2).
Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
604020 Placebo 0.5 mg Placebo 0.5 mg M/73/33.1	呼吸器、胸郭および縦隔障害/ 急性呼吸不全/ Acute Respiratory Failure	30DEC2014/ Fatal	561	N	24	12	Y/ Severe	Y	Unlikely/ Not Applicable	N
605019 Sema 1.0 mg Sema 1.0 mg F/70/29.3	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 膵癌第４期/ Pancreatic Carcinoma Stage 4	29APR2014/ Fatal	189	N	12	3	Y/ Severe	Y	Unlikely/ Not Applicable	N
606020 Placebo 1.0 mg Placebo 1.0 mg M/76/30.3	一般・全身障害および投与部位の状態/ 死亡/ Unknown Cause Of Death	01MAR2015/ Fatal	454	N	1	1	Y/ Severe	Y	Unlikely/ Not Applicable	N
607008 Placebo 0.5 mg Placebo 0.5 mg F/56/30.0	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 急性骨髄性白血病/ Acute Myeloid Leukemia	26OCT2014/ Fatal	552	Y	7	15	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
607021 Sema 0.5 mg Sema 0.5 mg F/58/54.6	神経系障害/ 低酸素性虚血性脳症/ Cause Of Death Anoxic Encephalopathy	04APR2014/ Fatal	226	N	1	15	Y/ Mild	Y	Unlikely/ Not Applicable	N
608022 Sema 1.0 mg Sema 1.0 mg F/59/22.4	心臓障害/ 心停止/ Cardiac Arrest	20FEB2015/ Fatal	446	N	1	1	Y/ Severe	Y	Unlikely/ Not Applicable	N

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Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
613003 Placebo 0.5 mg Placebo 0.5 mg M/72/37.0	神経系障害/ 脳梗塞/ Subacute Left Occipital Infarct	29JUL2014/ Fatal	468	N	197	16	Y/ Moderate	Y	Unlikely/ Not Applicable	N
613004 Sema 0.5 mg Sema 0.5 mg M/81/27.4	心臓障害/ 慢性心不全/ End Stage Congestive Heart Failure	20MAY2014/ Fatal	398	N	9	28	Y/ Severe	Y	Unlikely/ Not Applicable	N
613008 Placebo 1.0 mg Placebo 1.0 mg M/75/31.8	感染症および寄生虫症/ ブドウ球菌性敗血症/ Mrsa Sepsis	25JAN2015/ Fatal	629	Y	13	32	Y/ Severe	Y	Unlikely/ Not Applicable	N
	腎および尿路障害/ 急性腎不全/ Acute Renal Failure (On Top Of Chronic Renal Failure)	25JAN2015/ Fatal	629	Y	13	31	Y/ Severe	Y	Unlikely/ Not Applicable	N
	代謝および栄養障害/ 成長障害/ Malnutrition (Failure To Thrive)	25JAN2015/ Fatal	629	Y	13	30	Y/ Severe	Y	Unlikely/ Not Applicable	N
	感染症および寄生虫症/ ブドウ球菌性尿路感染/ Urinary Tract Infection (Mrsa)	25JAN2015/ Fatal	629	Y	13	26	Y/ Severe	Y	Unlikely/ Not Applicable	N
613013 Placebo 0.5 mg Placebo 0.5 mg M/71/34.2	心臓障害/ 心停止/ Cardiac Arrest	31JUL2015/ Fatal	670	Y	1	31	Y/ Severe	Y	Unlikely/ Not Applicable	N

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Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
614010 Placebo 1.0 mg Placebo 1.0 mg F/61/33.1	神経系障害/ 脳血管発作/ Cerebral Vascular Accident	21OCT2015/ Fatal	715	N	1	22	Y/ Severe	Y	Unlikely/ Not Applicable	N
624007 Placebo 1.0 mg Placebo 1.0 mg M/66/36.3	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 退形成星細胞腫/ Brain Tumor. Pathology Anaplastic Astrocytoma	11DEC2014/ Fatal	438	Y	133	9	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
627004 Placebo 1.0 mg Placebo 1.0 mg M/65/35.3	心臓障害/ 心筋梗塞/ Massive Myocardial Infarction Leading To Death	25MAY2015/ Fatal	693	N	1	9	Y/ Severe	Y	Unlikely/ Not Applicable	N
632014 Sema 1.0 mg Sema 1.0 mg M/68/29.3	傷害、中毒および処置合併症/ 硬膜下血腫/ Subdural Hematoma	21MAR2014/ Fatal	229	Y	63	11	Y/ Severe	N	Unlikely/ Dose Not Changed	N
	心臓障害/ うっ血性心不全/ Worsening Congestive Heart Failure	26MAR2014/ Fatal	234	Y	58	13	Y/ Moderate	Y	Unlikely/ Dose Not Changed	N
632018 Placebo 1.0 mg Placebo 1.0 mg M/69/39.6	一般・全身障害および投与部位の状態/ 死亡/ Death By Natural Cause	15NOV2013/ Fatal	81	Y	1	1	Y/ Severe	Y	Unlikely/ Dose Not Changed	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
633003 Placebo 1.0 mg Placebo 1.0 mg F/70/34.4	心臓障害/ 心停止/ Cardiac Arrest	14DEC2014/ Fatal	626	Y	1	11	Y/ Severe	Y	Possible/ Not Applicable	N
636028 Sema 0.5 mg Sema 0.5 mg F/63/42.7	心臓障害/ 心肺停止/ Cardiopulmonary Arrest	17NOV2015/ Fatal	751	Y	1	6	Y/ Severe	Y	Unlikely/ Not Applicable	N
638023 Sema 0.5 mg Sema 0.5 mg F/62/21.5	心臓障害/ 心停止/ Cardiac Arrest	22MAR2015/ Fatal	486	N	1	20	Y/ Severe	Y	Unlikely/ Not Applicable	N
	心臓障害/ 心筋梗塞/ Mi (Myocardial Infarction)	22MAR2015/ Fatal	486	N	1	10	Y/ Severe	Y	Unlikely/ Not Applicable	N
638024 Sema 1.0 mg Sema 1.0 mg M/63/23.0	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 肺癌第４期、細胞タイプ不明/ Stage Iv Lung Cancer	25AUG2014/ Fatal	274	Y	300	2	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 中枢神経系転移/ Metastatic Disease To The Brain	22FEB2015/ Fatal	455	Y	119	11	Y/ Severe	Y	Unlikely/ Dose Not Changed	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
638024 Sema 1.0 mg Sema 1.0 mg M/63/23.0	血液およびリンパ系障害/ 縦隔リンパ節腫脹/ Progressive Mediastinal Adenopathy	22FEB2015/ Fatal	455	Y	119	8	Y/ Moderate	Y	Unlikely/ Dose Not Changed	N
640024 Sema 1.0 mg Sema 1.0 mg M/62/29.2	心臓障害/ 不整脈/ Fatal Cardiac Arrythmia	04MAR2015/ Fatal	507	N	1	19	Y/ Severe	Y	Unlikely/ Not Applicable	N
640027 Sema 0.5 mg Sema 0.5 mg M/51/37.2	心臓障害/ 急性心筋梗塞/ Nstemi Myocardial Infarction	19NOV2015/ Fatal	752	N	2	35	Y/ Severe	Y	Unlikely/ Not Applicable	N
643003 Sema 0.5 mg Sema 0.5 mg F/62/40.8	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 卵巣上皮癌/ Ovarian Adenocarcinoma	24NOV2013/ Fatal	244	Y	736	21	Y/ Severe	Y	Unlikely/ Drug Withdrawn	N
643011 Sema 1.0 mg Sema 1.0 mg M/53/25.9	代謝および栄養障害/ 糖尿病/ Diabetes Melltus - Natural Causes	21JUL2013/ Fatal	7	Y	1	1	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
653029 Placebo 0.5 mg Placebo 0.5 mg M/72/44.1	神経系障害/ 脳血管発作/ Cerebrovascular Event-Stroke	06DEC2014/ Fatal	366	Y	3	14	Y/ Moderate	Y	Unlikely/ Dose Not Changed	N

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Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
656002 Sema 1.0 mg Sema 1.0 mg M/69/33.0	心臓障害/ 冠動脈疾患/ Worsening Of Caronary Artery Disease	03APR2015/ Fatal	695	Y	1	7	Y/ Severe	Y	Unlikely/ Not Applicable	N
	呼吸器、胸郭および縦隔障害/ 慢性閉塞性肺疾患/ Worsening Of Chronic Obstructive Pulmonary Disease	03APR2015/ Fatal	695	Y	1	8	Y/ Severe	Y	Unlikely/ Not Applicable	N
656014 Sema 0.5 mg Sema 0.5 mg M/82/31.6	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 遠隔転移を伴う胃癌/ End-Stage Metastatic Gastric Carcinoma	04JUL2014/ Fatal	214	Y	50	3	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
657003 Sema 1.0 mg Sema 1.0 mg M/62/30.7	心臓障害/ うっ血性心不全/ Chf	29APR2015/ Fatal	514	Y	2	6	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	心臓障害/ 心室性頻脈/ Ventricular Tachycardia	29APR2015/ Fatal	514	Y	2	9	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	心臓障害/ 心停止/ Cardiac Arrest	30APR2015/ Fatal	515	Y	1	10	Y/ Severe	Y	Unlikely/ Not Applicable	N

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Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
659017 Sema 1.0 mg Sema 1.0 mg F/59/34.9	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 小細胞肺癌/ Small Cell Lung Cancer	04MAR2014/ Fatal	134	Y	237	6	Y/ Severe	Y	Unlikely/ Not Applicable	N
663022 Sema 1.0 mg Sema 1.0 mg F/61/34.6	心臓障害/ 心肺停止/ Cardio-Pulmonary Arrest	07AUG2014/ Fatal	262	Y	2	2	Y/ Severe	Y	Unlikely/ Not Applicable	N
666010 Placebo 0.5 mg Placebo 0.5 mg M/58/34.4	心臓障害/ 心停止/ Cardiac Arrest	28FEB2015/ Fatal	494	N	1	1	Y/ Severe	Y	Unlikely/ Not Applicable	N
671017 Sema 0.5 mg Sema 0.5 mg M/72/37.9	感染症および寄生虫症/ 肺炎/ Bilateral Pneumonia	01JAN2014/ Fatal	29	Y	6	1	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	呼吸器、胸郭および縦隔障害/ 呼吸不全/ Respiratory Failure	01JAN2014/ Fatal	29	Y	6	2	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	感染症および寄生虫症/ 敗血症/ Sepsis	01JAN2014/ Fatal	29	Y	6	3	Y/ Severe	Y	Unlikely/ Dose Not Changed	N

MedDRA version 18.0 ,
Age (years), M: Male,F: Female, BMI: Body mass index (kg/m^2).
Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
675011 Placebo 0.5 mg Placebo 0.5 mg M/69/31.3	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 肝内胆管癌/ 1/30/2014 Metastatic Cholangiocarcinoma Liver	17DEC2013/ Fatal	140	Y	123	4	Y/ Severe	Y	Unlikely/ Drug Withdrawn	N
	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 肝内胆管癌/ Metastatic Cholangiocarcinoma Lymph Node	17DEC2013/ Fatal	140	Y	123	6	Y/ Severe	Y	Unlikely/ Drug Withdrawn	N
681016 Placebo 0.5 mg Placebo 0.5 mg M/72/39.3	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 肺の悪性新生物/ Malignant Neoplasm Of Brohchus/Lung	05MAR2015/ Fatal	477	Y	13	14	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
683008 Placebo 0.5 mg Placebo 0.5 mg M/56/48.1	心臓障害/ うっ血性心不全/ Exacerbation Of Congestive Heart Failure	29MAY2015/ Fatal	724	Y	50	18	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	心臓障害/ 心原性ショック/ Cardiogenic Shock	17JUL2015/ Fatal	773	Y	1	20	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
	血管障害/ 低血圧/ Hypotension	17JUL2015/ Fatal	773	Y	1	19	Y/ Severe	Y	Unlikely/ Not Applicable	N

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Adverse events with fatal outcome - listing - in-trial - all randomised subjects

Subject ID Planned treatment Actual treatment Sex/Age/BMI	System organ class/ Preferred term/ Reported term	Onset date/ Outcome	Trial day of onset	On-treatment (Y/N)	Duration of event (days)	AE reference id	Serious (Y/N)/ Severity	MESI (Y/N)	Relation/ Action	Related to technical complaint (Y/N)
690002 Sema 0.5 mg Sema 0.5 mg M/76/35.3	心臓障害/ 心停止/ Death (Cardiac Asystole)	23MAY2014/ Fatal	415	Y	1	15	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
690019 Placebo 0.5 mg Placebo 0.5 mg F/53/31.4	感染症および寄生虫症/ 肺炎球菌性肺炎/ Bilateral Pneumococcal Pneumonia	23DEC2014/ Fatal	382	Y	30	17	Y/ Severe	Y	Unlikely/ Drug Withdrawn	N
	感染症および寄生虫症/ 敗血症性ショック/ Septic Shock	25DEC2014/ Fatal	384	Y	28	21	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
699019 Placebo 0.5 mg Placebo 0.5 mg M/72/23.9	呼吸器、胸郭および縦隔障害/ 呼吸不全/ Respiratory Failure	15SEP2015/ Fatal	687	Y	38	3	Y/ Severe	Y	Unlikely/ Dose Not Changed	N
703018 Sema 1.0 mg Sema 1.0 mg M/60/30.5	心臓障害/ 心筋梗塞/ Myocardial Infraction With Arrhythmia	12SEP2015/ Fatal	733	Y	7	5	Y/ Severe	Y	Unlikely/ Not Applicable	N

MedDRA version 18.0 ,
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Y: Yes, N: No, NA: Not applicable. MESI: Medical events of special interest.
Relationship to trial products is based on investigator's assessment.

2.7.6.26 NN9924-3790

2.7.6.26.1 臨床試験概要

Trial Registration ID-number： NCT01923181	UTN：U1111-1136-4716 IND number：114,464 EudraCT number：2012-004994-16
治験の標題： 2 型糖尿病患者を対象とした、セマグルチド（経口投与）の用量範囲、用量漸増法、有効性の検討 －反復投与試験－	
治験責任医師名： 治験実施施設（全 100 施設）ごとに 1 名（セルビアのみ：3 名）の治験責任医師が任命された。以下の治験責任医師が治験総括報告書の内容を確認し、署名する「治験総括報告書への署名責任を有する医師（signatory investigator）」に指名された。 [redacted]	
治験実施施設： 本試験は以下の 14 ヵ国 100 施設において実施された：オーストリア（6 施設）、ブルガリア（3 施設）、カナダ（6 施設）、デンマーク（6 施設）、ドイツ（6 施設）、イスラエル（6 施設）、イタリア（4 施設）、マレーシア（4 施設）、セルビア〔1 施設（3 施設が同一敷地内にあり、1 施設とみなした）〕、南アフリカ（3 施設）、スペイン（5 施設）、スウェーデン（3 施設）、英国（8 施設）及び米国（39 施設）	
公表文献（引用文献）： 本臨床試験概要作成時点での公表文献はなし	
治験期間： 開始日：2013 年 12 月 2 日 終了日：2014 年 12 月 11 日	**開発のフェーズ**： 第 2 相
Cut-off date： ここに提示する結果は、2015 年 1 月 26 日の時点での臨床データベースに基づいている。	
報告書作成日： [redacted]	
目的： 投与後 26 週に評価した本試験の目的は以下のとおりであった： <u>主要目的</u>： • 2型糖尿病患者を対象とし、血糖コントロールに対するセマグルチド（経口投与、SNACを添加剤として含む）の有効性をプラセボと比較する。 <u>副次的目的</u>： • 2型糖尿病患者を対象とし、血糖コントロールに対するセマグルチド（経口投与、SNACを添加剤として含む）の有効性をセマグルチド（皮下投与）と比較する。 • 2型糖尿病患者を対象とし、セマグルチド（経口投与、SNACを添加剤として含む）26週間投与における3種類の用量漸増法（最終用量は同じ）の安全性及び忍容性を比較する。 • 投与後26週における以下のエンドポイントを指標とした、有効性、安全性及び忍容性パラメータならびに母集団薬物動態を比較する。 薬物動態及び／又は薬力学的作用のモデリングは、ノボ ノルディスク社の Quantitative Clinical	

Pharmacology が実施し、本臨床試験報告とは別途に報告する。

治験方法：

試験デザイン

本試験は、以下の 9 投与群〔7 つのセマグルチド（経口投与）群、1 つのプラセボ（経口投与）群及び 1 つのセマグルチド（皮下投与）群〕の並行群間、無作為割り付け、部分盲検、用量範囲、用量漸増法、多施設共同試験であった。セマグルチド（経口投与）群及びプラセボ群（経口投与）は二重盲検であったが、実薬投与対照群であるセマグルチド（皮下投与）群は非盲検であった。セマグルチド（経口投与）の維持用量は 2.5 mg、5 mg、10 mg、20 mg 及び 40 mg（いずれも 1 日 1 回投与）であった。セマグルチド（皮下投与）の維持用量は、1.0 mg（週 1 回投与）であった。プラセボは 1 日 1 回経口投与した。本試験には、セマグルチド（経口投与）を用いた 3 種類の用量漸増法が設定され、いずれも維持用量は 40 mg であった。用量漸増法は、標準的な用量漸増法〔4 週ごとに用量漸増を実施：セマグルチド（経口投与）40 mg〕、緩徐な用量漸増法〔8 週ごとに用量漸増を実施：セマグルチド（経口投与）40 mg S〕及び急速な用量漸増法〔2 週ごとに用量漸増を実施：セマグルチド（経口投与）40 mg F〕であった。投与群ごとに異なる用量漸増法が用いられており、その群で報告された有害事象は必ずしも発現日における実際の投与量を反映しているわけではない。

スクリーニング来院（来院 1）で被験者の適格性を評価し、その約 2 週間後に無作為割り付け来院（来院 2）を実施した。その後、26 週間の投与期間が設定された（来院 3～10）。すべての被験者は投与完了後又は治験薬の投与中止後に、予定されていた投与終了来院（来院 11）を実施した。事後調査来院（来院 12）は、投与終了来院（来院 11）の 5 週間後以降（来院許容範囲は+5 日間）であった。治験薬の投与を中止した被験者も、決められていた投与終了来院の日（すなわち無作為割り付けの 26 週間後）に投与終了 - 中止来院（来院 11X）を実施することとなっていた。本試験のいずれかの時点で中止となったすべての被験者にも、事後調査来院（来院 12）を実施することとなっていた。

無作為割り付け来院時、適格例は以下の 9 投与群いずれか 1 群に、等しい割合で無作為に割り付けられた（カッコ内の投与量は維持用量を表す）：

1. セマグルチド錠1日1回：2.5 mgを26週間（2.5 mg）
2. セマグルチド錠1日1回：2.5 mgを4週間、続いて5 mgを22週間（5 mg）
3. セマグルチド錠1日1回：5 mgを4週間、続いて10 mgを22週間（10 mg）
4. セマグルチド錠1日1回：5 mgを4週間、続いて10 mgを4週間、さらに20 mgを18週間（20 mg）
5. セマグルチド錠1日1回：5 mgを4週間、続いて10 mgを4週間、さらに20 mgを4週間、最後に40 mgを14週間（40 mg）
6. セマグルチド錠1日1回：5 mgを8週間、続いて10 mgを8週間、さらに20 mgを8週間、最後に40 mgを2週間（40 mg S）
7. セマグルチド錠1日1回：5 mgを2週間、続いて10 mgを2週間、さらに20 mgを2週間、最後に40 mgを20週間（40 mg F）
8. プラセボ錠1日1回：26週間
9. セマグルチド注射剤1週1回：0.25 mgを4週間、続いて0.50 mgを4週間、さらに1.0 mgを18週間（1.0 mg）

すべての投与群において治験薬はそれまでのメトホルミンに追加して投与するか、食事・運動療法のみを行っていた場合は単剤投与とした。

試験集団

試験集団は、食事・運動療法及び／又はメトホルミンで十分なコントロールが得られていない 2 型糖尿病患者で、年齢 18 歳以上の男女であった。

投与方法

セマグルチド（経口投与）は、N-[8-(2-ヒドロキシベンゾイル)アミノ]カプリル酸ナトリウム（SNAC）300 mg を添加剤として含む錠剤として 1 日 1 回投与し、維持用量は 2.5 mg、5 mg、10 mg、20 mg 又は 40 mg とした。プラセボは、錠剤として 1 日 1 回投与した。プラセボ錠は SNAC を含有しなかった。セマグルチド（皮下投与）は注射剤として 1 週間に 1 回投与し、維持用量を 1.0 mg とした。

投与群への割り付けと盲検化
無作為割り付け来院（来院 2）で、適格例は 9 投与群のいずれか 1 群に割付けられた。無作為割り付けは、IV/IWRS システム（interactive voice/web response system）を用いて、割り付け割合を等しくした。スクリーニング時点でのメトホルミンの使用（あり又はなし）で、無作為割り付けを層別した。経口投与（セマグルチド及びプラセボ）について、被験者及び治験責任医師を盲検化したが、皮下投与（セマグルチド）は非盲検下で投与した。
データモニタリング
本試験は治験依頼者によってモニタリングされ、以下の事項を確認するのに十分な頻度の施設訪問、電話確認、及び症例報告書の定期的な調査を行った：被験者の組み入れ、治験実施計画書の遵守状況、原資料、治験薬管理記録、ならびに有害事象の記録との照合による電子症例報告書データの完全性及び正確性。試験実施中の安全性調査は、社内のノボ ノルディスク社の経口 GLP-1 安全性委員会が実施した。外部の独立イベント判定委員会は、事前に設定した診断基準に従って、選定した有害事象の定性的又は定量的な評価を行った。この評価は、事前に設定したある特定の有害事象に関連する臨床データの評価に基づいて行われた。カルシトニンが 20 ng/L 以上の場合、関連する補足情報とともに甲状腺専門医からなる独立カルシトニンモニタリング委員会に提出された。独立カルシトニンモニタリング委員会は、当該被験者のさらなる調査及び治療に関して、治験責任医師への提案を行った。また、すべての心電図を中央評価した。
中間解析
本試験では中間解析を行わなかった。

計画及び解析された被験者数：
計画された被験者数
スクリーニング予定症例数：1005 例
無作為割り付け予定症例数：603 例
試験完了予定症例数：482 例
解析された被験者数
スクリーニングされた 1106 例のうち、474 例がスクリーニング不適格例であった。474 例のスクリーニング不適格例のうち、457 例が 1 つ以上の選択基準違反又は除外基準抵触例であり、主に HbA1c が規定した値から外れていたためであった（スクリーニング不適格例のうち 361 例）。残りの 17 例のスクリーニング不適格例は、同意の撤回もしくは追跡不能、又は治験責任医師の判断による治験不参加のいずれかであった。
計 632 例が 9 投与群（各投与群につき 70 又は 71 例）に均等に無作為割り付けされた。2 例〔セマグルチド（経口投与）10 mg 群で 1 例及びセマグルチド（皮下投与）1.0 mg 群で 1 例〕を除き、すべての無作為割り付けされた被験者が治験薬の投与を受けた。治験薬の投与を受けた 630 例が、最大の解析対象集団〔full analysis set（FAS）〕及び安全性解析対象集団〔safety analysis set（SAS）〕の両集団に含まれた。治験薬の投与を受けなかった 2 例は、いずれの解析集団からも除外された。
計 583 例（92%、投与群別：87～96%）が本試験を完了し、計 492 例（78%、投与群別：64～92%）が治験薬の投与を完了し、計 463 例（73%、投与群別：64～83%）がレスキュー治療薬を使用することなく本試験を完了した。本試験を完了した被験者の割合は投与群を通して同様であったが、セマグルチド（経口投与）20 mg 群、40 mg 群、40 mg S 群、40 mg F 群及びセマグルチド（皮下投与）1.0 mg 群と比較してセマグルチド（経口投与）2.5 mg 群、5 mg 群、10 mg 群及びプラセボ群でわずかに高かった（レスキュー治療薬の使用の有無を問わず）。
計 140 例（22%）が治験薬の投与を中止した。そのうち 92 例（15%）は有害事象、24 例（4%）は脱落（治験実施計画書不遵守、妊娠、被験者の申し出、又はその他）、残りの 24 例（4%）はその他の理由のためであった。脱落及びその他の理由により投与を中止した被験者の割合は投与群間で差は無かった。一方で、有害事象により投与を中止した被験者の割合は、セマグルチド（経口投与）2.5 mg 群（9%）、5 mg 群（6%）、10 mg 群（11%）、40 mg S 群（14%）、セマグルチド（皮下投与）1.0 mg 群（14%）及びプラセボ群（1%）と比較して、セマグルチド（経口投与）20 mg 群（27%）、40 mg 群（23%）及び 40 mg F 群

（26%）で高かった。
計 11 例（2%）が投与の中止後に試験を中止した。その理由は、治験実施計画書の不遵守（3 例）、被験者の申し出（7 例）又はその他の理由（1 例）のいずれかであった。試験中止となった被験者数が少なく、傾向を検討することはできなかった（各投与群で 1～4 例が試験を中止した）。さらに、10 例（2%）が追跡不能となった。

診断及び主要な組入れ基準：

主な選択基準

- 年齢が18歳以上の男女（同意取得時点）
- BMI（kg/m^2）：25以上40以下
- スクリーニングの30日以上前から食事・運動療法及び／又はメトホルミンによる安定した治療を受けている2型糖尿病患者
- HbA1c 7.0%以上9.5%以下（53～80 mmol/mol）

主な除外基準

- ワルファリン、ジゴキシン、三環系抗うつ薬、リチウム、アミノフィリン、テオフィリン、抗けいれん薬などの治療域の狭い経口薬剤を使用している被験者
- 慢性膵炎又は特発性急性膵炎の既往歴を有する被験者
- 慢性吸収不良（原因を問わない）を有する被験者
- クローン病、潰瘍性大腸炎又はその他の炎症性腸疾患を有する被験者
- スクリーニング来院前90日以内に、選択基準に記載のメトホルミン以外の血糖降下薬の投与を受けた被験者

主な中止基準

被験者は自由意志によりいつでも試験を中止することができ、安全性の懸念がある場合は治験責任医師の判断により試験を中止することができた。
被験者は、以下に該当する場合に試験を中止した：

- 選択基準に違反又は除外基準に抵触して試験に組み入れられた場合
- 被験者が妊娠した場合
- 被験者が妊娠を希望した場合

被験薬、用量及び投与方法、ロット番号：

本試験で用いられた治験薬は以下のとおりであった。

治験薬	用量	投与経路	ロット番号
セマグルチド 300 mg SNAC	2.5 mg	錠剤	C2RI123
			C2RI053
			D2RI002
セマグルチド 300 mg SNAC	5.0 mg	錠剤	C2RI054
			C2RI125
			C2RI109
セマグルチド 300 mg SNAC	10.0 mg	錠剤	C2RI110
			C2RI055
セマグルチド 300 mg SNAC	20.0 mg	錠剤	C2RI056
			C2RI111
セマグルチド 300 mg SNAC	40.0 mg	錠剤	C2RI057
			C2RI124

			C2RI112
セマグルチド	1.34 mg/mL	注射剤〔PDS290 ペン型注入器（1.5 mL）と一体化したプレフィルド製剤〕	CV40201
プラセボ	N/A	錠剤	C2RI105 C2RI052 D2RI001
プラセボ [a]	N/A	注射剤（テストペン）	CV40204

N/A：該当せず [a]プラセボ注射剤は、セマグルチド（皮下投与）群でのみテストのために用いられた。

投与期間：
予定投与期間は、26 週間であった。

対照薬、用量及び投与方法、ロット番号：
セマグルチドプラセボ（錠剤及び注射剤）。上述の表を参照のこと。プラセボ注射剤は、セマグルチド皮下投与群でのみテストのために用いられた。

評価基準：有効性

プライマリーエンドポイント

- ベースラインから投与後26週までのHbA1cの変化量

有効性に関するセカンダリーエンドポイント

- 投与後26週に、HbA1c 7%以下（53 mmol/mol）を達成した被験者
- ベースラインから投与後26週までの空腹時血糖値、C-ペプチド、空腹時インスリン及びグルカゴンの変化量
- ベースラインから投与後26週までのインスリン抵抗性〔インスリン抵抗性指数（HOMA-IR）〕及びβ細胞機能〔β細胞機能指数（HOMA-B）〕の変化量
- ベースラインから投与後26週までの空腹時脂質プロファイル〔総コレステロール、低比重リポタンパク（LDL）、高比重リポタンパク（HDL）、超低比重リポタンパク（VLDL）、トリグリセリド及び遊離脂肪酸〕の変化量
- ベースラインから投与後26週までの患者報告アウトカム〔SF-36（Medical Outcomes Study 36-Item Short-Form Health Survey）（全般的質問票）〕の変化量
- ベースラインから投与後26週までの体重の変化量
- ベースラインから投与後26週までのウエスト周囲径の変化量
- ベースラインから投与後26週までのBMIの変化量

評価基準：安全性

安全性に関するセカンダリーエンドポイント

- ベースラインから投与後31週までの治験薬投与下で発現した有害事象（Treatment Emergent Adverse Event、以下、有害事象とする）の発現件数
- ベースラインから投与後31週までの確定低血糖の発現件数
- ベースラインから投与後26週までのバイタルサイン（脈拍数、収縮期及び拡張期血圧）の変化量
- 26週間の投与期間及び事後調査時における抗セマグルチド抗体の産生（陽性／陰性）
- ベースラインから投与後26週までの安全性に関する臨床検査項目（血液学的検査、血液生化学的検査、ホルモン検査及び尿検査）

統計手法：

検出力の算出

セマグルチド（経口投与）の有効性を示すために必要な被験者数は、HbA1c のベースラインから投与終了（投与後 26 週）までの変化量の最初の比較、つまり a) 最終用量 40 mg とした標準用量漸増法及び急速な

用量漸増法を用いた 2 投与群を併合したものと b) プラセボ群の比較に基づいている。必要な被験者数の計算に関する仮定として、HbA1c のベースラインからの変化量の SD に 1.2%を選択した。リラグルチド（皮下投与）を 26 週間投与したいくつかの第 3 相試験で観察された SD から、SD は 1.1%未満になることが示唆された。しかし、セマグルチド（皮下投与）と比較して曝露量の変動が大きくなり、それによって治療効果の変動が大きくなるかどうかは不明であったため、SD を 1.2%と仮定した。

NN9535-1821 試験〔セマグルチド（皮下投与）を週 1 回投与〕において、投与量 0.2～0.8 mg における中止率は 16～24%であった。本試験では、胃腸障害が用量漸増法によって軽減されることにより、中止率はいずれの投与群でも同様に 20%になると予想した。完了例について、併合した 40 mg 投与群とプラセボ群の間の群間差は 0.64%以上と予想したが、中止例について、群間差は保守的に 0.32%に設定した。従って、検出可能な群間差の平均は 0.58%となる。これらの仮定に基づき、有意水準を 5%とした両側 t 検定を用いると、併合した 40 mg 投与群に 134 例、プラセボ群に 67 例の被験者を割り付けると、プラセボ群に対する併合した 40 mg 投与群の優越性を示す検出力は 90%である。投与群間で例数を等しくするため、無作為割り付けする被験者数は 9 投与群にそれぞれ 67 例とし、計 603 例となった。

解析集団

- FAS：無作為割り付けされセマグルチド（経口又は皮下投与）又はプラセボの投与を少なくとも1回受けたすべての被験者が含まれた。FASの被験者は「無作為割り付けされたとおり（as randomised）」の評価に寄与した。
- SAS：無作為割り付けされセマグルチド（経口又は皮下投与）又はプラセボの投与を少なくとも1回受けたすべての被験者が含まれた。SASの被験者は「治療されたとおりの（as treated）」の評価に寄与した。

無作為割り付けされた 632 例のうち 630 例が治験薬の投与を受け、FAS 及び SAS の両集団に含まれた。治験薬を投与されなかった被験者〔セマグルチド（経口投与）10 mg 群の 1 例、及びセマグルチド（皮下投与）1.0 mg 群の 1 例〕は、いずれの解析集団からも除外した。除外した 2 例は、いずれも治験実施計画書の不遵守によるものであった。

統計解析

観察期間

本試験では、以下の 3 つの観察期間を定義した；

- In-trial期間：有効性及び安全性の評価のための補足的な観察期間
- On-treatment期間：安全性評価のための主要観察期間（最終投与後の5週間の期間が含まれる）
- レスキュー治療を伴わないon-treatment期間：有効性評価のための主要観察期間

プライマリーエンドポイントの解析

プライマリーエンドポイントであるベースラインから投与後 26 週までの HbA1c の変化量を、標準的な繰り返し測定に対する混合モデル（標準的 MMRM と呼ぶ）によって解析した。このモデルには、投与群、国、層別変数を固定効果、対応するベースライン値を共変量として含めた。すべての効果と共変量を来院内で入れ子にした。このモデルでは、同一被験者内で無構造共分散行列を仮定した。

統計解析の結果は、投与群間に差はないという検定に対する p 値とともに、信頼係数を 95%とした両側信頼区間を提示した。層別変数は、メトホルミンの使用の有無（はい／いいえ）による 2 つの水準と定義した。

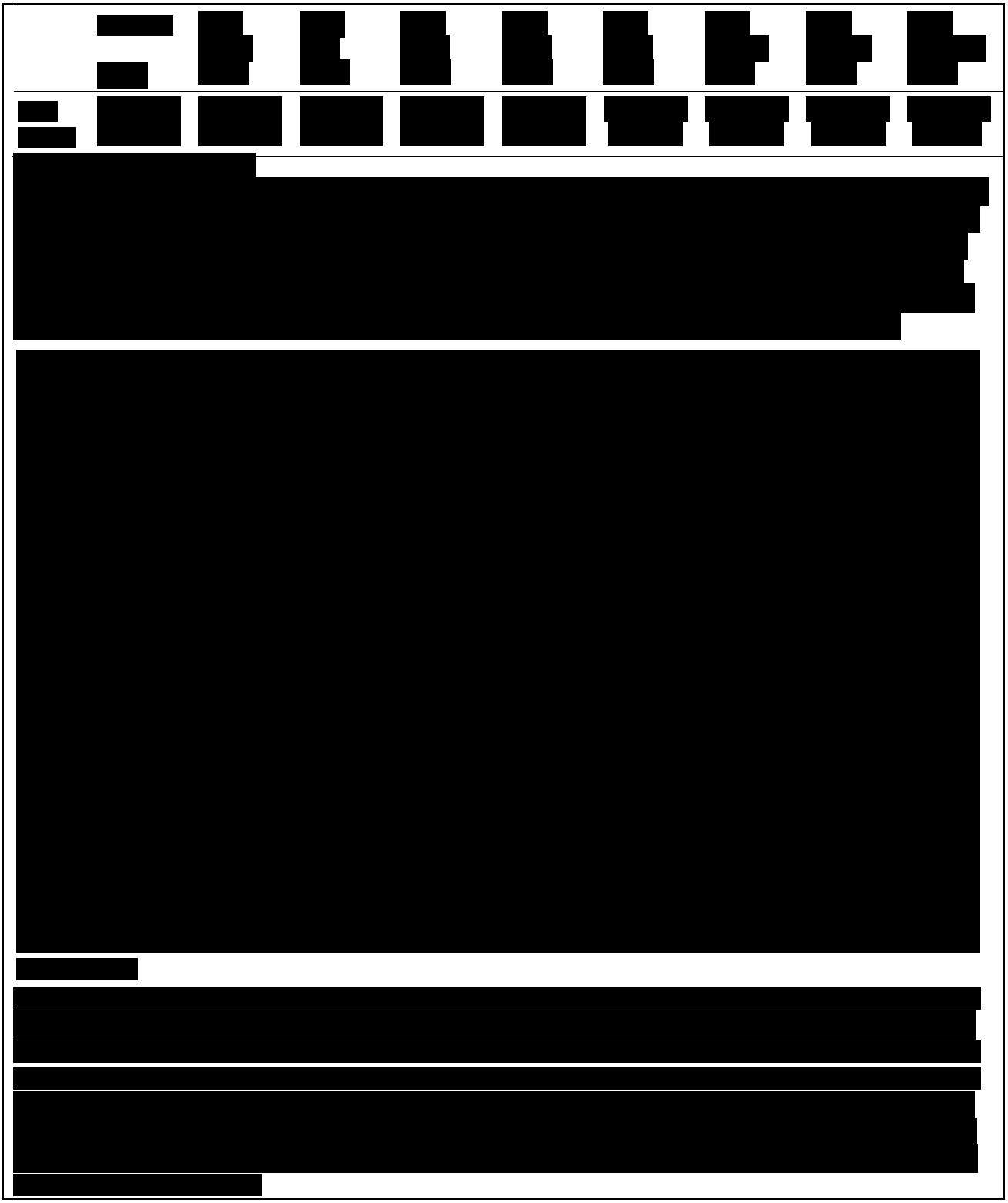
セマグルチド（経口投与）の有効性を、第一種の過誤のリスクを増大させることなく検証するために、プライマリーエンドポイントについての最初の比較を a) 最終用量 40 mg とした標準用量漸増法及び急速な用量漸増法を用いた 2 投与群を併合した投与群と b) プラセボ群の間で実施した。本比較にあたっては、標準用量漸増法を用いた 40 mg 群と急速な用量漸増法を用いた 40 mg 群を併合し、この併合群とプラセボ群の群間差を標準的 MMRM で推定することとした。投与群間の比較として以下の比較が計画された：a) セマグルチド（経口投与）の各群とプラセボ群、b) セマグルチド（皮下投与）群とプラセボ群、c) セマグルチド（経口投与）の各群とセマグルチド（皮下投与）群、及び d) 最終用量を 40 mg としたセマグルチド（経口投与）の 3 投与群間。

セカンダリーエンドポイントの解析
連続量のセカンダリーエンドポイントの解析には標準的 MMRM を用いた。
投与後 26 週において HbA1c が 7%（53 mmol/mol）未満を達成した被験者数についてのエンドポイントは、ロジスティック回帰モデルで解析した。モデルには投与群及び層別変数を固定効果、ベースラインの HbA1c を共変量として含めた。計画されていた投与群間の比較については、投与後 26 週におけるオッズ比の推定値を対応する両側 p 値及び 95%信頼区間とともに提示した。投与後 26 週の欠測データは、HbA1c の主要解析に用いた MMRM に基づいて補完した。ベースラインから投与後 26 週までの空腹時血糖値、C-ペプチド、空腹時インスリン、グルカゴン、HOMA-IR、HOMA-B、総コレステロール、LDL コレステロール、HDL コレステロール、VLDL コレステロール、トリグリセリド及び遊離脂肪酸の変化量といったエンドポイントについては、各週における値を対数変換した後に標準的 MMRM で解析した。投与後 26 週における群差の推定値及び対応する 95%信頼区間を比に変換し、両側 p 値とともに提示した。逆変換した平均の推定値の標準誤差は、デルタ法を用いて計算した。ベースラインから投与後 26 週までの体重、BMI 及びウエスト周囲径の変化量といったエンドポイントは、標準的 MMRM で解析した。体重については、ベースラインからの絶対的な体重変化量（kg）及び相対的な体重変化量（%）の両方を解析した。SF-36 質問票の全体及び各ドメイン内の総スコアを集計した。これらのスコアをそれぞれ標準的 MMRM で解析した。
治験薬投与下で発現した有害事象及び確定低血糖の発現件数といった安全性エンドポイントは、記述的に要約した。治験薬投与下で発現した確定低血糖の発現件数は、対数リンク関数を仮定し、治験薬投与下であると考えられる期間の対数をオフセット項とする負の二項分布回帰モデルで解析した。このモデルには投与群、国及び層別変数を固定効果、ベースラインの HbA1c 値を共変量として含めた。ベースラインから投与後 26 週までの脈拍数、収縮期及び拡張期血圧の変化量は、標準的 MMRM を用いて解析した。リパーゼ及びアミラーゼのエンドポイントについては、各週における値を対数変換した後に標準的 MMRM で解析した。投与後 26 週目における群差の推定値及び対応する 95%信頼区間を比に逆変換し、両側 p 値とともに提示した。デルタ法を用いて平均の標準誤差を計算した。その他の安全性に関する臨床検査項目（血液学的検査及び血液生化学的検査）は、記述統計量を用いて要約した。

被験者背景：
全体的に、被験者背景及びベースライン特性は 9 投与群間で同程度であった。試験集団は、男性及び女性の 2 型糖尿病患者で構成され、平均年齢は 57.1 歳（投与群別：55.7～58.9 歳）、被験者の 75.7%（投与群別：67.6～81.4%）が 18～64 歳であった。2 型糖尿病の平均罹病期間は 6.29 年（投与群別：5.33～7.67 年）、平均 HbA1c は 7.89%〔62.70 mmol/mol、投与群別：7.77～8.05%（61.34～64.45 mmol/mol）〕であった。平均体重及び平均 BMI（kg/m^2）はそれぞれ、92.33 kg（投与群別：88.80～93.81 kg）及び 31.73（投与群別：30.72～32.58）であった。被験者の大部分（83.0%、投与群別：77.1～90.0%）は白人で、2 番目に多かったのは黒人又はアフリカ系アメリカ人であった（7.5%、投与群別：2.9～10.1%）。組み入れられた被験者のうち 27.1%（投与群別：20.0～31.4%）が、米国の被験者であったが、残りの被験者は 13 ヵ国間にほぼ均等に分布していた。女性よりも男性が多く組み入れられた（62.7%、投与群別：56.3～69.6%）。全体として、被験者の 84.9%（投与群別：81.7～87.1%）がメトホルミンによる治療を受けていた。

有効性の結果：

[redacted]





[redacted]





安全性の結果：

有害事象：全体で、計 1886 件の有害事象が 475 例（75.4%）から報告された。有害事象を発現した被験者の割合及び有害事象の発現件数は、セマグルチド（経口投与）の用量とともに増加する傾向が示され〔67.1%・142 件（セマグルチド経口投与 2.5 mg）～85.7%・245 件（セマグルチド経口投与 40 mg F）〕、プラセボ（67.6%・127 件）と比較してセマグルチド（経口投与）10 mg 以上で多かった。セマグルチド（皮下投与）1.0 mg では、有害事象を発現した被験者の割合及び有害事象の発現件数はそれぞれ 81.2%及び 218 件であった。このプラセボとの差は主に、セマグルチド（経口投与）10 mg 以上及びセマグルチド（皮下投与）1.0 mg で、器官別大分類の胃腸障害に分類される有害事象が多く報告されたことに起因していた。セマグルチド（経口投与）で最も高頻度で報告された有害事象は器官別大分類の胃腸障害に分類される有害事象であり、最も高頻度で報告された基本語は悪心、下痢及び嘔吐であった。悪心及び下痢を発現した被験者の割合は、セマグルチド（経口投与）10 mg 以上とセマグルチド（皮下投与）1.0 mg で同程度であった。一方、嘔吐を発現した被験者の割合は、セマグルチド（皮下投与）1.0 mg と比較してセマグルチド（経口投与）10 mg 以上で高かった。

死亡及び重篤な有害事象：本試験期間中に死亡は報告されず、予期しない安全性の所見は特定されなかった。重篤な有害事象を発現した被験者の割合及び重篤な有害事象の発現件数は、投与群間で同程度であった：セマグルチド（経口投与）では 0～5 例で 0～9 件、セマグルチド（皮下投与）1.0 mg では 2 例で 2 件、プラセボでは 5 例で 8 件の重篤な有害事象が報告された。投与群との明らかな関連は認められなかった。報告された重篤な有害事象は、すべての投与群で様々な基本語にわたっており、特定の重篤な有害事象が多く発現したということはなかった。

妊娠：本試験期間中、1 件の妊娠が報告された。被験者は健康な乳児を出産し、生後 1 ヵ月の期間において先天性異常及び健康上の問題は認められなかった。

投与の中止に至った有害事象：全体として、計 92 例（14.6%）が 180 件の有害事象により投与を中止した。有害事象により投与を中止した被験者の割合は、セマグルチド（経口投与）2.5 mg、5 mg、10 mg 及び 40 mg S（8.6%、5.7%、11.6%及び 14.3%）ならびにセマグルチド（皮下投与）1.0 mg（14.5%）と比較し

て、セマグルチド（経口投与）20 mg、40 mg 及び 40 mg F（27.1%、22.5%及び 25.7%）で高かった。プラセボでは、1 例（1.4%）が有害事象により投与を中止した。最も高頻度で報告された投与の中止に至った有害事象は、器官別大分類の胃腸障害に分類される有害事象であった（180 件のうち 125 件）。この器官別大分類の有害事象を発現した被験者の割合は、セマグルチド（経口投与）2.5 mg、5 mg、10 mg 及び 40 mg S（4.3%、4.3%、11.6%及び 11.4%）ならびにセマグルチド（皮下投与）1.0 mg（11.6%）と比較して、経口投与のセマグルチド（経口投与）20 mg、40 mg 及び 40 mg F（21.4%、18.3%及び 21.4%）で高かった。プラセボでは投与の中止に至った胃腸障害の有害事象は報告されなかった。最も高頻度で報告された投与の中止に至った有害事象は、悪心、嘔吐であった。これらの有害事象を発現した被験者の割合は、その他のすべての投与群と比較してセマグルチド（経口投与）20 mg、40 mg 及び 40 mg F で高かった。投与の中止に至った重篤な有害事象が 4 例 7 件報告された；セマグルチド（経口投与）5 mg の 1 例で膵酵素増加、10 mg の 1 例で嘔吐、悪心及び急性腎不全、40 mg F の 1 例で胃腸炎及びプラセボの 1 例で尿管結石及び副腎新生物であった。

特に注目すべき医学的事象：

心血管系事象：イベント判定委員会により、5 例 6 件の心血管系事象が確認された；4 件〔プラセボで 2 件、セマグルチド（経口投与）10 mg で 1 件及びセマグルチド（経口投与）40 mg S で 1 件〕は治験薬投与下で発現した。2 件は治験薬非投与下で発現した〔いずれもセマグルチド（経口投与）40 mg S〕。

新生物：イベント判定委員会により、3 例 3 件の新生物が確認された；セマグルチド（経口投与）10 mg で 1 件（基底細胞癌）、セマグルチド（経口投与）40 mg F で 1 件（胃腸管腺腫）、セマグルチド（皮下投与）1.0 mg で 1 件（ケラトアカントーマ）であった。確認された事象はすべて、治験薬投与下で発現した。

膵炎：イベント判定委員会により、3 例 3 件の膵炎が確認された；セマグルチド（経口投与）20 mg で 1 件、セマグルチド（経口投与）40 mg で 1 件、セマグルチド（皮下投与）1.0 mg で 1 件であった。3 件の確認された事象はすべて、治験薬投与下で発現した。

甲状腺疾患（甲状腺切除を必要とする場合）：イベント判定委員会により確認された甲状腺の事象はなかった。

低血糖：低血糖を発現した被験者数及び低血糖の発現件数は、すべての投与群で低く、低血糖の大部分は確定症候性低血糖又は無症候性低血糖であった。重大な低血糖〔米国糖尿病学会（ADA）の低血糖の分類に基づく〕又は血糖値確定症候性低血糖〔低血糖症状が認められ、血糖値が 3.1 mmol/L（56 mg/dL）未満と確認された低血糖〕の発現は少なく、投与群間の発現の分布は同様であった：セマグルチド（経口投与）で 1～3 例（1～6 件）、プラセボで 2 例（3 件）及びセマグルチド（皮下投与）1.0 mg で 4 例（4 件）であった。以下の 2 例が重大な低血糖（ADA の低血糖の分類に基づく）を発現した；セマグルチド（経口投与）40 mg F で 1 例及びセマグルチド（皮下投与）1.0 mg で 1 例。

臨床検査項目：セマグルチド（経口投与）でリパーゼ及びアミラーゼの増加が認められた。リパーゼの増加は、プラセボと比較して、セマグルチド（経口投与）10 mg、40 mg、40 mg S 及び 40 mg F で有意に大きかった。同様の傾向がアミラーゼにも認められたが、その増加量はリパーゼほど顕著ではなかった。アミラーゼの増加量は、プラセボと比較してセマグルチド（経口投与）40 mg S 及び 40 mg F で有意に大きかった。リパーゼ及びアミラーゼの増加量は、セマグルチド（経口投与）5 mg 以上とセマグルチド（皮下投与）1.0 mg の間で有意な差は認められなかった。その他の血液学的及び血液生化学的パラメータについて、投与群間で顕著な違いは認められなかった。

抗体：試験期間中、セマグルチド（経口投与）2.5 mg、5 mg、10 mg 及び 20 mg の 9 例で抗セマグルチド抗体が認められた。抗セマグルチド抗体陽性例の抗体価は低く、投与群との明らかな関連は認められなかった。*in vitro* において、セマグルチドに対する中和作用を有する検体はなかった。4 つの検体が 内因性 GLP-1 に対する交叉抗体を有していたが、*in vitro* において GLP-1 に対する中和作用を有する検体はなかった。

バイタルサイン：脈拍数について、プラセボと比較してセマグルチド（経口投与）5 mg 以上及びセマグルチド（皮下投与）1.0 mg で有意な増加が認められた。脈拍数の増加量は、セマグルチド（経口投与）5 mg 以上とセマグルチド（皮下投与）1.0 mg で同程度であった。収縮期及び拡張期血圧について、プラセボと比較して有意な収縮期血圧の低下が認められたセマグルチド（経口投与）10 mg を除いて、いずれの投与

群間でも統計的に有意な差は認められなかった。さらに、ベースライン及び投与後 26 週における身体所見および心電図は、投与群間で同程度であった。

全体の結論：

本試験（無作為割り付け、部分盲検、用量範囲、用量漸増法、多施設共同、26 週間投与試験）では、食事・運動療法及び／又はメトホルミンで十分なコントロールが得られていない 2 型糖尿病患者を対象として、SNAC を添加剤として含むセマグルチド（経口投与）2.5 mg、5 mg、10 mg、20 mg 及び 40 mg を投与した時の有効性及び安全性をプラセボ及びセマグルチド（皮下投与）1.0 mg と比較した。さらに、本試験ではセマグルチド（経口投与）における維持量を 40 mg とした 3 種類の用量漸増方法（標準、緩徐、急速）の安全性及び忍容性を比較した。

試験成績より、以下の結論が導かれた：

- [redacted]
- [redacted]
- [redacted]
- 全体として、セマグルチド（経口投与）は安全で良好な忍容性を示し、セマグルチド（経口投与）による予期しない安全性の問題は特定されなかった。
- 有害事象を発現した被験者の割合及び有害事象の発現件数は、セマグルチド（経口投与）の用量とともに増加する傾向を示し、プラセボと比較してセマグルチド（経口投与）10 mg以上で多かった。プラセボとの差は主にセマグルチド（経口投与）10 mg以上で悪心、下痢及び嘔吐を発現した被験者の割合が高かったことに起因するが、これらの事象の大部分は軽度又は中等度であった。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と比較してセマグルチド（経口投与）で高く、セマグルチド（経口投与）2.5 mg、5 mg、10 mg及び40 mg Sと比較して、セマグルチド（経口投与）20 mg、40 mg及び40 mg Fで高かった。投与の中止に至った有害事象は主に胃腸障害の有害事象であった。特定の重篤な有害事象が多く発現したということはなく、すべての投与群から様々な基本語の重篤な有害事象が報告された。
- 低血糖について、投与群間で明らかな差は認められなかった。
- [redacted]さらに、胃腸障害の有害事象の発現件数は緩徐な用量漸増法と比較して急速な用量漸増法で多かった。
- [redacted]

本試験は、ヘルシンキ宣言（2013）、ICH-GCP（1996）及び FDA 21 CFR 312.120（2013）を遵守して実施された。