ソグルーヤ皮下注 5mg
ソグルーヤ皮下注 10mg
ソグルーヤ皮下注 15mg

成長ホルモン分泌不全性低身長症及び
15 mg 製剤剤形追加

2.7.4 臨床的安全性

ノボ ノルディスク ファーマ株式会社

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略語一覧

AE	:	adverse events（有害事象）
AGHD	:	adult growth hormone deficiency（成人成長ホルモン分泌不全症）
BMI	:	body mass index〔体容量指数：体重(kg)／身長$(m)^2$〕
CI	:	confidence interval（信頼区間）
C_{max}	:	maximum concentration（最高血中濃度）
CT	:	computed tomography（コンピュータ断層撮影法）
EMA	:	European Medicines Agency（欧州医薬品庁）
FAS	:	full analysis set（最大の解析対象集団）
FDA	:	US Food and Drug Administration（米国食品医薬品局）
GCP	:	good clinical practice（医薬品の臨床試験の実施の基準）
GLP-1	:	glucagon like peptide-1（グルカゴン様ペプチド-1）
GH	:	growth hormone（成長ホルモン）
GHD	:	growth hormone deficiency（成長ホルモン分泌不全／成長ホルモン分泌不全性低身長）
HbA1c	:	glycosylated haemoglobin A1c（グリコヘモグロビン A1c）
hGH	:	human growth hormone（ヒト成長ホルモン）
HLGT	:	high level group term（高位グループ語）
HLT	:	high level term（高位語）
HSDS	:	height standard deviation score（身長 SD スコア）
HV	:	height velocity（成長速度）
ICH	:	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IGF-I	:	insulin-like growth factor I（インスリン様成長因子-I）
MD	:	multiple-dose（反復投与）
MedDRA	:	Medical Dictionary for Regulatory Activities（国際医薬用語集）
NA	:	not applicable（該当せず）
PD	:	Pharmacodynamics（薬力学的作用）又は protocol deviation（治験実施計画書からの逸脱）
PK	:	Pharmacokinetics（薬物動態）
PYE	:	patient years of exposure
SAE	:	serious adverse event（重篤な有害事象）
s.c.	:	Subcutaneous（皮下）
SD	:	single dose（単回投与）
SD	:	standard deviation (in a statistical context)（標準偏差）
SDS	:	standard deviation score（SD スコア）
SmPC	:	summary of product characteristics
SMQ	:	standardised MedDRA queries（MedDRA 標準検索式）
SOC	:	system organ class（器官別大分類）
$t_{1/2}$	:	terminal half-life（終末相半減期）

本臨床概要では、somapacitan を日本語で表記する場合は、医薬品一般名称（JAN）に従いソマプシタンを用いる。

臨床試験の表記：
本臨床概要では、個々の臨床試験（NN8640-xxxx）を「xxxx 試験」と表記する（例：「NN8640-4263」の場合「4263 試験」と表記する）。

製剤の表記：
本臨床概要では、ソマプシタン 5 mg/1.5mL、10 mg/1.5 mL 及び 15 mg/1.5 mL 製剤を、それぞれ、ソマプシタン 5 mg、10 mg 及び 15 mg 製剤と表記する。

2.7.4.1　医薬品への曝露

2.7.4.1.1　背景

ノボ ノルディスク社は、成長ホルモン分泌不全性低身長症（小児 GHD）患者に対する治療に用いる製剤として週 1 回皮下投与の長時間作用型成長ホルモン（GH）であるソマプシタン（遺伝子組換え）を開発している。今回の承認申請は、当該効能又は効果の承認取得を目的とした承認事項の一部変更承認申請（一変申請）とソマプシタン 15mg 含有製剤の剤型追加からなる。さらなる詳細は、Module 2.7.3.1.1 に示す。

本邦では「成人成長ホルモン分泌不全症（重症に限る）」の効能又は効果で 2021 年 1 月 22 日に製造販売承認を受けている。また、米国（2020 年 8 月 28 日）、欧州（2021 年 3 月 31 日）及びその他の数ヵ国でも、成人成長ホルモン分泌不全症（AGHD）の適応症で承認を受けている。現在、成長の catch-up がみられなかった small for gestational age 性低身長症に対する治療の開発が進行中である。

ソマプシタンは長時間作用型遺伝子組換えヒト成長ホルモン（hGH）アナログであり、単一置換（101 位のロイシンからシステインへの置換）を含むアミノ酸骨格とアルブミン結合部位からなる。アルブミン結合部位（側鎖）は、親水性のスペーサー及び 16 鎖の脂肪酸部位から構成され、化学結合により hGH のアミノ酸骨格の 101 位に結合している。内因性アルブミンとの可逆的な非共有結合によりソマプシタンの消失が遅延し、その結果、*in vivo* での半減期（$t_{1/2}$）及び作用持続時間が延長する。この方法は、インスリン及びグルカゴン様ペプチド-1（GLP-1）（レベミル、ビクトーザ及びオゼンピック等）の半減期の延長において用いられたものと同様の方法である[1,2,3]。さらなる詳細は、Module 2.7.3.1.1 に示す。

ソマプシタンの薬理作用は hGH と同様である。GH は、小児の正常な長軸成長に必要不可欠であり、成長板に対する GH を介する直接作用及び肝臓でのインスリン様成長因子-I（IGF-I）分泌促進により成長を促す[4]。成長促進作用のほかに、GH 及び IGF-I は複数の臓器及び組織に対する作用を有し、小児のみならず成人における様々な代謝過程に関与している[5]。さらなる詳細は、Module 2.7.3.1.1 に示す。

週 1 回投与のソマプシタンは、新たな治療選択肢であり、1 日 1 回投与の hGH 製剤（ノルディトロピン等）と同様の安全性及び忍容性を有している。1 日 1 回投与の hGH 製剤（ノルディトロピンを含む）は、25 年を超える臨床経験から、小児 GHD 患者において有効かつ容認できる安全性プロファイルを有することが示されている[6,7,8,9]。

本臨床概要では、小児 GHD の適応症取得を目的としたソマプシタンの開発プログラムに含まれる、すべての完了した臨床試験から得られた安全性データを提示する。

安全性データのカットオフ日は、4172 試験（208 週）では 2021 年 11 月 19 日（208 週のデータベースロック）、4263 試験（52 週）では 2021 年 12 月 3 日（52 週の 1 回目のデータベースロック：いくつかの抗ソマプシタン抗体、薬物動態及び 4 つの骨年齢の評価を除くすべてのデータ）、2021 年 12 月 17 日（52 週の 2 回目のデータベースロック：抗ソマプシタン抗体、薬物動態及び骨年齢の評価のうち含まれていなかったものを追加）及び 2022 年 12 月 22 日（104 週）とした。

2.7.4.1.2　総括的安全性評価計画及び安全性試験の記述

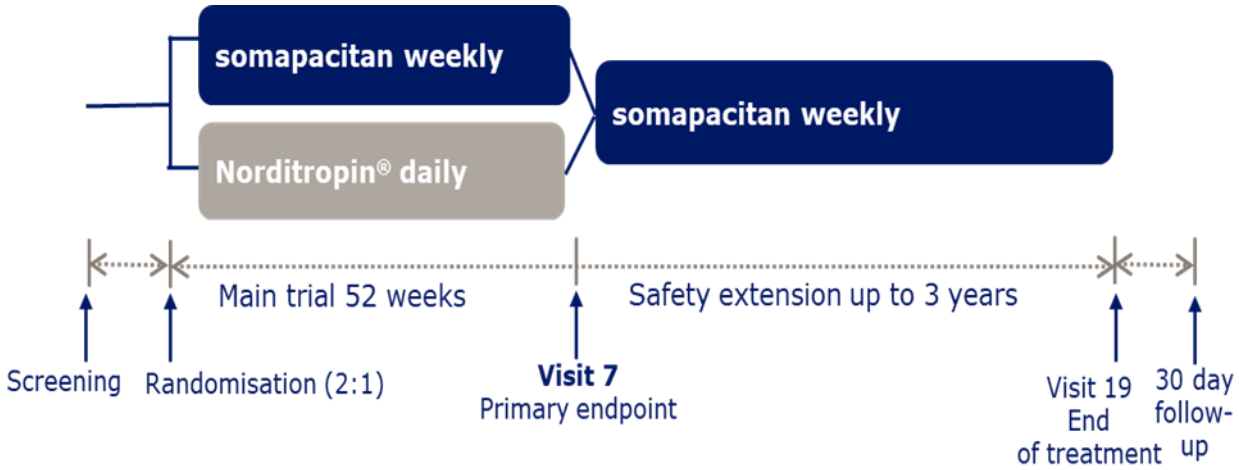
2.7.4.1.2.1 本臨床概要に含める臨床試験

本臨床概要に含めるソマプシタンの安全性情報は、小児 GHD 患者を対象とした 3 試験〔4042 試験（第 1 相試験）、4172 試験（第 2 相試験）及び 4263 試験（第 3 相試験）〕から得られたデータに基づいている。各試験のデザイン、対象集団、用法・用量及び対照薬の概要を表 2.7.4.1-1 に示す。

国際共同第 3 相検証的試験である 4263 試験は、安全性評価における主要な試験であり、本試験では完了した主要期間（52 週間）の安全性データが得られている。4263 試験の安全性データは、第 2 相試験である 4172 試験のデータ及びこれら 2 つの試験でソマプシタン 0.16 mg/kg/週の投与を受けたすべての被験者の安全性データからなる安全性併合データにより補足される。

4263 試験では、hGH 製剤による治療歴がない小児 GHD 患者を対象として、週 1 回投与のソマプシタンの有効性及び安全性を 1 日 1 回投与のノルディトロピンと比較検討した。本試験は、ソマプシタンとノルディトロピンを比較する 52 週間の主要期間と、すべての被験者がソマプシタンの投与を受ける 3 年間の安全性延長期間からなる（図 2.7.4.1-1）。各被験者の試験期間は最長で 4 年間となる。本試験は、主要期間が完了し、安全性延長期間が進行中である。本試験は 2024 年に完了予定である（4 年間のデータ）。

図 2.7.4.1-1　　第 3 相検証的試験（4263 試験）の試験デザイン

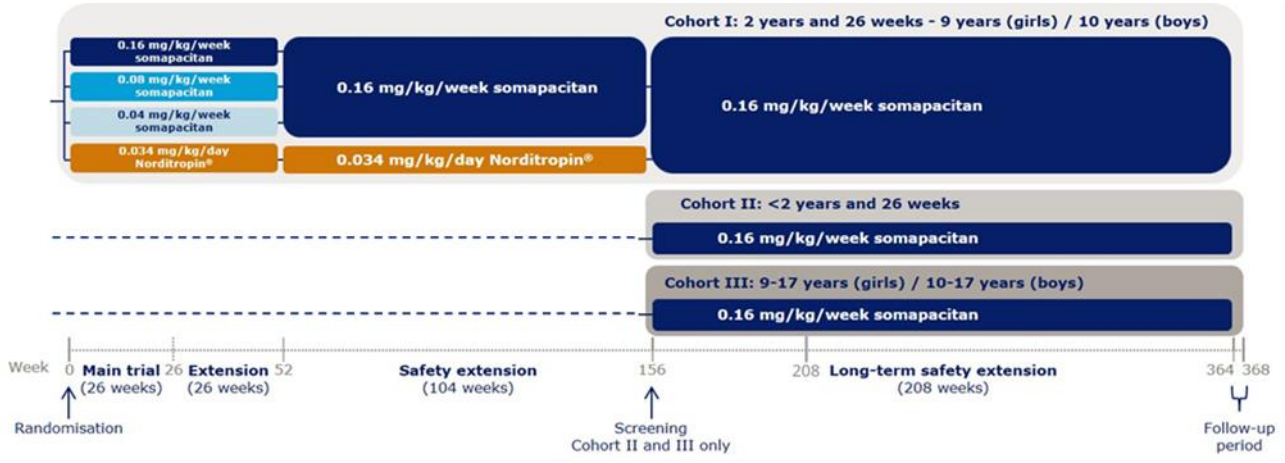


第 2 相用量設定補足的試験（4172 試験）でも、hGH 製剤による治療歴がない小児 GHD 患者を対象として、週 1 回投与のソマプシタンの有効性及び安全性を 1 日 1 回投与のノルディトロピンと比較検討した。被験者は、26 週の主要期間及び 26 週の延長期間の週 1 回投与のソマプシタン（0.04、0.08 又は 0.16 mg/kg/週）あるいは 1 日 1 回投与のノルディトロピン（0.034 mg/kg/日）に、1：1：1：1 の比率で無作為に割り付けられた（図 2.7.4.1-2）。主要期間では、異なる用量のソマプシタンの週 1 回投与は二重盲検とし、実対照薬群であるノルディトロピンの 1 日 1 回投与は非盲検であった。

本試験の安全性データは第 3 相試験の安全性を補足するものである。本試験の最初の期間（52 週まで）では、ノルディトロピンに対するソマプシタンの用量レベル（0.04、0.08 又は 0.16 mg/kg/週）間の比較データが得られている。156 週までの期間では、3 つのソマプシタン群及びノルディトロピン群の

さらなる安全性データが得られ、試験を延長することで、最長 4 年間の安全性データが得られている。本試験は、最初の 4 年間が完了し、長期安全性延長期間が進行中である（最長 7 年間の安全性データを収集予定）。

図 2.7.4.1-2　　第 2 相補足的試験（4172 試験）の試験デザイン



4042 試験は、hGH 製剤の治療歴のある小児 GHD 患者を対象とした単回投与試験であり、ソマプシタンの曝露は少なかった（各用量コホートに 6 例）（表 2.7.4.1-1）。

すべての臨床試験で、ソマプシタンは体重当たりの投与量で週 1 回皮下注射された。

臨床試験の有効性の要約は、Module 2.7.3.2 に示した。試験デザイン、対象集団、用法・用量及び対照薬の詳細は、Module 2.7.3.1.3（4263 試験及び 4172 試験）及び Module 2.7.2.1.4（4042 試験）に示した。個々の試験の詳細については、Module 2.7.6（個々の試験のまとめ）ならびに M 5.3.3.2 及び M 5.3.5.1（各治験総括報告書）を参照のこと。すべての臨床試験は、ICH-GCP[10]、関連規制要件及びヘルシンキ宣言[11]を遵守して実施された。

表 2.7.4.1-1　ソマプシタンの臨床試験（小児 GHD 患者を対象とした試験）

試験 ID（相）	試験デザイン	曝露被験者数	用法・用量
4042（第 1 相）	安全性、忍容性、薬物動態、薬力学的作用 無作為割り付け、非盲検、実薬対照、国際共同、用量漸増試験 試験の状況：完了 試験期間：28～35 日	hGH 製剤で治療中の二次性徴発来前の小児 GHD 患者 32 例 参加国 オーストリア、ベルギー、フランス、イスラエル、マケドニア、スロベニア、スペイン及びスウェーデン 女児 9 例及び男児 23 例 年齢 6.0～11.0 歳	0.02、0.04、0.08 及び 0.16 mg/kg のソマプシタン単回投与 又は 0.03 mg/kg/日のノルディトロピン 7 日間 1 日 1 回投与
4172[#]（第 2 相）	有効性及び安全性 無作為割り付け、国際共同、多施設共同、実薬対照（非盲検）、用量設定（二重盲検）、並行群間比較試験 [a] 試験の状況：進行中（208 週までは完了） 総試験期間：364 週間（7 年間）	コホート I hGH 製剤による治療歴のない、二次性徴発来前の小児 GHD 患者 59 例 年齢 2.7～9.7 歳 参加国 日本（12 例）を含む複数国 [b] 2 例が選択基準又は除外基準違反のために最大の解析対象集団から除外された 女児 23 例及び男児 34 例 [c]	0～52 週（26 週間の主要期間及び 26 週間の延長期間） 0.04、0.08 又は 0.16 mg/kg/週のソマプシタン又は 0.034 mg/kg/日のノルディトロピン（1：1：1：1） 52～156 週（安全性延長期間） 0.16 mg/kg/週のソマプシタン又は 0.034 mg/kg/日のノルディトロピン（3：1） 156～364 週（長期安全性延長期間） 0.16 mg/kg/週のソマプシタン（全例）
	試験の状況：被験者の組み入れが進行中	コホート II[d] 1 例（組み入れ時点で年齢 2.5 歳未満） コホート III[d] 9 例（組み入れ時点で年齢 9 歳超（女児）／10 歳超（男児）、17 歳以下）	156～364 週（長期安全性延長期間） 0.16 mg/kg/週のソマプシタン（全例）
4263[#]（第 3 相）	有効性及び安全性 無作為割り付け、国際共同、多施設共同、非盲検、実薬対照、並行群間比較試験 試験の状況：進行中（104 週までは完了） 総試験期間：208 週間（4 年間）	hGH 製剤による治療歴のない、二次性徴発来前の小児 GHD 患者 200 例 年齢 2.5～11.0 歳 参加国 日本（30 例）を含む複数国 [e] 女児 51 例及び男児 149 例	0～52 週（主要期間） 0.16 mg/kg/週のソマプシタン又は 0.034 mg/kg/日のノルディトロピン（2：1） 52～208 週（延長期間） 0.16 mg/kg/週のソマプシタン（全例）
4468（第 3 相）	有効性及び安全性	hGH 製剤による治療歴のない、二次性徴発来前の小児 GHD 患者 108 例（予定）	0.16 mg/kg/週のソマプシタン又は 0.034 mg/kg/日のノルディトロピン

試験 ID（相）	試験デザイン	曝露被験者数	用法・用量
	試験の状況：進行中（組み入れが進行中） 試験期間：52 週間	参加国 中国 無作為割り付け被験者 29 例、曝露被験者 28 例	

[a]: 4172 試験では、ソマプシタン及びノルディトロピンの比較は非盲検であったが、ソマプシタンの用量間の比較は二重盲検であった（0～52 週）。

[b]: 4172 試験：オーストリア、ブラジル、ドイツ、インド、イスラエル、日本、スロベニア、スウェーデン、トルコ、ウクライナ及び米国

[c]: 最大の解析対象集団（57 例）に基づく。

[d]: 週 1 回投与のソマプシタンを 7 年以上投与するよう計画された（26 週間の主要期間、26 週間の延長期間、104 週間の安全性延長期間及び 208 週間の長期安全性延長期間）。最初の 52 週間の治療を完了後、ソマプシタン投与を受けていた被験者は、0.16 mg/kg/週のソマプシタン投与に再度割り当てられ、0.034 mg/kg/日のノルディトロピン投与を受けていた被験者はノルディトロピンの投与を継続した。156 週後、ノルディトロピン投与を受けていたすべての被験者は、0.16 mg/kg/週のソマプシタン投与に切り替えた。4 年まで（208 週まで）の結果が報告されている。長期安全性延長期間（156～364 週）では、最初の試験対象集団（コホート I）に加え、2 つのコホート（コホート II 及び III）を追加した。コホート II にはスクリーニング時の年齢が 2.5 歳未満の被験者を、コホート III にはスクリーニング時の年齢が 9 歳（女児）／10 歳（男児）歳超、17 歳以下の被験者を組み入れた。

[e]: 4263 試験：オーストリア、カナダ、フランス、ドイツ、インド、イスラエル、イタリア、日本、韓国、ラトビア、ポーランド、ロシア、セルビア、スロベニア、スペイン、スイス、タイ、ウクライナ、英国及び米国

[#]日本人被験者を含む試験

注：ソマプシタンは週 1 回皮下投与、ノルディトロピンは 1 日 1 回皮下投与

2.7.4.1.2.2 安全性の評価

安全性評価は、ソマプシタンの臨床試験で収集した以下の安全性情報に基づく。

- 有害事象及び重篤な有害事象
- 特に注目すべき安全性領域
- 臨床検査項目：血液学的検査及び血液生化学的検査等（糖代謝、甲状腺機能及び副腎機能検査を含む）
- IGF-I
- バイタルサイン（収縮期／拡張期血圧及び脈拍数）
- 体重
- 骨年齢
- 身体所見
- 心電図

各試験で観察した安全性評価項目の一覧は、各試験の治験実施計画書〔4042 試験（M5.3.3.2）Section 4.2、4172 試験（M 5.3.5.1）Section 4.2、4263 試験（M 5.3.5.1）Section 9〕に詳細に示す。

有害事象

有害事象は、各試験の治験実施計画書〔4042 試験（M5.3.3.2）Section 12.1～12.3、4172 試験（M 5.3.5.1）Section 12.1～12.3、4263 試験（M 5.3.5.1）Section 9.2 及び Appendix 4〕で規定したとおり、ICH E2A に従って定義し、報告した。

特に注目すべき安全性領域

小児 GHD におけるソマプシタンの安全性プロファイルは、市販されている既存の hGH 製剤（ノルディトロピン等）と同様であると予測された。ノルディトロピンの安全性プロファイルの詳細は、Summary of Product Characteristics（SmPC）[9]、米国及び日本の添付文書[12,13]に示す。

ソマプシタンの臨床経験、規制当局からの助言及び要求事項に基づき、ソマプシタンの安全性評価において特に関連のある事象として、特に注目すべき安全性領域を定義した（表 2.7.4.2-14）。特に注目すべき安全性領域は、器官別又は症候群別有害事象の解析の項（2.7.4.2.5）に示す。それぞれの特に注目すべき安全性領域は、各領域に特有の国際医薬用語集（MedDRA）標準検索（狭義）に基づき評価した。詳細は 2.7.4.2.5 に示す。

MedDRA 標準検索式（SMQ）、器官別大分類（SOC）／高位グループ語（HLGT）／高位語（HLT）／基本語を用いて検索した。適切な SMQ がない場合は、関連する基本語又は高位語に基づいて特定の MedDRA 検索式を構築した（NNMQ）。各国際共同試験で該当する有害事象を検索し、試験別に提示した。主な評価は第 3 相検証的試験である 4263 試験で行い、第 2 相試験である 4172 試験の結果で補足した。また、SMQ による検索は、安全性併合解析データである 0.16 mg/kg/週のソマプシタン投与及びノルディトロピン投与の併合（2.7.4.1.2.3.2）でも行った。

hGH 製剤の投与は、インスリン感受性を低下させることがあり、特に、反応性の高い患者に高用量を投与した場合に起きやすい。また、hGH 製剤の投与によるインスリン感受性の低下は、小児患者よりも成人患者で起こりやすい。そのような場合、インスリン分泌能が不十分な患者では高血糖状態になる可能性がある。その結果、hGH 製剤による治療中に、これまでに診断されていない耐糖能異常又は糖尿病が現れることがある。そのため、耐糖能異常の徴候を示した被験者を特定するために、糖代謝に関する詳細な調査を行うこととした。

他の注射剤と同様に、ソマプシタンの皮下投与後にも、注射部位において発赤、腫脹、そう痒及び圧痛といった好ましくない局所的な副作用がみられることがある。局所忍容性は、注射部位反応を観察することで評価した。

あらゆるタンパク質性医薬品による治療時と同様、ソマプシタンでも抗体が産生される可能性がある。抗体の産生は、頻度はごく低いものの、これまでに他の hGH 製剤による治療でもみられている。ソマプシタンの投与を行った臨床試験では、*in vitro* の中和抗体を含めた、ソマプシタン又は hGH 製剤に対する抗体の測定を実施した。本臨床概要には、抗薬物抗体産生に関する主な結果と結論を示し、抗体評価に関する詳細は、Integrated summary of immunogenicity（M 5.3.5.3）に示す。

臨床検査項目

血液学的検査及び血液生化学的検査等（糖代謝、甲状腺機能及び副腎機能検査を含む）、標準的な臨床検査項目を評価した。臨床的に問題のある変化は、有害事象として報告された。

IGF-I

小児 GHD における GH 治療中の IGF-I レベルについて明確な基準を示したガイドラインはないが、IGF-I は可能なかぎり基準範囲内に維持すべきである。ただし、特定の状況下において+2 を大きくない

程度に超えることが許容される場合もあり、GH 治療を受けた小児において、血清 IGF-I 濃度の大きくない程度の一時的な上昇と有害事象の関連はないとの報告がある[14]。小児 GHD 患者を対象とした臨床試験（4263 試験及び 4172 試験）では、IGF-I 濃度を長期間にわたり基準範囲外になることがないように定期的に測定した。

バイタルサイン

医薬品が長期的に使用される場合、特に心血管リスクが高い患者集団では、数 mmHg のわずかな血圧上昇であっても、懸念となる可能性がある[15]。そのため、血圧及び脈拍数のベースラインからの変化量を検討した。

心電図

スクリーニング及び試験中では年 1 回の頻度で心電図を測定した。治験責任医師は、心電図結果を評価し、「正常」、「異常／臨床的に問題なし」又は「異常／臨床的に問題あり」のいずれかに分類した。

体重

小児では、成長中に体重増加が見込まれる。体重のベースラインからの変化量を検討した。

2.7.4.1.2.3 安全性データの表示

2.7.4.1.2.3.1 試験別での表示

安全性データを試験別に示し、主に国際共同第 3 相検証的試験である 4263 試験（主要期間）の結果を示す（表 2.7.4.1-1）。各臨床試験で収集した安全性データの評価の詳細は、各治験総括報告書に記載した。

国際共同第 3 相検証的試験である 4263 試験は、安全性評価における主要な試験であり、主要期間では、対照群（ノルディトロピン）に対するソマプシタンの 52 週間の安全性データが得られた（図 2.7.4.1-1）。対照群を設定して評価することで、製剤の一般的な安全性の問題に関連する最も意味のあるデータが得られることとなり、安全性のデータを治療間で比較することができる。なお、4263 試験の全被験者の 104 週までの成績（0 週にソマプシタン群に割り付けられた被験者：104 週間のソマプシタン投与、0 週にノルディトロピンに割り付けられ、52 週にソマプシタン投与に切り替えた被験者：52 週間のソマプシタン投与）は審査中に提出した。

追加で提出した 4263 試験の 104 週までの成績は以下の項に示す。

- 治験薬の曝露の情報：2.7.4.1.3.5
- 有害事象：2.7.4.2.7
- 臨床検査値：2.7.4.3.4
- バイタルサイン、身体所見及び安全性に関する他の観察項目：2.7.4.4.7

第 2 相試験である 4172 試験の安全性データは第 3 相試験の安全性を補足するものである。52 週間のノルディトロピンに対するソマプシタンの用量レベル（0.04、0.08 又は 0.16 mg/kg/週）間の比較デー

タ、156 週間の安全性データ（ソマプシタン群とノルディトロピン群の比較）及び延長試験の完了部分で最長 4 年間の安全性データ（0.16 mg/kg/週のソマプシタン）が得られている〔コホート I では、ソマプシタンの投与を受けていた被験者は、52 週時に 0.16 mg/kg/週のソマプシタン投与に移行し、0.034 mg/kg/日のノルディトロピン投与を受けていた被験者は、試験期間の 4 年目（156 週から）に 0.16 mg/kg/週のソマプシタン投与に切り替えた〕（図 2.7.4.1-2）。さらに、本試験では、組み入れ時点で年齢 2.5 歳未満の被験者（コホート II）及び 9 歳超（女児）／10 歳超（男児）17 歳以下の被験者（コホート III）の安全性データが得られている。また、ノルディトロピンから切り替え後 1 年のデータが得られている。

4172 試験の主な安全性評価は、0～208 週間の併合されたデータである。2 つのソマプシタン併合群を定義し、比較した。

- ソマプシタン 0.04/0.08/0.16 mg/kg/週併合群：0～208 週までに 0.04、0.08 又は 0.16 mg/kg/週のソマプシタン投与を受けた被験者（すなわち、52 週時に 0.04 又は 0.08 mg/kg 週から 0.16 mg/kg/週のソマプシタン投与に切り替えた被験者は含まれ、156 週時にノルディトロピンから 0.16 mg/kg/週のソマプシタン投与に切り替えた被験者は含まれない）。
- ソマプシタン 0.16 mg/kg/週併合群：0.16 mg/kg/週のソマプシタン投与を受けたすべての被験者（0.16 mg/kg/週のソマプシタン投与を開始した時点から）。0 週から 0.16 mg/kg/週のソマプシタン投与を受けた被験者、52 週時に 0.04 又は 0.08 mg/kg 週から 0.16 mg/kg/週のソマプシタン投与に切り替えた被験者及び 156 週時にノルディトロピンから 0.16 mg/kg/週のソマプシタン投与に切り替えた被験者からなる。

4172 試験の結果は、3 つの治験総括報告書に示されている。

- 26 週間の主要期間の治験総括報告書：用量別の比較
- 156 週間の治験総括報告書：52 週間の用量別の比較及び 3 年間のノルディトロピンとの比較
- 208 週間の治験総括報告書：追加の患者コホート〔年齢が 2.5 歳未満の被験者及び 9 歳超（女児）／10 歳超（男児）17 歳以下の被験者〕、ノルディトロピンからソマプシタン投与に切り替え後 1 年のデータ、ソマプシタン 0.04/0.08/0.16 mg/kg/週併合群とソマプシタン 0.16 mg/kg/週併合群の比較

さらに、これらの安全性データは、安全性併合データにより補足される（2.7.4.1.2.3.2）。

日本人被験者の安全性

「国際共同治験に関する基本的考え方について」[16]及び機構の助言に従い、4263 試験（52 週）及び 4172 試験（208 週）の全集団と日本人集団の結果の一貫性を評価した。全集団と日本人集団で安全性の結果に一貫性がみられた場合、全集団の結果を日本人集団に外挿することが可能と考えられる。

2 つの集団間の安全性の一貫性を評価するため、日本人集団の安全性データ（有害事象プロファイル）を試験別に要約し、全集団における安全性データと比較した。当該評価に関連する帳票を付録 2.7.4.7.2 に含めた。

日本人小児 GHD 患者は、日本の治験実施医療機関から組み入れられた被験者と定義した。

臨床薬理試験

第 1 相試験である 4042 試験（単回投与）の関連する安全性データを提示する。4042 試験は曝露期間が短いため（単回投与）、本試験から得られた安全性データは限られている。本試験の安全性情報の詳細は、治験総括報告書〔4042 試験（M 5.3.3.2）Section 12〕に示す。

2.7.4.1.2.3.2 安全性併合データ

ソマプシタンの安全性（有害事象）に関する評価を、第 2 相試験（4172 試験）及び第 3 相試験（4263 試験、主要期間）で 0.16 mg/kg/週のソマプシタン投与又はノルディトロピン投与を受けたすべての被験者からなる安全性併合データで補足する。

安全性併合データの解析対象集団は、第 2 相試験（4172 試験）及び第 3 相試験（4263 試験）で、0.16 mg/kg/週のソマプシタン投与又はノルディトロピン投与を開始した来院から、当該治療を少なくとも 1 回受けたすべての被験者で構成される。表 2.7.4.1-2 には、いずれの治療群又は期間が併合した治療群に寄与するかを示す。被験者が用量を減量した場合でも、安全性併合データに含めた。

ソマプシタンの安全性に関する総合評価を補足し、潜在的な安全性シグナルを検出する可能性を高めるため、小児 GHD 患者を対象とした臨床試験（4263 試験及び 4172 試験）で、0.16 mg/kg/週のソマプシタンの投与を開始した来院から、当該治療を受けたすべての被験者から得られた曝露及び有害事象のデータを併合した。試験データを併合することの適切性を確認するため、またデータを併合することで、安全性の問題が検出されなくなることを回避するため、併合データ内の各試験間の一貫性も評価した。いずれの試験もノルディトロピンと比較したソマプシタンの安全性データを含み（4263 試験：52 週間、4172 試験：156 週）、試験対象集団は hGH 製剤による治療歴のない小児 GHD 患者である。

ノルディトロピンと比較して最適で有効な用量と考えられる 0.16 mg/kg/週を小児 GHD におけるソマプシタンの用量として選択した。本用量は、第 3 相試験（4263 試験）において、ノルディトロピンに対する検証的な比較を行う際に用いられ、市販後に世界的に小児 GHD で使用予定の用量である。4172 試験では、0.16 mg/kg/週のソマプシタンの投与を受けた被験者の一部は、0.16 mg/kg/週に移行前に低用量（0.04 及び 0.08 mg/kg/週）のソマプシタンの投与を受けた。これらの低用量のソマプシタンの投与を受けた被験者の安全性データは、4172 試験の安全性を記述する際に提示される。

実際に投与を受けた治療に基づいて被験者を分類した。すなわち、4172 試験で最初にノルディトロピン投与を受けた後ソマプシタン投与に切り替えた被験者は、いずれの群にも含まれた。有害事象の因果関係は、有害事象発現時に投与されていた治験薬との関連性を評価した。ノルディトロピンからソマプシタン投与に切り替え後に発現した有害事象は、いずれの治療群にも寄与した。

ソマプシタンの安全性プロファイルについて、第 2 相試験及び第 3 相試験の被験者集団間で明らかな違いはみられなかった（各試験の安全性データに基づく）。このことは、安全性データを併合することを支持する。

4042 試験では、曝露の程度が小さいことから（6 例の被験者が 0.16 mg/kg のソマプシタンの単回投与を受けた）、併合データには含めなかった。

表 2.7.4.1-2　　併合した安全性データ（群別）

Trial ID	52 weeks	Extension	
Trial 4263	Somapacitan 0.16 mg/kg/week	NA (ongoing)	
	Norditropin	NA (ongoing)	
Trial 4172	**Main + extension** **Year 1** (Weeks 0-52)	**Safety extension** **Year 2 and 3** (Weeks 52-156)	**Long-term safety extension** **Year 4** (Weeks 156 to 208)
Cohort I	Somapacitan 0.16 mg/kg/week	Somapacitan 0.16 mg/kg/week[a]	Somapacitan 0.16 mg/kg/week
	Norditropin	Norditropin	Somapacitan 0.16 mg/kg/week[b]
Cohorts II and III	NA	NA	Somapacitan 0.16 mg/kg/week[c]

[a] Some children were previously exposed to lower somapacitan dose levels (0.04 or 0.08 mg/kg/week).
[b] Children were previously exposed to Norditropin and switched the last year to somapacitan 0.16 mg/kg/week.
[c] Cohorts II and III were included in the trial in addition to the original trial population (cohort I). Cohort II enrolled children below 2 years and 26 weeks at screening, and cohort III enrolled children above 9 years (girls)/10 years (boys) and ≤ 17 years at screening.
Notes: In trial 4172, children treated with somapacitan in the first 52 weeks continued their once-weekly somapacitan treatment in the extension part, where all children were treated with somapacitan 0.16 mg/kg/week. Children treated with Norditropin in the first 156 weeks were switched to somapacitan 0.16 mg/kg/ week in the long-term safety extension. The long-term safety extension is ongoing (Weeks 156 to 364; 52 of 208 weeks long-term extension have been reported).
Abbreviations: NA: not applicable.

併合された被験者集団の群別の被験者の内訳及びベースライン特性は、4172 試験の最初の 156 週間に行った治療の変更に関わらず、ベースラインのデータに基づいている（たとえば、ノルディトロピン/ソマプシタン群の被験者では、ノルディトロピン群及びソマプシタン群のいずれの評価においても、ベースラインデータは同一である）。

安全性データの併合の概要を表 2.7.4.1-3 に示す。

表 2.7.4.1-3　　小児 GHD 患者を対象とした臨床試験の併合の概要

Trial ID (duration)	**Number of exposed children** (randomisation ratio)	**Children with GHD**	**Treatment group**[a]
Trial 4263 (52 weeks)	N=200 (2:1)	GH treatment naïve	Somapacitan 0.16 mg/kg/week or Norditropin
Trial 4172 Cohort I (up to 208 weeks)	N=59 (1:1:1:1)	GH treatment naïve	Somapacitan 0.16 mg/kg/week and/or Norditropin
Cohorts II and III	N=10	GH treatment naïve or previously treated	Somapacitan 0.16 mg/kg/week

[a] Trial 4263: somapacitan s.c. 0.16 mg/kg week. Norditropin s.c. 0.034 mg/kg/day.
Trial 4172: weeks 0−52: somapacitan s.c. 0.04, 0.08 or 0.16 mg/kg week; weeks 52−364: somapacitan s.c. 0.16 mg/kg/week. Norditropin s.c. 0.034 mg/kg/day (up to week 156, whereafter all children were allocated to somapacitan 0.16 mg/kg/week).
Abbreviations: GH: growth hormone; GHD: growth hormone deficiency.

2.7.4.1.2.3.3 安全性データの提示順序

安全性データは以下の順序で提示した。

- 主要な第 3 相試験（4263 試験）：52 週の結果（データベースロックは 2021 年 12 月 3 日及び 17 日）

  - 日本人集団の結果
- 補足的な情報
  - 第 2 相試験（4172 試験）：208 週の結果（データベースロックは 2021 年 11 月 19 日）
    - 日本人集団の結果
  - 安全性併合データ：第 3 相試験（4263 試験）及び第 2 相試験（4172 試験）（曝露及び有害事象）
  - 臨床薬理試験（4042 試験）：単回投与、用量漸増の結果

2.7.4.1.2.3.4 有害事象

安全性データは、記述統計量を用いて示した。有害事象は、MedDRA（version. 17.1～24.1、完了時点で試験別に作成したデータ）を用いてコード化し、器官別大分類（SOC）及び基本語（PT）別に集計した。本申請における併合データでは、MedDRA version. 24.1 を用いた。

有害事象及び重篤な有害事象の記述及び評価には、主に有害事象を発現した被験者の割合を使用し、有害事象の単位時間あたりの発現件数又は有害事象の発現件数は適宜提示した。さらに、重症度、有害事象の種類、治験薬との因果関係及び転帰も用いた。有害事象は試験別及び治療別に提示した。

さらに、0.16 mg/kg/週のソマプシタン投与又はノルディトロピン投与の有害事象のデータを併合して提示する（4172 試験及び 4263 試験の併合）。併合の手法は 2.7.4.1.2.3.2 に記載した。

重篤な有害事象ならびに治験薬の投与中止に至った有害事象についての叙述を各治験総括報告書（M 5.3.5.1）に示す。

その他の重要な有害事象（新生物、注射部位反応等）は、本臨床概要の本文中に適宜詳述した（ただし、上記のカテゴリーに該当しない場合は、治験総括報告書に叙述を含めていない）。

2.7.4.1.2.3.5 臨床検査項目

試験ごとに異なる来院時期に測定した値を併合することは困難であるため、血液学的検査、血液生化学的検査及び免疫原性試験を含む臨床検査項目の評価は、試験別に記述した（各試験の治験総括報告書に基づく）。

血液学的検査及び血液生化学的検査についてはベースラインからの変化量を評価した。基準範囲外の臨床検査値については、基準範囲より高いか低いかを示した。

糖代謝については、米国糖尿病学会（ADA）の糖尿病診断基準〔空腹時血糖値及び HbA1c について ADA（Diabetes Care vol.39, suppl.1, Jan 2016）の基準を超える被験者を特定（試験中に 1 回以上の来院で空腹時血糖値が 7.0 mmol/L 以上又は HbA1c が 6.5%以上）〕を適用して耐糖能障害の徴候を示した被験者を特定した。

2.7.4.1.2.3.6 IGF-I SD スコア

年齢及び性別における正常な集団の値[17]に基づいて IGF-I SD スコアを算出した。

IGF-I SD スコアが+2 超（連続 2 回以上の来院）となった被験者の IGF-I SD スコアの推移図を試験別に提示した。

2.7.4.1.2.3.7 バイタルサイン、心電図及び体重

バイタルサイン（収縮期／拡張期血圧及び脈拍数）、心電図及び体重については試験別に記述した（各試験の治験総括報告書に基づく）。ベースラインからの変化を検討した。

2.7.4.1.2.4 部分集団における安全性

ICH M4E ガイドライン[18]に従い、以下の部分集団における有害事象も評価した。

- 性別（男児又は女児）
- 年齢（6 歳未満又は 6 歳以上、無作為割り付け時の層別割り付けの水準）

これらの部分集団における安全性を検討するため、第 3 相試験である 4263 試験の有害事象の要約表を示した。部分集団別の有害事象を 2.7.4.5.1 に示す。

さらに、組み入れ時点で年齢 2.5 歳未満の被験者（4172 試験のコホート II）及び 9 歳超（女児）／10 歳超（男児）17 歳以下の被験者（4172 試験のコホート III）の安全性データが得られている。当該データを 2.7.4.2.1.2.1 に示す。

2.7.4.1.2.5 AGHD における安全性

ソマプシタン（遺伝子組換え）（販売名：ソグルーヤ®皮下注 5 mg/ソグルーヤ®皮下注 10 mg）は、「成人成長ホルモン分泌不全症（重症に限る）」の効能又は効果で 2021 年 1 月 22 日に製造販売承認を受けており、米国（2020 年 8 月 28 日）及び欧州（2021 年 3 月 31 日）でも成人成長ホルモン分泌不全症（AGHD）の適応症で承認を受けている。

AGHD におけるソマプシタンの安全性は、1 日 1 回投与の hGH 製剤（ノルディトロピン等）と同様であった。AGHD における臨床開発プログラムで得られた結果の詳細は、本剤の Summary of Product Characteristics（SmPC）又は AGHD の適応症取得を目的とした初回の製造販売承認申請時（既承認申請時）に提出した資料に示す。

2.7.4.1.2.5.1 非臨床における所見

非臨床におけるソマプシタンの安全性評価に関する報告では、ヒトに対する長期的な皮下投与を妨げるような安全性の問題は示されなかった。非臨床における安全性評価の詳細については、既承認申請時に提出した資料（Module 2.4）を参照のこと。

2.7.4.1.3 全般的な曝露状況

試験別の曝露状況の詳細は、治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Section 10.3.1、4172 試験（26 週）（M 5.3.5.1）Section 10.3.1、4172 試験（156 週）（M 5.3.5.1）Section 10.3.1、4172 試験（208 週）（M 5.3.5.1）Section 10.3.1 及び 4042 試験（M 5.3.3.2） Section 10.3〕に示す。試験デザインの詳細は、Module 2.7.6 に示す。

2.7.4.1.3.1 主要な第 3 相試験（4263 試験、主要期間）の曝露

小児 GHD 患者 132 例が第 3 相試験の完了した期間でソマプシタンの投与を受けた（表 2.7.4.1-4）。第 3 相試験（4263 試験、主要期間）では、52 週までのソマプシタン投与を評価した。

第 3 相試験（4263 試験、主要期間）では、0.16 mg/kg のソマプシタンを週 1 回投与し、実対照薬として 0.034 mg/kg のノルディトロピンの 1 日 1 回投与を含めた。

総曝露期間はノルディトロピン（約 69 人・年、総曝露日数 25166 日）と比較してソマプシタン（約 133 人・年、総曝露日数 48734 日）で約 2 倍長く、割り付け比率が 2：1 であったことと 52 週間の主要期間中に投与を中止した被験者が 1 例のみ（ソマプシタン群）であったことを反映している（表 2.7.4.1-4）。被験者あたりの曝露期間の平均は、いずれの群でも約 1 年であり、治験薬の投与を完了した被験者の割合が高かったことを反映している。

表 2.7.4.1-4　曝露状況の要約（安全性解析対象集団）（4263 試験、主要期間）

	Norditropin	somapacitan
Number of subjects	68	132
Total exposure (days)	25166	48734
Exposure (days)		
N	68	132
Mean (SD)	370.1 (3.7)	369.2 (28.8)
Median	369.0	370.0
Min ; Max	364 ; 387	56 ; 458

N: Number of subjects, SD: Standard deviation
Exposure days in the treatment period are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan or to visit 7 (week 52), whichever comes first.

大部分の被験者が計画された投与を受け、治療遵守率の平均（治験薬投与を中止した 1 例の被験者の中止後の期間は含めていない）は、ソマプシタン群で 95.8%、ノルディトロピン群で 88.3%であった（表 2.7.4.1-5）。

表 2.7.4.1-5　治療遵守状況（4263 試験、主要期間）

	Norditropin	somapacitan	Total
Number of subjects	68	132	200
Number of reported dosings	23710	6708	30418
Number of dosings in adherence	22203	6691	28894
Adherence according to diary*			
Mean (SD)	88.3 (23.57)	95.8 (10.19)	93.3 (16.38)
Median	96.9	100.0	98.9
Min; Max	4.2; 100.0	20.8; 100.0	4.2; 100.0

SD: Standard deviation
Dosings in adherence: All injections recorded between visit 2 and visit 7 in the diary with a dose above 0. A dose for Norditropin® will be counted in adherence if taken at or after 3 pm and before 3 am the following day. A dose of somapacitan will be counted in adherence if taken within 1 day before to 2 days after planned date of dosing.
For subjects discontinuing treatment, the planned number of dosings will be counted up until last day on treatment.
* Number of reported dosings from diary in adherence divided by number of planned dosings multiplied by 100.

2.7.4.1.3.1.1 主要な第 3 相試験（4263 試験、主要期間）の曝露（日本人集団）

4263 試験の日本人集団及び全集団における曝露状況を要約する（要約表の相互参照を以下に示す）。

4263 試験（主要期間）では、日本人小児 GHD 患者 19 例にソマプシタンを投与し（総曝露期間 19 人・年）、11 例にノルディトロピンを投与した（総曝露期間 11 人・年）（付録 2.7.4.7.2、Table 24）。すべての日本人小児 GHD 患者が 52 週間の投与を完了した。日本人小児 GHD 患者における曝露を付録 2.7.4.7.2、Table 24～26（4263 試験、主要期間）に要約する。

4263 試験では、曝露について日本人集団と全集団との間に意味のある違いは認められなかった。

2.7.4.1.3.2 補足的な情報

2.7.4.1.3.2.1 4172 試験（第 2 相試験）の曝露

第 2 相用量設定試験（4172 試験）の完了した期間でソマプシタンの投与を受けた小児 GHD 患者の被験者数〔曝露期間（人・年、PYE）を含む〕を表 2.7.4.1-6 に要約する。第 2 相試験では、4 年（208 週）までのソマプシタン投与を評価した。4172 試験は試験期間中に治療を変更する試験デザインであったため、曝露状況を試験の異なる期間に対して要約する。

第 2 相試験では、最初の 1 年間に 0.04 mg/kg、0.08 mg/kg 又は 0.16 mg/kg/週のソマプシタンを投与し、その後ソマプシタンの投与を受けたすべての被験者が 0.16 mg/kg/週のソマプシタン投与に移行した。0.034 mg/kg/日のノルディトロピン投与を受けた被験者は、最初の 3 年間終了後に 0.16 mg/kg/週のソマプシタン投与に移行した。4 つの群は以下のとおり表記する。

- ノルディトロピン/ソマプシタン（Norditropin 0.034 mg/kg/day/somapacitan 0.16 mg/kg/week）
- ソマプシタン 0.04/0.16 mg/kg/週（somapacitan 0.04/0.16 mg/kg/week）
- ソマプシタン 0.08/0.16 mg/kg/週（somapacitan 0.08/0.16 mg/kg/week）

- ソマプシタン 0.16/0.16 mg/kg/週（somapacitan 0.16/0.16 mg/kg/week）

さらに、4172 試験のソマプシタン併合群（ソマプシタン 0.04/0.08/0.16 mg/kg/週）の曝露状況を表 2.7.4.1-6 に提示した。

本試験には実対照薬として 0.034 mg/kg のノルディトロピンの 1 日 1 回投与を含めた。

表 2.7.4.1-6　曝露状況の要約（治療別及び期間別）（4172 試験、コホート I）

Treatment group Main + Extension/ Safety extension	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week) N	PYE	somapacitan (0.04mg/kg/week)/ somapacitan (0.16mg/kg/week) N	PYE	somapacitan (0.08mg/kg/week)/ somapacitan (0.16mg/kg/week) N	PYE	somapacitan (0.16mg/kg/week)/ somapacitan (0.16mg/kg/week) N	PYE	somapacitan (0.04/0.08/0.16 mg/kg/week) pooled N	PYE
Main (Weeks 0-26)	14	6.7	16	7.3	15	7.6	14	7.2	45	22.0
Extension (Weeks 0-52)	13	13.0	14	14.1	15	15.1	14	14.3	43	43.4
Safety extension (Weeks 52-156)	11	22.2	13	25.7	14	28.1	13	25.7	40	79.5
Long-term safety ext (Weeks 156-208)	11	10.8	12	11.7	14	14.0	13	13.1	39	38.8

N: Number of subjects, PYE: Patient years of exposure

[a] The 11 children who switched to somapacitan 0.16 mg/kg/week after 156 weeks were not included in the trial 4172 somapacitan 0.04/0.08/0.16 mg/kg/week pool.

Notes: The treatment in the main/extension periods of the trial is indicated by e.g. somapacitan/somapacitan.

Abbreviations: PYE: patient years of exposure; Norditropin: Norditropin FlexPro.

長期安全性延長期間に追加した 2 つのコホート〔組み入れ時点で年齢 2.5 歳未満の被験者（コホート II）及び 9 歳超（女児）／10 歳超（男児）17 歳以下の被験者（コホート III）〕でもソマプシタンを投与したデータが得られている（表 2.7.4.1-7）。

表 2.7.4.1-7　曝露状況の要約〔治療別、コホート II（年齢 2.5 歳未満の被験者）及び III（年齢 9 歳超（女児）／10 歳超（男児）17 歳以下の被験者）〕（4172 試験）

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Number of subjects	1	2	7
Total exposure (days)	366	676	1022
Exposure (days)			
N	1	2	7
Mean (SD)	366.0 (.)	338.0 (59.4)	146.0 (75.7)
Median	366.0	338.0	161.0
Min ; Max	366 ; 366	296 ; 380	7 ; 242

N: Number of subjects, SD: Standard deviation. Exposure days in the treatment period are calculated as time from first date on treatment to last date on treatment plus six days.

大部分の被験者が計画された投与を受け、治療遵守率の平均は、ソマプシタン 0.04/0.08/0.16 mg/kg/週併合群で 96.8%、ノルディトロピン/ソマプシタン群（156～208 週）で 96.2%、ノルディトロピン群（0～156 週）で 98.6%であった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.2.9〕。

コホート II では、データベースロック時点の治療遵守率は 100%（1 例）であった。コホート III では、データベースロック時点の治療遵守率は hGH 製剤による治療歴のない被験者で 76.1%（2 例）、治療歴のある被験者で 67.4%（7 例）であった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.2.13〕。コホート III で治療遵守率が低かったのは、投与忘れではなく投与データの欠測によるものであった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Section 10.3.1〕。

2.7.4.1.3.2.1.1 第 2 相試験（4172 試験）の曝露（日本人集団）

4172 試験の日本人集団及び全集団における曝露状況を要約する（要約表の相互参照を以下に示す）。

4172 試験では、日本人小児 GHD 患者 9 例にソマプシタンを投与し（総曝露期間 36 人・年、総曝露日数約 13264 日）、3 年後にさらに 2 例の日本人被験者がノルディトロピンからソマプシタンの投与に切り替えた（付録 2.7.4.7.2、Listing 35）。3 例の日本人被験者にノルディトロピンを投与した（総曝露期間 7 人・年、総曝露日数約 2553 日）（付録 2.7.4.7.2、Table 15）。

被験者あたりの曝露期間の平均はソマプシタン群で 4 年（ソマプシタン群に無作為割り付けされた日本人被験者 9 例が 4 年間の投与を完了）、ノルディトロピン群で 2.3 年（日本人被験者 2 例が 3 年間、1 例が 1 年間の投与を完了）であった。ソマプシタン群の曝露日数の中央値は日本人集団〔中央値 1473 日、平均（SD）1473.8（4.5）日（約 4 年）〕と全集団〔中央値 1471 日、平均（SD）1324.1（403.8）日（約 3.6 年）〕で同様であった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.2.1〕。

日本人被験者における曝露を付録 2.7.4.7.2、Table 1～3（4172 試験、156 週）及び Table 15～17（4172 試験、208 週）に要約する。

4172 試験では、曝露について日本人集団と全集団との間に意味のある違いは認められなかった。

2.7.4.1.3.2.2 安全性併合データの結果

安全性併合データにおけるソマプシタンの曝露状況を表 2.7.4.1-8 に要約する。

小児 GHD 患者を対象とした 2 つの進行中の試験（4172 試験及び 4263 試験）では、194 例が 0.16 mg/kg/週のソマプシタン投与を受けた。4172 試験では、0.16 mg/kg/週のソマプシタン投与を受けた被験者の一部は、最初に 0.04 又は 0.08 mg/kg/週のソマプシタン投与に無作為割り付けされ、52 週時に 0.16 mg/kg/週のソマプシタン投与に移行した。安全性併合データには、4263 試験及び 4172 試験で 0.16 mg/kg/週のソマプシタン投与を受けたすべての被験者の、0.16 mg/kg/週での投与開始以降のデータを含めた。208 週までのソマプシタンの曝露状況を評価した（4172 試験は進行中）。

小児 GHD 患者を対象とした試験では、82 例が実対照薬である 1 日 1 回のノルディトロピン投与（0.034 mg/kg/日）を受けた（曝露期間は 156 週まで）。

総曝露期間はソマプシタン 0.16 mg/kg/週安全性併合群で 282.8 人・年、ノルディトロピン安全性併合群で 104.5 人・年であった。

表 2.7.4.1-8　　小児 GHD 患者における曝露状況の要約（安全性併合データ）

	Norditropin	somapacitan (0.16mg/kg/week) safety pooled[a]
Number of exposed subject	82	194
Days of exposure*		
Mean (SD)	464.32 (255.79)	533.38 (360.98)
Median	369.0	371.0
Min ; Max	45 ; 1196	7 ; 1484
Treatment dose** (mg)		
Mean (SD)	2.79 (1.23)	3.90 (1.26)
Median	2.88	3.80
Min ; Max	0.40 ; 5.20	2.00 ; 9.90
Treatment dose** (mg/kg)		
Mean (SD)	0.03 (0.0007)	0.16 (0.0011)
Median	0.03	0.16
Min ; Max	0.03 ; 0.04	0.16 ; 0.16
Total patient years at risk (on treatment)	104.54	282.75

N: Number of subjects, SD: Standard deviation
*Exposure days in the treatment period are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan or to visit 20 (week 208 for cohort I and week 52 for cohort II and III) for 4172 and for 4263 to visit 7 (week 52), which ever comes first.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.
**Last prescribed dose.
[a]Children previously exposed to Norditropin who switched at week 156 to somapacitan 0.16 mg/kg/week are included in the somapacitan pool.

小児 GHD のソマプシタン臨床開発プログラムでは、188 例（96.9%）に 6 ヵ月以上、183 例（94.3%）に 12 ヵ月以上、39 例（20.1%）に 21 ヵ月以上ソマプシタンを投与した（表 2.7.4.1-9）。

表 2.7.4.1-9　小児 GHD 患者における 3 ヵ月ごとの曝露状況の要約（安全性併合データ）

	Norditropin N (%)	somapacitan (0.16mg/kg/week) safety pooled N (%)
Number of Subjects	82	194
Exposure period		
>0 months	82 (100.0)	194 (100.0)
>3 months	81 (98.8)	192 (99.0)
>6 months	81 (98.8)	188 (96.9)
>9 months	81 (98.8)	186 (95.9)
>12 months	81 (98.8)	183 (94.3)
>15 months	11 (13.4)	41 (21.1)
>18 months	11 (13.4)	39 (20.1)
>21 months	11 (13.4)	39 (20.1)

N: Number of subjects, %: Percentage. Month = 30 days.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

被験者の治療遵守率は 2 つの群いずれにおいても高かった（表 2.7.4.1-10）。

表 2.7.4.1-10　被験者の治療遵守率（最大の解析対象集団）（安全性併合データ）

	Norditropin N (%)	somapacitan (0.16mg/kg/week) safety pooled N (%)
Number of subjects	82	194
Number of reported dosings	36448	15622
Number of dosings in adherence	34938	15581
Number of planned dosings	39860	16519
Number of planned dosings until treatment discontinuation**	38085	16239
Adherence according to diary*		
<80%	10 (12.2)	20 (10.3)
80 - 95%	19 (23.2)	26 (13.4)
>95%	53 (64.6)	148 (76.3)
Adherence according to diary until treatment discontinuation**		
<80%	8 (9.8)	17 (8.8)
80 - 95%	19 (23.2)	27 (13.9)
>95%	55 (67.1)	150 (77.3)

N: Number of subjects, %: Percentage
* Number of reported dosings from diary in adherence divided by number of planned dosings multiplied by 100.
** For subjects discontinuing treatment, the planned number of dosings will be counted up until last day on treatment.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.
Dosings in adherence: 4263: All injections recorded between visit 2 and visit 7 in the diary with a dose above 0. A dose for Norditropin® will be counted in adherence if taken at or after 3 pm and before 3 am the following day. A dose of somapacitan will be counted in adherence if taken within 1 day before to 2 days after planned date of dosing. 4172: All injections recorded between visit 2 and visit 20 in the diary with a dose above 0. A dose for Norditropin® will be counted in adherence if taken at or after 3 am and before 3 am the following day. A dose of somapacitan will be counted in adherence if taken within 2 days before or 2 days after planned date of dosing.
06APR2022:09:06:20 - tsladhergroupsumfas.sas/tsladhergroupsumfaspool.txt
Notes: Full analysis set (FAS): All randomised subjects. Subjects were analysed "as randomised".

2.7.4.1.3.2.3 臨床薬理試験（4042 試験）の結果

4042 試験の曝露状況を表 2.7.4.1-11 に要約する。曝露状況の詳細は治験総括報告書に示す。4042 試験の試験デザインの詳細は Module 2.7.2.1.4 に示す。

第 1 相試験である 4042 試験では、計 24 例の小児 GHD 患者がソマプシタンの単回投与（0.02、0.04、0.08 及び 0.16 mg/kg の 4 つの用量レベル）を受けた。体重当たりの皮下注射としてソマプシタンを投与した。

表 2.7.4.1-11　小児 GHD 患者における臨床薬理試験の曝露状況の要約（4042 試験）

Trial ID	Population	Dose/duration	Somapacitan	Norditropin
Phase 1			N	N
Trial NN8640-4042	GHD children	Somapacitan SD 0.02, 0.04, 0.08 or 0.16 mg/kg Norditropin MD 0.03 mg/kg/day for 7 days	24	8

Abbreviations: GHD: growth hormone deficiency; MD: multiple dose; SD: single dose.

第 1 相試験では日本人被験者に対する曝露はなかった。

2.7.4.1.3.3 試験を中止・脱落した被験者数

完了した臨床試験において試験を中止・脱落した被験者又は治験薬投与を中止した被験者の数を試験別に表 2.7.4.1-12 に示す。

第 3 相試験（4263 試験、主要期間）では、試験を中止した被験者及び有害事象により治験薬の投与中止に至った被験者はいなかった。ソマプシタン群の 1 例が治験実施計画書違反により治験薬の投与を中止した（選択基準／除外基準を違反していたため）。

第 2 相試験（4172 試験）では、試験を中止した被験者の割合はソマプシタン群（13.3%）とノルディトロピン群（14.3%）で同様であった。ソマプシタン群では 6 例が試験を中止し、有害事象により治験薬の投与中止に至った被験者はいなかった。ノルディトロピン群では 2 例が試験を中止し、2 例が有害事象により治験薬の投与中止に至った。治験薬の投与中止に至った有害事象の詳細を 2.7.4.2.4.1 に示す。

表 2.7.4.1-12　試験を中止・脱落した被験者又は治験薬投与を中止した被験者の要約

Trial ID	Number (%) of children withdrawn of total randomised	Reason for withdrawal	Discontinued trial product
Phase 3			
Trial 4263	somapacitan: 0.0%	NA	PD (1 child)
	Norditropin: 0.0%	NA	NA
Phase 2			
Trial 4172	somapacitan: 6 of 45 (13.3%)	Withdrawn by parent/LAR (2 children) Lost to follow-up (1 child)	Withdrawn by parent/LAR (2 children) PD (4 children)

Trial ID	Number (%) of children withdrawn of total randomised	Reason for withdrawal	Discontinued trial product
		Other (3 children)	
	Norditropin: 2 of 14 (14.3%)	PD (1 child, JP) Other (1 child)	AEs: (2 children): drug hypersensitivity and nephrotic syndrome
Phase 1			
Trial 4042	None	NA	NA

Abbreviations: AE: adverse events; GHD: growth hormone deficiency; LAR: Legally acceptable representative; PD: protocol deviation; NA: not applicable. JP: Japanese (Subject ID [redacted]002).

2.7.4.1.3.4 用量レベルの調整

4263 試験では、連続 2 回以上の来院で IGF-I SD スコアが+2.5 を超えた被験者 2 例が 25%の用量減量を行った（ソマプシタン群 1 例、ノルディトロピン群 1 例）。この 2 例において IGF-I SD スコアが +2.5 を超えたことに関連する安全性の問題は認められなかった（2.7.4.2.5.15）。このほか、3 例が有害事象により用量を減量した〔ソマプシタン群 1 例（軽度の「空腹時血中ブドウ糖不良」）、ノルディトロピン群 2 例（「頭痛」）〕（2.7.4.2.4.2.1）。

4172 試験（208 週まで）では有害事象による用量レベルの調整は行われなかった。単回投与試験である 4042 試験では用量レベルの調整は適用されなかった。

2.7.4.1.3.5 4263 試験の安全性延長期間（104 週）の曝露

4263 試験では、安全性延長期間に移行したすべての被験者（ソマプシタン/ソマプシタン群の 131 例及びノルディトロピン/ソマプシタン群の 68 例）がソマプシタンの投与を受けた（52～104 週）。安全性延長期間（52～104 週）では、曝露期間の平均は、ソマプシタン/ソマプシタン群及びノルディトロピン/ソマプシタン群で同様であった。曝露に関する詳細は治験総括報告書に示す〔4263 試験（104 週）（M 5.3.5.1）Section 10.3.1〕。

2.7.4.1.4 治験対象集団の人口統計学的特性及びその他の特性

2.7.4.1.4.1 組み入れ基準

被験者の組み入れ基準については、Module 2.7.3.1.3.5 を参照のこと。

2.7.4.1.4.2 主要な第 3 相試験（4263 試験、主要期間）の結果

被験者背景は、ソマプシタン群とノルディトロピン群で概ね同様であった（表 2.7.4.1-13）。表 2.7.4.1-13 には、小児 GHD 患者の主なベースライン特性も示す。

小児 GHD 患者 200 例が 4263 試験で検討された（男児 74.5%、女児 25.5%）。これらの被験者は、hGH 製剤による治療歴がなく、スクリーニング時点で二次性徴発来前（Tanner stage 1）であった。ベースラインの年齢の平均は両群ともに 6.4 歳であり、97 例（48.5%）が 6 歳未満、103 例（51.5%）が 6 歳以上であった。

本試験は国際共同試験であり、大部分の被験者が米国（26.0%）、日本（15.0%）、ロシア（10.5%）及びインド（10.0%）で組み入れられた。GHD の原因は器質性（12%）又は特発性（88%）であった。

表 2.7.4.1-13　被験者背景及びベースラインの特性の要約（4263 試験、主要期間）

Trial 4263		**Norditropin**	**Somapacitan**
Number of subjects		68	132
GH treatment naive		Yes	Yes
Age (years), mean (SD)		6.43 (2.42)	6.38 (2.23)
Age group	<6 years, n (%)	33 (48.5%)	64 (48.5%)
	≥6 years, n (%)	35 (51.5%)	68 (51.5%)
Sex	Male, n (%)	50 (73.5%)	99 (75.0%)
	Female, n (%)	18 (26.5%)	33 (25.0%)
Race	White, n (%)	36 (52.9%)	78 (59.1%)
	Asian, n (%)	28 (41.2%)	46 (34.8%)
	Black or African American, n (%)	1 (1.5%)	0
Cause of GHD	Idiopathic, n (%)	61 (89.7%)	115 (87.1%)
	Organic, n (%)	7 (10.3%)	17 (12.9%)
HV (cm/year), mean (SD)		4.1 (1.4)	4.3 (1.4)
HVSDS, mean (SD)		-2.52 (1.55)	-2.35 (1.51)
Height (cm), mean (SD)		100.2 (15.0)	102.3 (12.5)
HSDS, mean (SD)		-3.47 (1.52)	-2.99 (1.02)
IGF-I SDS, mean (SD)		-2.33 (1.03)	-2.03 (0.97)

Abbreviations: GHD: growth hormone deficiency; HV: height velocity; HVSDS: height velocity standard deviation score; HSDS: height standard deviation score; IGF-I SDS: insulin-like growth factor I standard deviation score.

試験別の被験者背景及びベースライン特性の詳細は、Module 2.7.3.3.1.2.1 又は治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Section 10.2〕に示す。

併発疾患及び併用薬剤の情報は、治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Table 14.1.6 及び 14.1.7〕に示す。

2.7.4.1.4.2.1 主要な第 3 相試験（4263 試験、主要期間）の結果（日本人集団）

日本人小児 GHD 患者 30 例が 4263 試験で検討された。このうち 19 例がソマプシタン投与を受けた。

試験別の被験者背景及びベースライン特性の詳細は、Module 2.7.3.3.1.2.1 に示す。

2.7.4.1.4.3 補足的な情報

2.7.4.1.4.3.1 第 2 相試験（4172 試験）の結果

被験者背景及びベースライン特性は、ソマプシタン群とノルディトロピン群で概ね同様であった（表 2.7.4.1-14）。

補足的試験である 4172 試験のコホート I に組み入れられた被験者は、hGH 製剤による治療歴のない、二次性徴発来前の小児 GHD 患者であった（女児 2.5 歳以上 9 歳未満、男児 2.5 歳以上 10 歳未満）。

コホート I で最大の解析対象集団（FAS）に含まれた 57 例のうち、6 歳未満が 31 例（54.4%）、6 歳以上が 26 例（45.6%）であった。女児が 23 例（40.4%）及び男児が 34 例（59.6%）であった。本試験は国際共同試験であり、インド（24.6%）、日本（21.1%）、米国（14.0%）及びウクライナ（12.3%）から多くの被験者が組み入れられた。GHD の原因は器質性（7%）又は特発性（93%）であった。

表 2.7.4.1-14　被験者背景及びベースラインの特性の要約（4172 試験、コホート I）

Trial 4172 (cohort I)		**Norditropin 0.034 mg/kg/day**	**Somapacitan (pooled)**
Number of subjects		14	43
GH treatment naive		Yes	Yes
Age (years), mean (SD)		5.89 (1.98)	5.89 (1.95)
Age group	<6 years, n (%)	7 (50.0%)	24 (55.8%)
	≥6 years, n (%)	7 (50.0%)	19 (44.2%)
Sex	Male, n (%)	9 (64.3%)	25 (58.1%)
	Female, n (%)	5 (35.7%)	18 (41.9%)
Race	White, n (%)	7 (50.0%)	21 (48.8%)
	Asian, n (%)	6 (42.9%)	22 (51.2%)
	Black or African American, n (%)	1 (7.1%)	0
HV (cm/year), mean (SD)		3.5 (1.6)	4.2 (1.6)
HSDS, mean (SD)		-3.39 (1.05)	-3.80 (1.79)
IGF-I SDS, mean (SD)		-2.07 (0.74)	-2.35 (0.93)

Abbreviations: GHD: growth hormone deficiency; HV: height velocity; HSDS: height standard deviation score; IGF-I SDS: insulin-like growth factor I standard deviation score.

コホート II 及び III

コホート II には、年齢[redacted].5 歳の hGH 製剤による治療歴のある被験者が 1 例組み入れられた。当該被験者は、日本で組み入れられたアジア人男児であり、GHD の原因は器質性であった。

コホート III には、hGH 製剤による治療歴のない 2 例（いずれも男児であり、年齢は 1[redacted].9 歳及び 1[redacted].7 歳）及び hGH 製剤による治療歴のある 7 例（6 例が男児、1 例が女児。年齢の平均は 13.27 歳、最小値：10.2 歳、最大値：16.1 歳）が組み入れられた。コホート III には、5 ヵ国から組み入れられた。8 例が白人であり、1 例がアジア人であった。GHD の原因は 8 例が特発性であり、1 例が器質性であった。

コホート III では、hGH 製剤による治療歴のない 2 例の被験者は 2 次性徴を発来（Tanner stage >1）しており、hGH 製剤による治療歴のある 7 例の被験者のうち、5 例は 2 次性徴発来前であったが、2 例はスクリーニング時に 2 次性徴を発来していた。

試験別の被験者背景及びベースラインの特性の詳細は、Module 2.7.3.3.1.2.2 及び治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Section 10.2〕に示す。

併発疾患及び併用薬剤の情報は、治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Table 14.1.11～14.1.14〕に示す。

2.7.4.1.4.3.1.1 第 2 相試験（4172 試験）の結果（日本人集団）

日本人小児 GHD 患者 12 例が 4172 試験で検討された。このうち 9 例にソマプシタンを 4 年間投与し、さらに 2 例が 3 年後にノルディトロピンからソマプシタンに切り替えた（付録 2.7.4.7.2、Listing 35）。

4172 試験の被験者背景及びベースライン特性の詳細は、Module 2.7.3.3.1.2.2 に示す。

2.7.4.1.4.3.2 安全性併合データの結果

2 つの小児 GHD 患者を対象とした試験〔第 3 相試験（4263 試験）及び第 2 相試験（4172 試験）〕のベースライン特性は同様であった。安全性併合データにおけるベースライン特性は及び試験別のベースライン特性と同様であった。付録 2.7.4.7.1、Table 4 及び 5 に要約を示す。

計 194 例の hGH 製剤による治療歴のない小児 GHD 患者〔平均年齢 6.5 歳（範囲 : [redacted].5～16.1 歳）、男児 71.1%及び女児 28.9%）が 0.16 mg/kg/週のソマプシタン投与の併合（第 3 相試験及び第 2 相試験）に含まれた。

人種の分布は国際共同試験を反映しており、0.16 mg/kg/週のソマプシタン投与の併合には白人が 57.2%及びアジア人が 38.7%含まれ、黒人／アフリカ系アメリカ人は含まれなかった（付録 2.7.4.7.1、Table 4）。

2.7.4.1.4.3.3 臨床薬理試験（4042 試験）の結果

臨床薬理試験（4042 試験）の被験者背景及びベースライン特性を Module 2.7.2.2.2 に示す。

2.7.4.2　有害事象

2.7.4.2.1　有害事象の解析

2.7.4.2.1.1 主要な第 3 相試験（4263 試験、主要期間）の結果（全集団）

4263 試験において、小児 GHD 患者に対する 52 週までのソマプシタン週 1 回投与の安全性プロファイルは既存の 1 日 1 回投与の hGH 製剤（ノルディトロピン等）の安全性プロファイルと同様であった。臨床的に問題となる安全性又は局所忍容性の所見は認められなかった。本試験では、3 年間の安全性延長試験が進行中である。

4263 試験の試験デザインは、図 2.7.4.1-1 に示す。

概して、ソマプシタンの安全性プロファイルの以下のとおりであった〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Section 12.6〕。

- 大部分の有害事象（98%）は、軽度又は中等度に分類された。
- ソマプシタン群では、8 件の重篤な有害事象が報告された。重篤な有害事象の転帰はすべて「回復」であり、治験責任医師により治験薬との因果関係は「なし」と判定された（すなわち、予測できない重篤な副作用の報告はなかった）。
- ソマプシタン群では治験薬の投与中止に至った有害事象はなかった。
- いずれの群でも注射部位反応の発現頻度は低く、ソマプシタン群では 2 例（1.5%）が「注射部位疼痛」を発現した。

有害事象を発現した被験者の割合は、ソマプシタン群で 71.2%であり、ノルディトロピン群で 60.3%であった（表 2.7.4.2-1）。有害事象の単位時間あたりの発現件数は、ソマプシタン群（232.3 件／100 人・年）とノルディトロピン群（212.8 件／100 人・年）で概ね同様であった。

有害事象の概要を表 2.7.4.2-1 及び図 2.7.4.2-1 に示す。

特に注目すべき安全性領域の要約を 2.7.4.2.5 に示す。概して、選択した安全性領域に含まれる有害事象の発現件数は少なかった。特に注目すべき安全性領域に分類された有害事象の評価により、ソマプシタン群とノルディトロピン群の安全性プロファイルが同様であることが支持された。

2 つの群（ソマプシタン群及びノルディトロピン群）の投与期間はいずれも 52 週間であるため、主に有害事象を発現した被験者の割合（ある有害事象を発現した被験者数／すべての被験者数）を用いて評価し、適切な場合、単位時間あたりの有害事象の発現件数を提示した。

4263 試験では、有害事象の評価は、in-trial 観察期間及び on-treatment 観察期間を用いて行った〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Section 9.7.1.1〕。以降では、on-treatment 観察期間における評価を提示する（on-treatment 観察期間の定義は表 2.7.4.2-1 の脚注に示す）。本試験では、試験中止に至った被験者はなく、治験薬投与中止に至った被験者は 1 例であったため〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 10-1〕、曝露人・年及び単位時間あたりの有害事象の発現件数の数値がわずかに異なることを除き、有害事象の評価は、in-trial 観察期間及び on-treatment 観察期間で同様であった。

表 2.7.4.2-1　有害事象の概要（On-treatment 観察期間、安全性解析対象集団、4263 試験、主要期間）

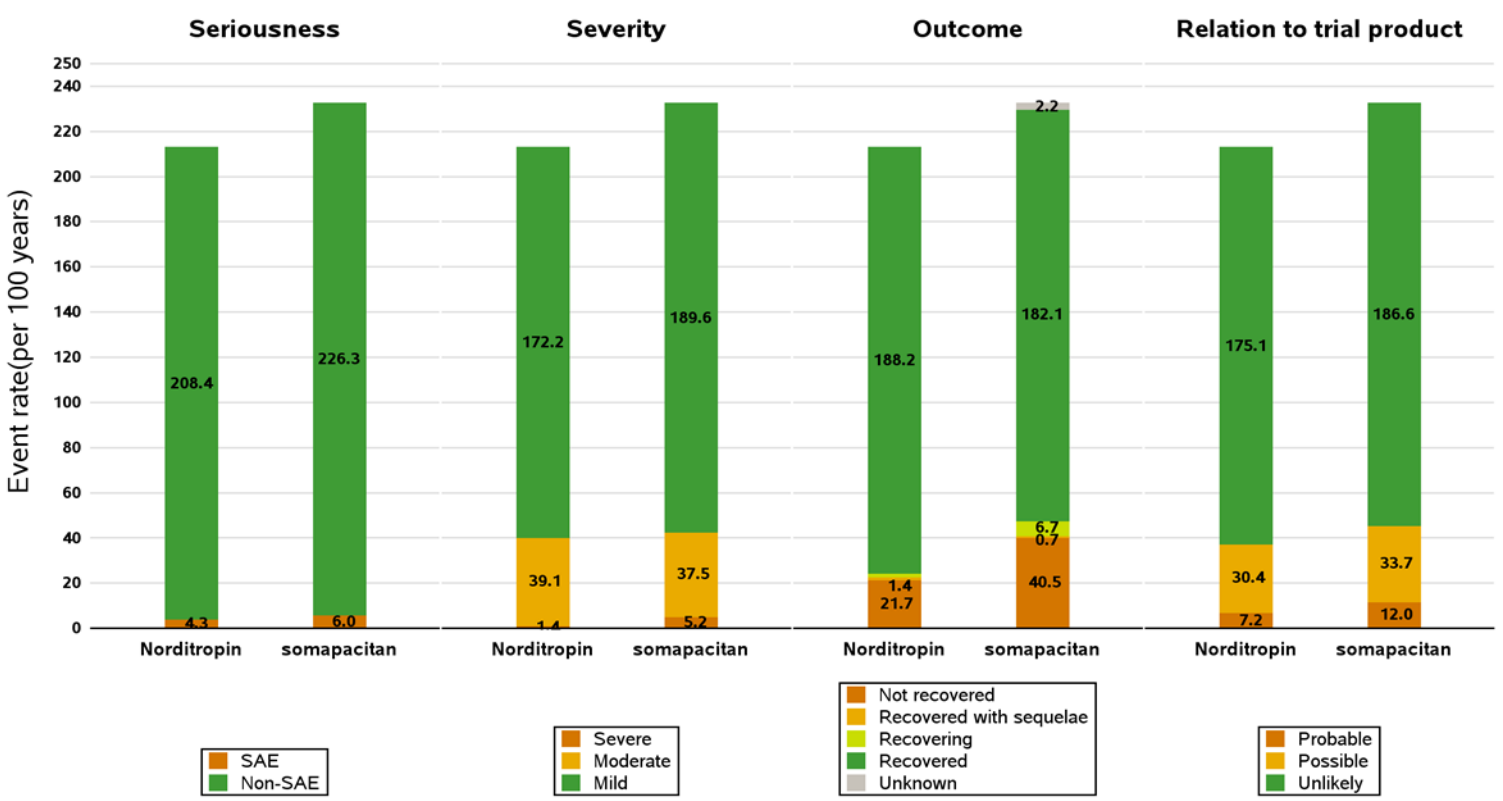
	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	68			132			200		
Total patient years at risk	69.1			133.4			202.5		
All adverse events	41 (60.3)	147	212.8	94 (71.2)	310	232.3	135 (67.5)	457	225.6
Serious adverse events									
Yes	2 (2.9)	3	4.3	6 (4.5)	8	6.0	8 (4.0)	11	5.4
No	41 (60.3)	144	208.4	93 (70.5)	302	226.3	134 (67.0)	446	220.2
Severity									
Mild	35 (51.5)	119	172.2	87 (65.9)	253	189.6	122 (61.0)	372	183.7
Moderate	12 (17.6)	27	39.1	27 (20.5)	50	37.5	39 (19.5)	77	38.0
Severe	1 (1.5)	1	1.4	4 (3.0)	7	5.2	5 (2.5)	8	3.9
Causality									
Probable	4 (5.9)	5	7.2	12 (9.1)	16	12.0	16 (8.0)	21	10.4
Possible	9 (13.2)	21	30.4	20 (15.2)	45	33.7	29 (14.5)	66	32.6
Unlikely	38 (55.9)	121	175.1	90 (68.2)	249	186.6	128 (64.0)	370	182.7
Missing	0			0			0		
Action taken to trial product due to AE									
Drug interrupted	5 (7.4)	5	7.2	2 (1.5)	2	1.5	7 (3.5)	7	3.5
Drug withdrawn	0			0			0		
Dose reduced	2 (2.9)	6	8.7	1 (0.8)	1	0.7	3 (1.5)	7	3.5
Dose increased	0			1 (0.8)	1	0.7	1 (0.5)	1	0.5
Dose not changed	40 (58.8)	136	196.9	89 (67.4)	289	216.6	129 (64.5)	425	209.8
Unknown	0			2 (1.5)	2	1.5	2 (1.0)	2	1.0
Missing	0			0			0		

Continued..

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Outcome									
Recovered/resolved	40	(58.8)	130 188.2	89	(67.4)	243 182.1	129	(64.5)	373 184.2
Recovering/resolving	1	(1.5)	1 1.4	5	(3.8)	9 6.7	6	(3.0)	10 4.9
Recovered/resolved with sequelae	1	(1.5)	1 1.4	1	(0.8)	1 0.7	2	(1.0)	2 1.0
Not recovered/not resolved	11	(16.2)	15 21.7	34	(25.8)	54 40.5	45	(22.5)	69 34.1
Fatal	0			0			0		
Unknown	0			1	(0.8)	3 2.2	1	(0.5)	3 1.5
Missing	0			0			0		
Treatment									
Treatment discontinuations due to adverse events	0			0			0		

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage, AE: Adverse event
AE causality is based on judgement of investigators.
On treatment: Measurement after first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until week 52 or 14 days after last trial drug administration, whichever comes first, for all other subjects.

図 2.7.4.2-1　　重篤度、重症度、転帰及び治験薬との関連性別の有害事象の概要（安全性解析対象集団）（4263 試験、主要期間）



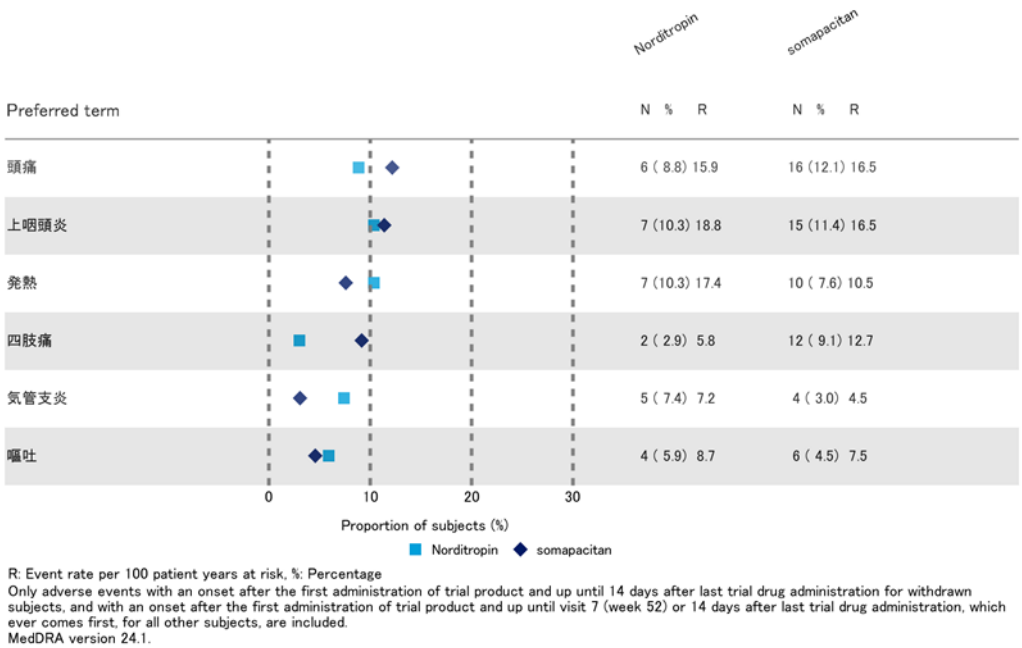
SAE: Serious adverse event
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
AE causality is based on judgement of investigators.

最も高頻度（いずれかの群で 5%以上）で報告された有害事象を基本語別に図 2.7.4.2-2 に要約する。すべての有害事象の器官別大分類別及び基本語別の要約を治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.4〕に示す。

ソマプシタン群で最も高頻度（5%以上）で報告された有害事象は、「頭痛」、「上咽頭炎」、「四肢痛」及び「発熱」（有害事象を発現した被験者の割合の順）であった。これらの有害事象は、治療及び基礎疾患に関わらず、小児でよくみられる事象であった。「四肢痛」はノルディトロピン群（2.9%）よりもソマプシタン群（9.1%）で比較的多く報告された。ソマプシタン群で認められた 17 件の「四肢痛」はいずれも非重篤であり、17 件中 15 件が軽度に分類され（重度の有害事象 2 件を以下に記載する）、17 件中 13 件の転帰が「回復」又は「軽快」であった〔4263 試験（52 週）（M 5.3.5.1）Listing 16.2.7.1〕。報告された事象の大部分は、脚痛（主に下肢や末梢部）に関連する事象であった。成長痛は GH 治療の影響としてよく知られているものである。17 件の「四肢痛」で、注射部位反応に関連する事象はなかった。高頻度で認められた有害事象にソマプシタン群とノルディトロピン群で大きな違いはみられなかった。

最も高頻度（いずれかの群で 2%以上）で報告された有害事象を治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Figure 14.3.1.57～14.3.1.59 及び Table 14.3.1.56〕に示す。

図 2.7.4.2-2　高頻度（いずれかの群で 5%以上）で報告された有害事象（基本語別）（安全性解析対象集団）（4263 試験、主要期間）



Notes: Sorted by percentage in either treatment group.

ソマプシタン群で最も高頻度（2%以上）で報告された治験薬との因果関係が「可能性あり」又は「あり」と判定された有害事象は、「頭痛」（ソマプシタン群で 3.8%、ノルディトロピン群で 8.8%）及び「四肢痛」（ソマプシタン群で 2.3%、ノルディトロピン群で 1.5%）であった（表 2.7.4.2-2）。その他の治験薬との因果関係が「可能性あり」又は「あり」と判定されたすべての有害事象は、1 例又は

2 例の被験者で報告され、異なる器官別大分類及び基本語にわたって報告された〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.14〕。これらの事象は 2.7.4.2.5 の「特に注目すべき安全性領域」に詳細に記載する。有害事象の発現について何らかの傾向はみられず、あるいは特定の有害事象が集中して発現することはなかった。ソマプシタンとの因果関係が「可能性あり」又は「あり」と判定された大部分の有害事象は、軽度又は中等度に分類され、重篤な有害事象として報告されたものはなかった〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.15 及び Appendix 16.2.7、Listing 16.2.7.4〕。

ノルディトロピン群で最も高頻度（2%以上）で報告された治験薬との因果関係が「可能性あり」又は「あり」と判定された有害事象は、「頭痛」（発現した被験者の割合は、上述のとおり）、「嘔吐」（ソマプシタン群で 1.5%、ノルディトロピン群で 2.9%）及び「高血糖」（ソマプシタン群で 0.8%、ノルディトロピン群で 2.9%）であった（表 2.7.4.2-2）。

治験責任医師により治験薬との因果関係が「可能性あり」又は「あり」と判定された有害事象を発現した被験者の割合は、ソマプシタン群では 20.5%、ノルディトロピン群では 16.2%であった（表 2.7.4.2-2）。

ソマプシタン群では、4 例（3%）7 件の有害事象が治験責任医師により重度に分類されたが、有害事象に特定のパターンはみられなかった（表 2.7.4.2-3）。ノルディトロピン群では 1 例（1.5%）1 件の有害事象が重度に分類された。治験薬の投与中断に至った重度の「頭痛」が各群 1 件ずつ発現した（ソマプシタン群の事象は重篤な有害事象）。ソマプシタン群の別の 1 例の被験者ではデータベースロック時点で「頭痛」の転帰は「未回復」であった。眼底検査の結果は正常であった。

表 2.7.4.2-2　高頻度（いずれかの群で 2%以上）で報告された治験薬との因果関係が「可能性あり」又は「あり」と判定された有害事象（基本語別）（安全性解析対象集団）（4263 試験、主要期間）

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	68			132			200		
Total patient years at risk	69.1			133.4			202.5		
Events	11	(16.2)	26 37.6	27	(20.5)	61 45.7	38	(19.0)	87 43.0
神経系障害									
頭痛	6	(8.8)	9 13.0	5	(3.8)	7 5.2	11	(5.5)	16 7.9
胃腸障害									
嘔吐	2	(2.9)	2 2.9	2	(1.5)	4 3.0	4	(2.0)	6 3.0
代謝および栄養障害									
高血糖	2	(2.9)	2 2.9	1	(0.8)	1 0.7	3	(1.5)	3 1.5
筋骨格系および結合組織障害									
四肢痛	1	(1.5)	2 2.9	3	(2.3)	8 6.0	4	(2.0)	10 4.9

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, whichever comes first, for all other subjects, are included.
MedDRA version 24.1.

表 2.7.4.2-3　重度の有害事象（安全性解析対象集団）（4263 試験、主要期間）

Trial product/ Subject ID	**Sex/Age/ BMI**	**AE preferred term**	**Onset day/ Period/ Duration** (Days)	**SAE**	**Causality**	**Outcome**	**Action taken**	**Additional information**
Somapacitan [redacted]008	M/[redacted].3/17.3	喘息	313/Main/46	Yes	Unlikely	Recovered	Trial product temporarily discontinued (1 week)	SAE case no. 800684
Somapacitan [redacted]001	M/[redacted].9/15.2	頭痛 [a]	35/Main/2	Yes	Unlikely	Recovered	Trial product temporarily discontinued (1 week)	SAE case no. 681612 Fundoscopy normal.
Somapacitan [redacted]002	M/[redacted].7/14.7	頭痛	2/Main	No	Possible	Not recovered	Dose not changed	Reported term: Headache, fundoscopy exam performed with normal results. Concomitant illnesses: multiple allergies and asthma.
Somapacitan [redacted]001	F/[redacted].1/17.2	疲労 (2 cases)	16 and 23/ Main/1	No	Possible	Recovered	Dose not changed	
		四肢痛 (2 cases)	16 and 23/ Main/1	No	Possible	Recovered	Dose not changed	Reported term: Lower extremity pain (both cases).
Norditropin [redacted]004	F/[redacted].7/18.8	頭痛	6/Main/10	No	Possible	Recovered	Trial product temporarily discontinued	No information on fundoscopy available.

[a] Chronic ear pain, fever while hospitalised.

Notes: Age in years.

Abbreviations: F: female; M: male; BMI: body mass index (kg/m^2) at baseline. AE: adverse event; SAE: serious adverse event.

2.7.4.2.1.1.1 主要な第 3 相試験（4263 試験、主要期間）の結果（日本人集団）

全集団の結果は、2.7.4.2.1.1 に示す。日本人集団では、有害事象の単位時間あたりの発現件数はソマプシタン群で 202.7 件/100 人・年、ノルディトロピン群で 188.1 件/100 人・年であった。有害事象によりソマプシタン投与の中止に至った被験者はいなかった。4263 試験の日本人集団の有害事象の概要を付録 2.7.4.7.2、Table 27 に示す。

日本人集団において最も高頻度で報告された有害事象は「上咽頭炎」であった〔図 2.7.4.2-2（全集団）、付録 2.7.4.7.2、Table 28（日本人集団）〕。日本人集団におけるこの他の有害事象は、いずれも 1 例又は 2 例で報告された。ソマプシタン群で因果関係が「可能性あり」又は「あり」と判定された有害事象はなかった（付録 2.7.4.7.2、Table 33）。

日本人集団と全集団との一貫性の評価

国際共同試験における 4263 試験における有害事象のプロファイルについて、ソマプシタンを投与した日本人集団と全集団で大きな違いはみられなかった〔表 2.7.4.2-1（全集団）、付録 2.7.4.7.2、Table 27（日本人集団）〕。

2.7.4.2.1.2 補足的な情報

2.7.4.2.1.2.1 第 2 相試験（4172 試験、208 週まで）の結果

4172 試験において、小児 GHD 患者に対する 208 週までのソマプシタン週 1 回投与の安全性プロファイルは既存の 1 日 1 回投与の hGH 製剤（ノルディトロピン等）の安全性プロファイルと同様であった。臨床的に問題となる安全性又は局所忍容性の所見は認められなかった。

4172 試験の試験デザインは、図 2.7.4.1-2 に示す。

4172 試験の主な安全性評価は、0～208 週間の併合されたデータである。2 つのソマプシタン併合群（ソマプシタン 0.04/0.08/0.16 mg/kg/週併合群及びソマプシタン 0.16 mg/kg/週併合群）を評価した（評価法については、2.7.4.1.2.3.1 に示す）。

本試験の最初のパート（26 週及び 52 週まで）ではノルディトロピンに対するソマプシタン 0.04、0.08 及び 0.16 mg/kg/週の用量反応を検討した。ソマプシタンは検討したすべての用量で良好な忍容性を示した。重篤な有害事象及び重度の有害事象の発現件数はソマプシタン用量群を通じて少なく、治験薬との因果関係が「可能性あり」又は「あり」と判定された有害事象を発現した被験者の割合は群を通じて同様であった。ソマプシタン用量群で、治験薬の用量減量又は投与中止に至った有害事象はなかった。156 週まで（安全性延長期間終了まで）において、安全性プロファイルは 3 つのソマプシタン群（ソマプシタン 0.04/0.16 mg/kg/週、0.08/0.16 mg/kg/週及び 0.16/0.16 mg/kg/週群）及びノルディトロピン群で同様であった。

0～208 週まででは、ソマプシタン 0.04/0.08/0.16 mg/kg/週併合群（248.2 件／100 人・年）及びソマプシタン 0.16 mg/kg/週併合群（232.9 件／100 人・年）の単位時間あたりの有害事象の発現件数は、ノルディトロピン群（270.8 件／100 人・年）と同様であった（表 2.7.4.2-4）。なお、ソマプシタン 0.16 mg/kg/週併合群には、コホート I の被験者のみが含められている。大部分の有害事象は、非重篤で、軽度又は中等度に分類された。ソマプシタン群において最も高頻度（いずれかの群で 10%以上）で発現

した有害事象は、「上咽頭炎」、「発熱」及び「インフルエンザ」（単位時間あたりの発現件数の順）であった（図 2.7.4.2-3）。

156～208 週まででは、ノルディトロピンからソマプシタンに切り替えた被験者（ノルディトロピン/ソマプシタン群）のデータも得られた。単位時間あたりの有害事象の発現件数は、2 つのソマプシタン併合群と比較してノルディトロピン/ソマプシタン群（111.2 件／100 人・年）で少なかったが、この群では曝露が少なかったことに留意すべきである。

さらに、156～208 週まででは、コホート II（2.5 歳未満の被験者）及び III〔9 歳超（女児）／10 歳超（男児）17 歳以下の被験者〕のデータが得られた。これらのコホートで 0.16 mg/kg/週のソマプシタン投与を受けた 10 例の被験者に、安全性で問題となる特定の所見は認められなかった（表 2.7.4.2-6）。

本試験の主要期間（26 週まで）及び延長期間（52 週まで及び 156 週まで）の詳細については、治験総括報告書〔4172 試験（26 週）（M 5.3.5.1）Section 12、4172 試験（156 週）（M 5.3.5.1）Section 12〕に示す。

有害事象の概要は、表 2.7.4.2-4（コホート I）及び治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.2（コホート I、156～208 週）及び Table 14.3.1.3（コホート II 及び III）〕に示す。

特に注目すべき安全性領域の評価を 2.7.4.2.5 に示す。概して、各安全性領域に含まれる有害事象の発現件数は少なかった。安全性領域に分類された有害事象の評価により、ソマプシタン群とノルディトロピン群の安全性プロファイルが同様であることが支持された。

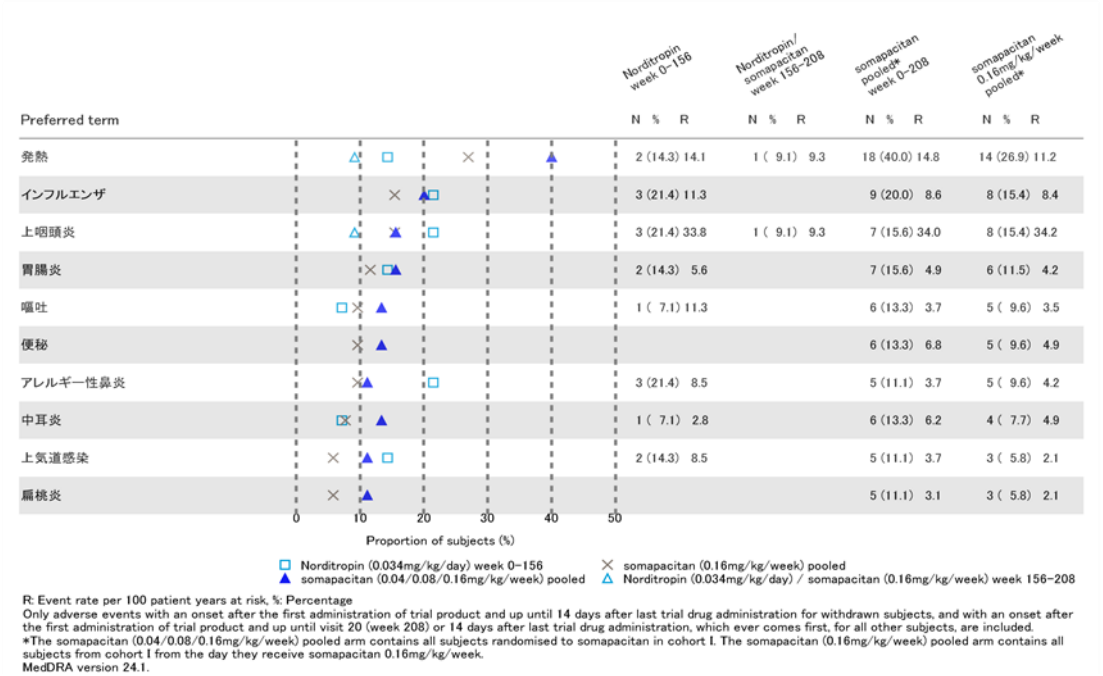
表 2.7.4.2-4　有害事象の概要（全集団、4172 試験、コホート I、208 週）

Cohort I Treatment group	Norditropin (0.034mg/kg/day) week 0-156 N (%) E R	Norditropin (0.034mg/kg/day) / somapacitan (0.16mg/kg/week) week 156-208 N (%) E R	somapacitan (0.04/0.08/0.16mg/kg/week) pooled* week 0-208 N (%) E R	somapacitan (0.16mg/kg/week) pooled* N (%) E R
Number of subjects	14	11	45	52
Total patient years at risk	35.5	10.8	162.0	143.4
All adverse events	14 (100.0) 96 270.8	8 (72.7) 12 111.2	42 (93.3) 402 248.2	44 (84.6) 334 232.9
Serious adverse events				
Yes	2 (14.3) 3 8.5	0	4 (8.9) 8 4.9	4 (7.7) 6 4.2
Severity				
Mild	14 (100.0) 85 239.7	7 (63.6) 9 83.4	41 (91.1) 351 216.7	41 (78.8) 294 205.0
Moderate	5 (35.7) 10 28.2	3 (27.3) 3 27.8	18 (40.0) 48 29.6	19 (36.5) 39 27.2
Severe	1 (7.1) 1 2.8	0	3 (6.7) 3 1.9	1 (1.9) 1 0.7
Causality related to Norditropin				
Probable	2 (14.3) 2 5.6	0	0	0
Possible	2 (14.3) 5 14.1	1 (9.1) 1 9.3	0	1 (1.9) 1 0.7
Unlikely	14 (100.0) 89 251.0	7 (63.6) 11 101.9	0	6 (11.5) 10 7.0
Causality related to somapacitan				
Probable	0	0	6 (13.3) 17 10.5	5 (9.6) 15 10.5
Possible	0	0	8 (17.8) 10 6.2	7 (13.5) 8 5.6
Unlikely	0	8 (72.7) 12 111.2	41 (91.1) 375 231.5	43 (82.7) 311 216.8
Action taken to trial product due to AE				
Drug interrupted	2 (14.3) 3 8.5	2 (18.2) 2 18.5	5 (11.1) 6 3.7	4 (7.7) 5 3.5
Drug withdrawn	2 (14.3) 2 5.6	0	0	0
Dose reduced	0	0	0	0
Dose not changed	14 (100.0) 91 256.7	6 (54.5) 10 92.7	42 (93.3) 395 243.9	42 (80.8) 328 228.7
Unknown	0	0	1 (2.2) 1 0.6	1 (1.9) 1 0.7
Outcome				
Recovered/resolved	14 (100.0) 83 234.1	7 (63.6) 9 83.4	41 (91.1) 370 228.4	43 (82.7) 309 215.4
Recovering/resolving	0	0	1 (2.2) 1 0.6	0
Recovered/resolved with sequela	0	0	1 (2.2) 1 0.6	1 (1.9) 1 0.7
Not recovered/not resolved	7 (50.0) 13 36.7	2 (18.2) 3 27.8	15 (33.3) 30 18.5	14 (26.9) 24 16.7
Fatal	0	0	0	0

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage, AE: Adverse event
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 20 (week 208) or 14 days after last trial drug administration, whichever comes first, for all other subjects, are included. AE causality is based on judgement of investigators.
*The somapacitan (0.04/0.08/0.16mg/kg/week) pooled arm contains all subjects randomised to somapacitan in cohort I. The somapacitan (0.16mg/kg/week) pooled arm contains all subjects from cohort I from the day they receive somapacitan 0.16mg/kg/week. For Norditropin week 156-208 action taken to trial drug, technical complaints and injection site reactions are only summarised for somapacitan.

コホートⅠでは、ソマプシタン群において最も高頻度（10%以上）で発現した有害事象は小児でよくみられる事象であり、「上咽頭炎」、「発熱」及び「インフルエンザ」を含んでいた（単位時間あたりの発現件数の順）（図 2.7.4.2-3）。最も高頻度（いずれかの群で 5%以上）で報告された有害事象を器官別大分類別及び基本語別に治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.13〕に要約する。すべての有害事象の要約を治療別に治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.10〕に示す。

図 2.7.4.2-3　　高頻度（いずれかの群で 10%以上）で報告された有害事象（基本語別）（4172 試験、コホートⅠ）



R: Event rate per 100 patient years at risk, %: Percentage
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
*The somapacitan (0.04/0.08/0.16mg/kg/week) pooled arm contains all subjects randomised to somapacitan in cohort I. The somapacitan (0.16mg/kg/week) pooled arm contains all subjects from cohort I from the day they receive somapacitan 0.16mg/kg/week.
MedDRA version 24.1.

大部分の有害事象は軽度又は中等度に分類された（表 2.7.4.2-4）。4 例 4 件の有害事象が治験責任医師により重度に分類された（表 2.7.4.2-5）。2 件の「脂肪組織萎縮症」の詳細は、2.7.4.2.5.7.2 に示す。

表 2.7.4.2-5　　重度の有害事象（4172 試験、コホートⅠ）

Treatment group Subject ID	Sex/Age /BMI	AE Preferred term	Study day/ Period/ Duration (days)	SAE	Causality	Outcome	Action taken to trial product
Somapacitan 0.04/0.16 mg/kg/week [redacted]001	F/[redacted].0/15.0	脂肪組織萎縮症	274/ Ext/ 275	No	Probably	Recovered	No change in dose
Somapacitan 0.04/0.16 mg/kg/week [redacted]002	M/[redacted].0/15.6	脂肪組織萎縮症	171/ Main/ 210	No	Probably	Recovered	No change in dose
Somapacitan 0.16/0.16 mg/kg/week [redacted]002	M/[redacted].3/15.9	骨折観血的整復	1374/ Long-term safety ext/ 1	No	Unlikely	Recovered	No change in dose

Treatment group Subject ID	Sex/Age /BMI	AE Preferred term	Study day/ Period/ Duration (days)	SAE	Causality	Outcome	Action taken to trial product
		(報告された事象名：internal fixation of left elbow)					
Norditropin 0.34 mg/kg/day/ Somapacitan 0.16 mg/kg/week [redacted]001	M/[redacted].3/15.4	アデノイド切除	381/ Safety ext/ 1	Yes	Unlikely	Recovered	No change in dose (Norditropin)

Notes: Age in years.
Abbreviations: F: female; M: male; BMI: body mass index (kg/m^2) at baseline. AE: adverse event; SAE: serious adverse event.

因果関係が「可能性あり」又は「あり」と判定された有害事象の単位時間あたりの発現件数は、ソマプシタン 0.04/0.08/0.16 mg/kg/週併合群（16.7 件/100 人・年）及びソマプシタン 0.16 mg/kg/週併合群（16.7 件/100 人・年）とノルディトロピン群（19.7 件/100 人・年）で同様であった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 12-4〕。

2 件の「脂肪組織萎縮症」（詳細は 2.7.4.2.5.7.2 参照）を除いて、治験責任医師によりソマプシタンとの因果関係が「可能性あり」又は「あり」と判定された有害事象はいずれも 1 例の被験者で発現し、異なる器官別大分類及び基本語にわたって報告された〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.42〕。ソマプシタンとの因果関係が「可能性あり」又は「あり」と判定された有害事象の大部分は非重篤であり、軽度又は中等度に分類された〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.6〕。特に注目すべき安全性領域における有害事象を 2.7.4.2.5.2 に示す。

因果関係が「あり」と判定された 2 件の有害事象（ソマプシタン 0.16 mg/kg/週群：「全身性浮腫」及び「嘔吐」）は重篤な有害事象として報告された（2.7.4.2.3.2.1 参照）。

延長期間では、主要期間と比較して安全性プロファイルに明らかな違いは認められなかった。詳細は治験総括報告書〔4172 試験（26 週）（M 5.3.5.1）Section 12、4172 試験（156 週）（M 5.3.5.1）Section 12 及び 4172 試験（208 週）（M 5.3.5.1）Section 12〕に示す。

コホート II 及び III

さらに、4172 試験では、組み入れ時点で年齢 2.5 歳未満の被験者 1 例（コホート II）及び 9 歳超（女児）／10 歳超（男児）17 歳以下の被験者 9 例（コホート III）の安全性データを収集した。これらの年齢グループで 0.16 mg/kg/週のソマプシタン投与を受けた 10 例の被験者に、安全性で問題となる特定の所見は認められなかった。

コホート II 及び III の 10 例のうち、有害事象を発現した被験者は 3 例であった。新たな安全性の問題は認められず、いずれの有害事象も軽度に分類され、非重篤であり、治験薬との因果関係は「なし」と判定された（表 2.7.4.2-6）。注射部位反応に関する事象は報告されなかった。

表 2.7.4.2-6　有害事象の一覧（4172 試験、コホート II 及び III）

Treatment group/ Subject ID	Sex/Age/ BMI	Preferred term	Trial day/ duration (days)	Severity/ Causality	Outcome	Action taken to trial product
Cohort II						
Somapacitan 0.16 mg/kg/week [redacted]003 Previously treated	M/[redacted].5/16.0	上気道感染	171/13	Mild/ Unlikely	Recovered	Dose not changed
		上気道感染	251/18	Mild/ Unlikely	Recovered	Dose not changed
		中耳炎	302/4	Mild/ Unlikely	Recovered	Dose not changed
		上気道感染	316/4	Mild/ Unlikely	Recovered	Dose not changed
Cohort III						
Somapacitan 0.16 mg/kg/week [redacted]005 Treatment naive	M/1[redacted].7/30.9	心電図 QT 延長 (for details, see 表 2.7.4.2-27)	380/-	Mild/ Unlikely	Not recovered	Dose not changed
Somapacitan 0.16 mg/kg/week [redacted]005 Previously treated	M/1[redacted].0/16.7	季節性アレルギー	99/-	Mild/ Unlikely	Not recovered	Dose not changed
		頭痛	113/-	Mild/ Unlikely	Not recovered	Dose not changed

Notes: Age in years.
Abbreviations: F: female; M: male; BMI: body mass index (kg/m^2) at baseline.

2.7.4.2.1.2.1.1 第 2 相試験（4172 試験）の結果（日本人集団）

全集団（4172 試験、208 週間）の結果は 2.7.4.2.1.2.1 に示す。日本人集団では、有害事象の単位時間あたりの発現件数はソマプシタン 0.04/0.08/0.16 mg/kg/週併合群（513.6 件/100 人・年）とノルディトロピン群（455.3 件/100 人・年）で同様であり、有害事象のパターンも同様であった。各群における日本人被験者数が少なかったことを考慮する必要がある（ソマプシタン群 9 例、ノルディトロピン群 3 例）。有害事象によりソマプシタン投与の中止に至った被験者はみられなかった。4172 試験（208 週）の日本人集団の有害事象の概要を付録 2.7.4.7.2、Table 18 に示す。

日本人集団において最も高頻度で報告された有害事象は「上咽頭炎」及び「インフルエンザ」であった〔図 2.7.4.2-3（全集団）、付録 2.7.4.7.2、Table 19（日本人集団）〕。日本人集団におけるこの他の有害事象は、いずれも 1～4 例で報告された。ソマプシタン群では、1 件の因果関係が「可能性あり」と判定された有害事象（「血中リン増加」、軽度、転帰は「回復」）が報告された（付録 2.7.4.7.2、Table 23）。

日本人集団と全集団との一貫性の評価

国際共同試験である 4172 試験における有害事象のプロファイルについて、ソマプシタンを投与した日本人集団と全集団で大きな違いはみられなかった〔表 2.7.4.2-4（全集団）、付録 2.7.4.7.2、Table 18（日本人集団）〕。

日本人集団では、延長期間において主要期間と比較して安全性プロファイルに明らかな違いは認められなかった。詳細は付録 2.7.4.7.2、Table 4～14（156 週まで）及び Table 18～23（208 週間）を参照のこと。

2.7.4.2.1.2.2 安全性併合データの結果

主要な第 3 相試験である 4263 試験に基づく結論は、安全性併合データにより支持された。安全性併合データの定義は、2.7.4.1.2.3.2 に示す。

小児 GHD 患者のソマプシタン 0.16 mg/kg/週安全性併合群とノルディトロピン安全性併合群における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を比較した要約を付録 2.7.4.7.1、Table 6～9 及び 11～18 ならびに Figure 10 及び 19～23 に示す。

ソマプシタン 0.16 mg/kg/週安全性併合群及びノルディトロピン安全性併合群の有害事象の概要を表 2.7.4.2-7 及び付録 2.7.4.7.1、Figure 10 に示す。ソマプシタン 0.16 mg/kg/週安全性併合群には 194 例（4263 試験の 132 例、4172 試験コホート I の 52 例、4172 試験コホート II 及び III の 10 例）が含まれる。ノルディトロピン安全性併合群には 82 例（4263 試験の 68 例及び 4172 試験の 14 例）が含まれる。4172 試験の 156 週時点で、11 例がノルディトロピンからソマプシタンに切り替えたため、安全性併合データには 265 例のデータが含まれる。

ソマプシタン 0.16 mg/kg/週安全性併合群とノルディトロピン安全性併合群の有害事象のパターンは主要な第 3 相試験である 4263 試験と同様であった。

有害事象を発現した被験者の割合はソマプシタン 0.16 mg/kg/週安全性併合群とノルディトロピン安全性併合群で同様であった（ソマプシタン 0.16 mg/kg/週安全性併合群 73.2%、ノルディトロピン安全性併合群 67.1%）。有害事象の単位時間あたりの発現件数はソマプシタン 0.16 mg/kg/週安全性併合群（230.9 件/100 人・年）とノルディトロピン安全性併合群（232.4 件/100 人・年）で同様であった（表 2.7.4.2-7）。いずれの安全性併合群でも大部分の有害事象は非重篤であった。すべての有害事象を器官別大分類別、基本語別及び治療別に付録 2.7.4.7.1、Table 8 に示す。

表 2.7.4.2-7　有害事象の概要（安全性併合データ）

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	82			194			265		
Total patient years at risk	104.5			282.7			387.3		
All adverse events	55	(67.1)	243 232.4	142	(73.2)	653 230.9	189	(71.3)	896 231.4
Serious adverse events									
Yes	4	(4.9)	6 5.7	10	(5.2)	14 5.0	14	(5.3)	20 5.2
No	55	(67.1)	237 226.7	141	(72.7)	639 226.0	188	(70.9)	876 226.2
Severity									
Mild	49	(59.8)	204 195.1	132	(68.0)	556 196.6	174	(65.7)	760 196.2
Moderate	17	(20.7)	37 35.4	46	(23.7)	89 31.5	62	(23.4)	126 32.5
Severe	2	(2.4)	2 1.9	5	(2.6)	8 2.8	7	(2.6)	10 2.6
Causality (Norditropin)									
Probable	6	(7.3)	7 6.7	0			6	(2.3)	7 1.8
Possible	11	(13.4)	26 24.9	1	(0.5)	1 0.4	12	(4.5)	27 7.0
Unlikely	52	(63.4)	205 196.1	7	(3.6)	11 3.9	52	(19.6)	216 55.8
Missing	1	(1.2)	5 4.8	134	(69.1)	641 226.7	135	(50.9)	646 166.8
Causality (somapacitan)									
Probable	0			17	(8.8)	31 11.0	17	(6.4)	31 8.0
Possible	0			27	(13.9)	53 18.7	27	(10.2)	53 13.7
Unlikely	1	(1.2)	5 4.8	137	(70.6)	569 201.2	138	(52.1)	574 148.2
Missing	55	(67.1)	238 227.7	0			55	(20.8)	238 61.5
Action taken to trial product due to AE (Norditropin)									
Drug interrupted	7	(8.5)	8 7.7	0			7	(2.6)	8 2.1
Drug withdrawn	2	(2.4)	2 1.9	0			2	(0.8)	2 0.5
Dose reduced	2	(2.4)	6 5.7	0			2	(0.8)	6 1.5
Dose increased	0			0			0		

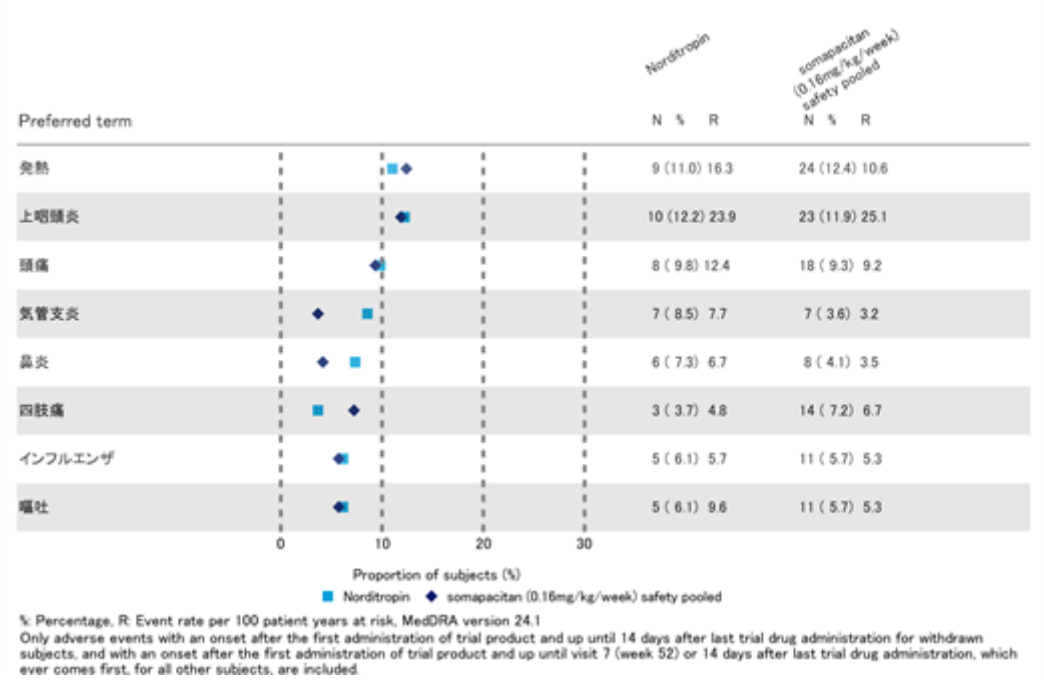
Summary of adverse events - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Dose not changed	54 (65.9)	222	212.4	0			54 (20.4)	222	57.3
Unknown	0			0			0		
Not Applicable	0			8 (4.1)	12	4.2	8 (3.0)	12	3.1
Missing	1 (1.2)	5	4.8	134 (69.1)	641	226.7	135 (50.9)	646	166.8
Action taken to trial product due to AE (somapacitan)									
Drug interrupted	0			6 (3.1)	7	2.5	6 (2.3)	7	1.8
Drug withdrawn	0			0			0		
Dose reduced	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Dose increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Dose not changed	1 (1.2)	5	4.8	135 (69.6)	626	221.4	136 (51.3)	631	162.9
Unknown	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Not Applicable	0			9 (4.6)	15	5.3	9 (3.4)	15	3.9
Missing	55 (67.1)	238	227.7	0			55 (20.8)	238	61.5
Outcome									
Recovered/resolved	54 (65.9)	213	203.7	133 (68.6)	557	197.0	180 (67.9)	770	198.8
Recovering/resolving	1 (1.2)	1	1.0	5 (2.6)	9	3.2	6 (2.3)	10	2.6
Recovered/resolved with sequelae	1 (1.2)	1	1.0	2 (1.0)	2	0.7	3 (1.1)	3	0.8
Not recovered/not resolved	18 (22.0)	28	26.8	51 (26.3)	82	29.0	68 (25.7)	110	28.4
Fatal	0			0			0		
Unknown	0			1 (0.5)	3	1.1	1 (0.4)	3	0.8
Treatment (Norditropin)									
Treatment discontinuations due to AE	2 (2.4)	2	1.9	0			2 (0.8)	2	0.5
Treatment (somapacitan)									
Treatment discontinuations due to AE	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1 , AE: Adverse event, On treatment: Measurement after first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects,and up until visit 20 (week 208 for cohort I and week 52 for cohort II and III) for 4172 and for 4263 until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects.
AE causality is based on judgement of investigators.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

ソマプシタン 0.16 mg/kg/週安全性併合群において最も高頻度（5%以上）で認められた有害事象は、「発熱」（12.4%）、「上咽頭炎」（11.9%）及び「頭痛」（9.3%）であった（有害事象を発現した被験者の割合の順）。これらの有害事象は、治療及び基礎疾患に関わらず、小児でよくみられる事象であった。5%以上で認められた有害事象を図 2.7.4.2-4、付録 2.7.4.7.1, Table 17 に示す。

図 2.7.4.2-4　　高頻度（5%以上）で報告された有害事象（安全性併合データ）



2%以上で認められた有害事象を付録 2.7.4.7.1, Table 18 及び Figure 20～23 に示す。

重症度

ソマプシタン 0.16 mg/kg/週安全性併合群では、大部分の有害事象は軽度又は中等度に分類された（表 2.7.4.2-7 及び付録 2.7.4.7.1、Table 12 及び 13）。重度に分類された有害事象は 5 例 8 件であり、いずれも小児で予想されるものであった（付録 2.7.4.7.1、Table 11）。重度の有害事象を発現した被験者の割合は群間で同様であった（ソマプシタン 0.16 mg/kg/週安全性併合群 2.6%、ノルディトロピン安全性併合群 2.4%）（付録 2.7.4.7.1、Table 11）。ソマプシタン 0.16 mg/kg/週安全性併合群では、8 件の重度の有害事象のうち 5 件が治験責任医師により治験薬との因果関係が「可能性あり」又は「あり」と判定され、ノルディトロピン安全性併合群では、2 件の重度の有害事象のうち 1 件が治験薬との因果関係が「可能性あり」又は「あり」と判定された（付録 2.7.4.7.1、Table 16）。

治験薬との因果関係が「可能性あり」又は「あり」と判定された有害事象

安全性併合データで、治験責任医師により治験薬との因果関係が「可能性あり」又は「あり」と判定された有害事象を発現した被験者の割合（ソマプシタン 0.16 mg/kg/週安全性併合群 20.1%、ノルディトロピン安全性併合群 18.3%）は、4263 試験と同様であった（付録 2.7.4.7.1、Table 14）。

ソマプシタン 0.16 mg/kg/週安全性併合群において最も高頻度（2%以上）で報告された因果関係が「可能性あり」又は「あり」と判定された有害事象は「頭痛」であった（ソマプシタン 0.16 mg/kg/週安全性併合群 2.6%、ノルディトロピン安全性併合群 8.5%）（付録 2.7.4.7.1、Table 14）。その他の治験薬との因果関係が「可能性あり」又は「あり」と判定されたすべての有害事象は、1～3 例の被験者で報告され、異なる器官別大分類及び基本語にわたって報告された。

治験薬（ソマプシタン）との因果関係が「可能性あり」又は「あり」と判定された有害事象の大部分は軽度又は中等度に分類され、非重篤であった。ソマプシタンとの因果関係が「可能性あり」又は「あり」と判定された有害事象で、重篤な有害事象として報告された事象は 2 件（「嘔吐」及び「全身性浮腫」）であった（付録 2.7.4.7.1、Table 15）。

ノルディトロピン安全性併合群において最も高頻度（2%以上）で報告された因果関係が「可能性あり」又は「あり」と判定された有害事象は、「頭痛」（割合は上述）、「四肢痛」（ソマプシタン 0.16 mg/kg/週安全性併合群 1.5%、ノルディトロピン安全性併合群 2.4%）、「嘔吐」（ソマプシタン 0.16 mg/kg/週安全性併合群 1.5%、ノルディトロピン安全性併合群 3.7%）及び「高血糖」（ソマプシタン 0.16 mg/kg/週安全性併合群 0.5%、ノルディトロピン安全性併合群 2.4%）であった（付録 2.7.4.7.1、Table 14）。

2.7.4.2.1.2.3 臨床薬理試験（4042 試験）の結果

小児 GHD 患者に対するソマプシタンの単回皮下投与の忍容性は、検討したすべての用量（0.02～0.16 mg/kg）で良好であり、臨床的に問題となる安全性の所見及び局所忍容性の問題はみられなかった。

重篤な有害事象の報告はなかった。試験中止に至った有害事象はなかった。

すべての有害事象は軽度に分類され（ソマプシタン単回投与後：11 例（46%）19 件、ノルディトロピン投与後：1 例（13%）2 件）、0.02 mg/kg のソマプシタン投与後に報告された 1 件の「血尿」が治験薬との因果関係が「可能性あり」と判定されたことを除き、治験薬との因果関係は「なし」と判定された。2 例以上の被験者で報告された有害事象は、「上咽頭炎」、「頭痛」及び「嘔吐」であった。器官別大分類内及び器官別大分類を通じた有害事象の種類及び頻度について、治療に依存する明らかな傾向はみられず、大部分の有害事象は 1 例又は 2 例の被験者で報告された。

詳細は、治験総括報告書に示す。〔4042 試験（M 5.3.3.2）Section 12.8〕

2.7.4.2.2 死亡

小児 GHD 患者を対象としたソマプシタンの臨床試験で、死亡の報告はなかった〔4263 試験（52 週間）、4172 試験（208 週間）、4042 試験（1 週間）〕〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Listing 14.3.2.1、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.1〕。

2.7.4.2.3　その他の重篤な有害事象

2.7.4.2.3.1 主要な第 3 相試験（4263 試験、主要期間）の結果

重篤な有害事象の単位時間あたりの発現件数はソマプシタン群、ノルディトロピン群のいずれにおいても少なかった。重篤な有害事象はソマプシタン群で 6 例（4.5%）8 件、ノルディトロピン群で 2 例（2.9%）3 件報告された（ソマプシタン群 6.0 件/100 人・年、ノルディトロピン群 4.3/100 人・年）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.2〕。重篤な有害事象を被験者別に表 2.7.4.2-8 に示す。

重篤な有害事象により治験薬の投与中止に至った被験者はなかった。重篤な有害事象の転帰はいずれも「回復」であった。治験責任医師により治験薬との因果関係が「可能性あり」又は「あり」と判定された重篤な有害事象はなかった（予測できない重篤な副作用の疑いは認められなかった）。

ソマプシタン群の 2 例（「喘息」及び「頭痛」）及びノルディトロピン群の 1 例（「COVID-19」）が重篤な有害事象により治験薬の投与中断に至った。3 件の重篤な有害事象はいずれも完全に回復した。

[redacted]歳の被験者（被験者 ID：[redacted]001）で認められた「頭痛」は、重度の羞明を伴う難治性頭痛として報告された。入院し検査を行った結果、頭蓋内圧亢進及び乳頭浮腫は否定され、頭部 CT は正常で、1 日以内に回復した。当該被験者は慢性耳痛を有し、入院中に発熱がみられた。頭痛は基礎疾患又はウイルス感染によるものと考えられた。

本試験の最初の 52 週間以内にノルディトロピン群で 1 件の「COVID-19」が重篤な有害事象として報告された。

重篤な有害事象の概要を治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.2〕に示す。重篤な有害事象を器官別大分類別及び基本語別に要約し、治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.10〕に示す。重篤な有害事象の一覧を治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Listing 14.3.2.2〕に示す。

重篤な有害事象の叙述を治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Section 14.3.3〕に示す。

表 2.7.4.2-8　重篤な有害事象の一覧（4263 試験、主要期間）

Treatment group Subject ID	Sex/Age/BMI	SAE preferred term	Onset date/ Outcome	Study day/ Duration (days)	Severity/ Causality	Action taken to trial product
Somapacitan [redacted]001	M/[redacted].5/17.2	嘔吐	10JUL21/ Recovered	271 /2	Moderate/ Unlikely	Dose not changed
		脱水	10JUL21/ Recovered	271/ 2	Moderate/ Unlikely	Dose not changed
Somapacitan [redacted]008	M/[redacted].3/17.3	喘息	28MAR21/ Recovered	313/ 46	Severe/ Unlikely	Trial product interrupted (1 week)
Somapacitan [redacted]001	M/[redacted].9/15.2	頭痛 [a]	25AUG19/ Recovered	35/ 2	Severe/ Unlikely	Trial product interrupted (1 week)
Somapacitan	F/[redacted].8/17.6	臍ヘルニア	10JUN21/	337/	Mild/	Dose not changed

Treatment group Subject ID	Sex/Age/BMI	SAE preferred term	Onset date/ Outcome	Study day/ Duration (days)	Severity/ Causality	Action taken to trial product
[redacted]002#			Recovered	66	Unlikely	
Somapacitan [redacted]002#	M/[redacted].1/16.2	中耳炎	25FEB21/ Recovered	289/ 71	Mild/ Unlikely	Dose not changed
		アデノイド肥大 [b]	25MAR21/ Recovered	317/ 14	Moderate/ Unlikely	Dose not changed.
Somapacitan [redacted]001	M/[redacted].9/14.5	停留精巣 [c]	05MAY21/ Recovered	185/ 8	Moderate/ Unlikely	Dose not changed.
Norditropin [redacted]002	F/[redacted].0/17.1	胃腸炎	02FEB20/ Recovered	26/ 1	Moderate/ Unlikely	Dose not changed
		急性副腎皮質機能不全	02FEB20/ Recovered	26 /1	Moderate/ Unlikely	Dose not changed
Norditropin [redacted]003	F/[redacted].7/16.3	COVID-19	10JUL21/ Recovered	332/ 17	Mild/ Unlikely	Trial product interrupted (2 weeks)

[a] Chronic ear pain, fever while hospitalised.
[b] Exacerbation of adenoid hypertrophy.
[c] SAE due to hospitalisation to have bilateral orchidopexy.
Japanese subjects〔治験総括報告書 4263 試験（52 週）（M 5.3.5.1）Listing 16.2.4.2〕
Notes: Somapacitan 0.16 mg/kg/week. Norditropin 0.034 mg/kg/day. Age in years at baseline.
Abbreviations: F: female; M: male; BMI: body mass index (kg/m^2) at baseline. AE: adverse event; SAE: serious adverse event.

2.7.4.2.3.1.1 主要な第 3 相試験（4263 試験、主要期間）の結果（日本人集団）

日本人集団では、ソマプシタン群の 2 例で重篤な有害事象が 3 件認められた（表 2.7.4.2-8）。3 件の重篤な有害事象はいずれも軽度又は中等度に分類された。報告された有害事象は小児において予想されるものであった。

2.7.4.2.3.2 補足的な情報

2.7.4.2.3.2.1 第 2 相試験（4172 試験、208 週まで）の結果

小児 GHD 患者を対象とした第 2 相試験では、第 3 相試験と同様に、重篤な有害事象を発現した被験者数は少なかった（表 2.7.4.2-9）。

重篤な有害事象の単位時間あたりの発現件数は、ソマプシタン 0.04/0.08/0.16 mg/kg/週併合群（4.9 件/100 人・年）及びソマプシタン 0.16 mg/kg/週併合群（4.2 件/100 人・年）のいずれにおいても少なく、また、ノルディトロピン群（8.5 件/100 人・年）においても少なかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.4〕。重篤な有害事象はソマプシタン 0.04/0.08/0.16 mg/kg/週併合群で 4 例（8.9%）8 件（208 週まで）、ノルディトロピン群では 2 例（14.3%）3 件（156 週まで）報告された。11 件の重篤な有害事象のうち、9 件は、治験責任医師により治験薬との因果関係は「なし」と判定された。

重篤な有害事象 2 件（「全身性浮腫」及び「嘔吐」）は治験薬（ソマプシタン 0.16 mg/kg/週）との因果関係が「あり」と判定され、いずれの被験者も、これらの事象により治験薬の投与中断に至った（2.7.4.2.4.2.2 及び 2.7.4.2.5.5.1）。

ソマプシタンを投与した 2 例の被験者で「アナフィラキシー反応」及び「アナフィラキシーショック」が認められた（2.7.4.2.5.6.2）。

表 2.7.4.2-9　　重篤な有害事象の一覧（4172 試験、208 週）

Treatment group Subject ID	Sex/Age/BMI	SAE preferred term	Study day/ Period/ Duration (days)	Severity/ Causality	Outcome	Action taken to trial product
Somapacitan 0.04/0.16 mg/kg/week [redacted]001[#]	F/[redacted].1/14.1	アナフィラキシー反応	683/Safety ext/2	Moderate/ Unlikely	Recovered	Dose not changed
Somapacitan 0.08/0.16 mg/kg/week [redacted]001	M/[redacted].8/16.0	下垂体機能低下症	96/Main	Mild/ Unlikely	Not recovered	Dose not changed
		胃腸炎	310/Ext/2	Moderate/ Unlikely	Recovered	Dose not changed
		胃腸炎	682/Safety ext/2	Moderate/ Unlikely	Recovered	Dose not changed
Somapacitan 0.16 mg/kg/week [redacted]005	F/[redacted].9/15.0	全身性浮腫	3/Main/9	Moderate/ Probable	Recovered	Drug interrupted
		嘔吐	4/Main/3	Moderate/ Probable	Recovered	Drug interrupted
		扁桃炎	366/Ext/10	Moderate/ Unlikely	Recovered	Dose not changed
Somapacitan 0.16 mg/kg/week [redacted]001[#]	M/[redacted].1/17.2	アナフィラキシーショック	861/Safety ext/2	Moderate/ Unlikely	Recovered	Dose not changed
Norditropin 0.034 mg/kg/day/ Somapacitan 0.16 mg/kg/week [redacted]001	M/[redacted].3/15.4	アデノイド切除	381/Safety ext/1	Severe/ Unlikely	Recovered	Dose not changed
Norditropin 0.034 mg/kg/day [redacted]002[#]	M/[redacted].1/15.6	RS ウイルス気管支炎	290/Ext/12	Moderate/ Unlikely	Recovered	Dose not changed
		ネフローゼ症候群	366/Ext	Moderate/ Unlikely	Not recovered	Drug withdrawn

[#] Japanese subjects 〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Listing 16.2.4.3〕.

Notes: Age in years at baseline.

Abbreviations: F: female; M: male; BMI: body mass index (kg/m^2) at baseline; SAE: serious adverse event.

重篤な有害事象の概要を治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.4〕に示す。重篤な有害事象を器官別大分類別及び基本語別に要約し、治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.38〕に示す。

重篤な有害事象の叙述及び症例報告書を治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Section 14.3.3〕に示す。

ノルディトロピン／ソマプシタン群の被験者で、ノルディトロピンからソマプシタンに切り替えた後に重篤な有害事象を報告した被験者はいなかった。

コホート II 及び III で、重篤な有害事象の報告はなかった〔4172 試験（208 週）（M 5.3.5.1）Listing 14.3.2.2〕。

2.7.4.2.3.2.1.1 第 2 相試験（4172 試験）の結果（日本人集団）

日本人集団では、ソマプシタン群の 2 例で重篤な有害事象が 2 件認められた（付録 2.7.4.7.2、Listing 21）。

2.7.4.2.3.2.2 安全性併合データの結果

ソマプシタン 0.16 mg/kg/週安全性併合群及びノルディトロピン安全性併合群で認められた重篤な有害事象の要約を表 2.7.4.2-10（カテゴリー別）及び表 2.7.4.2-11（器官別大分類別及び基本語別）に示す。

ソマプシタン 0.16 mg/kg/週安全性併合群における重篤な有害事象のパターンは、主要な第 3 相試験と同様であった。重篤な有害事象が認められた被験者の割合はいずれの群でも低かった〔ソマプシタン 0.16 mg/kg/週安全性併合群 10 例（5.2%）14 件、ノルディトロピン安全性併合群 4 例（4.9%）6 件〕。「嘔吐」の重篤な有害事象が 2 件報告されたことを除き、その他の事象は 1 例 1 件ずつ報告された。

重篤な有害事象 2 件（「全身性浮腫」及び「嘔吐」）は治験薬（ソマプシタン 0.16 mg/kg/週）との因果関係が「あり」と判定され（付録 2.7.4.7.1、Table 15）、いずれの被験者も、これらの事象により治験薬投与の中断に至った（2.7.4.2.5.5.1）。

表 2.7.4.2-10　重篤な有害事象の概要（安全性併合データ）

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
All adverse events	4	(4.9)	6	5.7	10	(5.2)	14	5.0	14	(5.3)	20	5.2
Severity												
Mild	1	(1.2)	1	1.0	2	(1.0)	2	0.7	3	(1.1)	3	0.8
Moderate	2	(2.4)	4	3.8	7	(3.6)	10	3.5	9	(3.4)	14	3.6
Severe	1	(1.2)	1	1.0	2	(1.0)	2	0.7	3	(1.1)	3	0.8
Causality (Norditropin)												
Probable	0				0				0			
Possible	0				0				0			
Unlikely	4	(4.9)	6	5.7	0				4	(1.5)	6	1.5
Missing	0				10	(5.2)	14	5.0	10	(3.8)	14	3.6
Causality (somapacitan)												
Probable	0				1	(0.5)	2	0.7	1	(0.4)	2	0.5
Possible	0				0				0			
Unlikely	0				10	(5.2)	12	4.2	10	(3.8)	12	3.1
Missing	4	(4.9)	6	5.7	0				4	(1.5)	6	1.5
Action taken to trial product due to AE (Norditropin)												
Drug interrupted	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Drug withdrawn	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Dose reduced	0				0				0			
Dose increased	0				0				0			
Dose not changed	3	(3.7)	4	3.8	0				3	(1.1)	4	1.0
Unknown	0				0				0			
Not Applicable	0				0				0			
Missing	0				10	(5.2)	14	5.0	10	(3.8)	14	3.6

Serious adverse events - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Action taken to trial product due to AE (somapacitan)												
Drug interrupted	0				3	(1.5)	4	1.4	3	(1.1)	4	1.0
Drug withdrawn	0				0				0			
Dose reduced	0				0				0			
Dose increased	0				0				0			
Dose not changed	0				8	(4.1)	10	3.5	8	(3.0)	10	2.6
Unknown	0				0				0			
Not Applicable	0				0				0			
Missing	4	(4.9)	6	5.7	0				4	(1.5)	6	1.5
Outcome												
Recovered/resolved	4	(4.9)	5	4.8	10	(5.2)	14	5.0	14	(5.3)	19	4.9
Recovering/resolving	0				0				0			
Recovered/resolved with sequelae	0				0				0			
Not recovered/not resolved	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Fatal	0				0				0			
Unknown	0				0				0			
Treatment (Norditropin)												
Treatment discontinuations due to AE	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Treatment (somapacitan)												
Treatment discontinuations due to AE	0				0				0			

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1 , AE: Adverse event
AE causality is based on judgement of investigators.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

表 2.7.4.2-11　重篤な有害事象の要約（器官別大分類及び基本語別）（安全性併合データ）

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	4	(4.9)	6	5.7	10	(5.2)	14	5.0	14	(5.3)	20	5.2
感染症および寄生虫症	3	(3.7)	3	2.9	3	(1.5)	3	1.1	6	(2.3)	6	1.5
胃腸炎	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
ＣＯＶＩＤ－１９	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
ＲＳウイルス気管支炎	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
中耳炎	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
扁桃炎	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
胃腸障害	0				3	(1.5)	3	1.1	3	(1.1)	3	0.8
嘔吐	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
臍ヘルニア	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
呼吸器、胸郭および縦隔障害	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
アデノイド肥大	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
喘息	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
免疫系障害	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
アナフィラキシーショック	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
アナフィラキシー反応	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
一般・全身障害および投与部位の状態	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
全身性浮腫	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
外科および内科処置	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of serious adverse events by system organ class and preferred term - on-treatment - safety analysis set - pooled global data

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
アデノイド切除	1 (1.2)		1	1.0	0				1 (0.4)		1	0.3
神経系障害	0				1 (0.5)		1	0.4	1 (0.4)		1	0.3
頭痛	0				1 (0.5)		1	0.4	1 (0.4)		1	0.3
腎および尿路障害	1 (1.2)		1	1.0	0				1 (0.4)		1	0.3
ネフローゼ症候群	1 (1.2)		1	1.0	0				1 (0.4)		1	0.3
先天性、家族性および遺伝性障害	0				1 (0.5)		1	0.4	1 (0.4)		1	0.3
停留精巣	0				1 (0.5)		1	0.4	1 (0.4)		1	0.3
代謝および栄養障害	0				1 (0.5)		1	0.4	1 (0.4)		1	0.3
脱水	0				1 (0.5)		1	0.4	1 (0.4)		1	0.3
内分泌障害	1 (1.2)		1	1.0	0				1 (0.4)		1	0.3
急性副腎皮質機能不全	1 (1.2)		1	1.0	0				1 (0.4)		1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

重篤な有害事象の詳細を 2.7.4.2.3.1 及び 2.7.4.2.3.1.1 に示す。

2.7.4.2.3.2.3 臨床薬理試験（4042 試験）の結果

4042 試験（単回投与、用量漸増試験）では重篤な有害事象の報告はなかった〔治験総括報告書、4042 試験（M 5.3.3.2）Section 12.8〕。

2.7.4.2.4 その他の重要な有害事象

2.7.4.2.4.1 治験薬の投与中止に至った有害事象

治験薬の投与中止に至った有害事象を試験別に表 2.7.4.2-12 に示す。

第 3 相試験（4263 試験、主要期間）の結果

4263 試験では、有害事象の発現により治験薬の投与中止に至った被験者はいなかった（表 2.7.4.2-12）。

第 2 相試験（4172 試験）

ソマプシタン投与を受けた被験者で、有害事象により治験薬の投与中止に至った被験者はいなかった（表 2.7.4.2-12）。

ノルディトロピン投与を受けた 2 例の被験者が、有害事象により治験薬の投与中止に至った（「薬物過敏症」及び「ネフローゼ症候群」）（表 2.7.4.2-12）。

表 2.7.4.2-12 治験薬の投与中止に至った被験者（試験別）

Treatment group/ Subject ID	Sex/Age/BMI	AE preferred term	Onset day/ Period/ Duration (days)	SAE	Severity/ Causality	Outcome	Action taken to trial product
Phase 3							
Trial 4263	Not applicable						
Phase 2							
Trial 4172							
Norditropin 0.034 mg/kg/day/ somapacitan 0.16 mg/kg/week [redacted]004	M/[redacted]0/13.9	薬物過敏症	45/Main	No	Mild/ Probably	Not recovered	Drug withdrawn
Norditropin 0.034 mg/kg/day/ somapacitan 0.16 mg/kg/week [redacted]002	M/[redacted]1/15.6	ネフローゼ症候群	366/Ext	Yes	Moderate/ Unlikely	Not recovered	Drug withdrawn

Notes: Age in years.
Abbreviations: M: male; BMI: body mass index (kg/m^2) at baseline. AE: adverse event; SAE: serious adverse event.

コホート II 及び III で、治験薬の投与中止に至った有害事象はなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.13〕。

治験薬の投与中止に至った有害事象の叙述を各治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Section 14.3.3 及び 16.3.1〕に示す。

臨床薬理試験（4042 試験）の結果

有害事象の発現により治験薬の投与中止に至った被験者はいなかった〔治験総括報告書、4042 試験（M 5.3.3.2）Section 12.8〕。

2.7.4.2.4.2 治験薬の用量減量又は投与中断に至った有害事象

2.7.4.2.4.2.1 主要な第 3 相試験（4263 試験、主要期間）の結果

ソマプシタン群の 1 例（被験者 ID：[redacted]002）が Day 369（52 週の来院時）に軽度の「空腹時血中ブドウ糖不良」により治験薬の用量減量に至った〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.5〕。

ノルディトロピン群の 2 例が「頭痛」〔被験者 ID：[redacted]001「頭痛」（Day 136）、被験者 ID：[redacted]001「頭痛」、「眼痛」／「霧視」、「腹痛」及び「嘔吐」（いずれも Day 9～16）〕により治験薬の用量減量に至った。治験薬の用量減量に至った有害事象は非重篤であり、被験者は完全に回復した。治験薬の用量減量に至った有害事象の一覧を治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.5〕に示す。

ソマプシタン群の 2 例及びノルディトロピン群の 5 例が有害事象により治験薬の投与中断に至った（表 2.7.4.2-13）。3 例が「頭痛」により治験薬の投与中断に至った。いずれの被験者も完全に回復し、投与を継続した。

表 2.7.4.2-13　治験薬の投与中断に至った有害事象（4263 試験、主要期間）

Treatment group	Sex/Age/BMI	AE preferred term	Trial day/ Period/ Duration (days)	SAE	Severity/ Causality	Outcome
Somapacitan	M/[redacted].3/17.3	喘息	313/Main/46	Yes	Severe/ Unlikely	Recovered
Somapacitan	M/[redacted].9/15.2	頭痛	35/Main/2	Yes	Severe/ Unlikely	Recovered (Section 2.7.4.2.3.1)

Treatment group	Sex/Age/BMI	AE preferred term	Trial day/ Period/ Duration (days)	SAE	Severity/ Causality	Outcome
Norditropin	F/[redacted].0/17.1	頭痛	286/Main/5	No	Moderate/ Possible	Recovered
Norditropin	F/[redacted].7/18.8	頭痛	6/Main/10	No	Severe/ Possible	Recovered
Norditropin	M/[redacted].7/14.2	偶発的過量投与	142/Main/1	No	Mild/ Unlikely	Recovered
Norditropin	F/[redacted].7/16.3	COVID-19	332/Main/17	Yes	Mild/ Unlikely	Recovered
Norditropin	M/[redacted].1/14.9	四肢痛	106/Main/24	No	Mild/ Unlikely	Recovered

Notes: Somapacitan 0.16 mg/kg/week. Norditropin 0.034 mg/kg/day. Age in years.
Abbreviations: F: female; M: male; BMI: Body mass index (kg/m^2) at baseline. AE: adverse event; SAE: serious adverse event.

2.7.4.2.4.2.2 補足的な情報

第 2 相試験（4172 試験、208 週）の結果

4 年間の試験期間中に治験薬の用量減量に至った有害事象はなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.1 及び 14.3.1.3〕。

ソマプシタンもしくはノルディトロピンの投与を受けた被験者 8 例が有害事象により治験薬の投与中断に至った〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 12-9〕。7 例で発現した治験薬の投与中断に至った有害事象は非重篤で、治験薬との因果関係は「なし」と判定された。

ソマプシタン 0.16 mg/kg/週の投与を受けた被験者 1 例が 2 件の重篤な有害事象（「全身性浮腫」及び「嘔吐」）により治験薬の投与中断に至った。いずれの重篤な有害事象も治験薬との因果関係が「あり」と判定された。いずれも完全に回復した。2 件の重篤な有害事象の叙述を治験総括報告書〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Section 14.3.3（症例番号：543799）〕に示す。2 件の重篤な有害事象は予測できない重篤な副作用の疑いとして報告された。

臨床薬理試験（4042 試験）の結果

治験薬の用量減量に至った有害事象はなかった〔治験総括報告書、4042 試験（M 5.3.3.2）Section 12.8〕。

2.7.4.2.5 器官別又は症候群別有害事象の解析

2.7.4.2.5.1 特に注目すべき安全性領域の選択方法

安全性の主要な評価は、第 3 相検証的試験である 4263 試験（主要期間）で行い、第 2 相試験である 4172 試験で得られたデータ及び安全性併合データ（0.16 mg/kg/週のソマプシタン併合及びノルディトロピン併合）で補足した。SMQ（2.7.4.1.2.2 参照）を用いて各国際共同試験及び安全性併合データで該

当する有害事象を検索し、試験別に提示した。2.7.4.2.5.3～2.7.4.2.5.14 には、主に 4263 試験（主要期間）での結果を示し、4172 試験及び安全性併合データの結果は相互参照で示した。

ソマプシタンの臨床経験、GH のクラスエフェクト、規制当局からの助言及び要求事項に基づき、ソマプシタンの安全性評価において特に関連のある事象として、特に注目すべき安全性領域を定義した（表 2.7.4.2-14）。それぞれの特に注目すべき安全性領域は、各領域で特有の SMQ（狭義）に基づき評価した。

表 2.7.4.2-14　特に注目すべき安全性領域

評価した安全性領域	MedDRA 検索式（SOC、SMQ 等）	MedDRA コード／NMQ コード
内分泌障害（2.7.4.2.5.3）		
甲状腺機能低下症	SMQ 甲状腺機能低下症	20000160
副腎皮質機能不全	HLT 副腎皮質機能低下	10001343
胃腸障害（2.7.4.2.5.4）		
膵炎	SMQ 急性膵炎	20000022
嘔吐	PT 嘔吐	10047700
一般・全身障害（2.7.4.2.5.5）		
末梢性浮腫	PT 末梢性浮腫	10030124
疲労	PT 疲労	10016256
無力症	PT 無力症	10003549
免疫系障害（2.7.4.2.5.6）		
アレルギー反応	SMQ 過敏症	20000214
アナフィラキシー反応	SMQ アナフィラキシー反応	20000021
傷害、処置及び投与部位の状態（2.7.4.2.5.7）		
注射部位反応	HLT 注射部位反応	10022097
脂肪肥大症／リポジストロフィー／脂肪組織萎縮症	HLT リポジストロフィー	10024606
感染症及び寄生虫症（2.7.4.2.5.8.1）		
新型コロナウイルス感染症	HLT コロナウイルス感染症	10084510
臨床検査（2.7.4.2.5.9）		
血中アルカリホスファターゼ増加（骨）	PT 血中アルカリホスファターゼ増加	10059570
薬物特異性抗体陽性	HLT 免疫学的検査 NEC	10021504
心電図に関連する有害事象	HLGT 不整脈	10007521
代謝系障害（2.7.4.2.5.10）		
高血糖／2 型糖尿病	SMQ 高血糖／糖尿病の発症	20000041
筋骨格系障害（2.7.4.2.5.11）		
関節痛	PT 関節痛	10003239
筋肉痛	PT 筋肉痛	10028411
関節硬直	PT 関節硬直	10023230
筋肉硬直	PT 筋骨格硬直	10052904
側弯症	PT 側弯症	10039722
新生物（2.7.4.2.5.12）		
新生物	SOC 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）	10029104
神経系障害（2.7.4.2.5.13）		

評価した安全性領域	MedDRA 検索式（SOC、SMQ 等）	MedDRA コード／NMQ コード
頭痛	HLT 頭痛 NEC	10019233
錯感覚	PT 錯感覚	10033775
脳卒中	SMQ 中枢神経系血管障害	20000060
手根管症候群	PT 手根管症候群	10007697
良性頭蓋内圧亢進	HLT 頭蓋内圧亢進性障害	
その他（2.7.4.2.5.14）		
まれな事象	NMQ まれな事象	99999033
投薬過誤	SMQ 投薬過誤	20000224
乱用又は誤用	NMQ 乱用／誤用	99999001
過量投与	NMQ 過量投与	99999029
製品を介する感染因子の伝播の疑い	NMQ 伝播	99999035

[a] Additional PTs were included in the evaluation of peripheral oedema: PT Oedema peripheral, PT Swelling face, PT Periorbital oedema, PT Face oedema and PT Swelling of eyelid, please refer to Section 2.7.4.2.5.5.1.

Abbreviations: HLGT: high level group term; HLT: high level term; PT: preferred term; SOC: system organ class; NMQ: Novo Nordisk medical query; SMQ: standard MedDRA queries.

2.7.4.2.5.2 特に注目すべき安全性領域の要約

第 3 相試験である 4263 試験（主要期間）で認められた特に注目すべき安全性領域における有害事象の概要を図 2.7.4.2-5 に示す（いずれの群でも有害事象の報告がなかった特に注目すべき安全性領域は、この概要には含めていない）。両群で認められた有害事象はクラスエフェクトとして予想される事象と一致していた。

概して、選択した安全性領域に含まれる有害事象の発現件数は少なく、特に注目すべき安全性領域に含まれる有害事象の評価により、ソマプシタンとノルディトロピンの安全性プロファイルが同様であることが示唆された。4263 試験（主要期間）における特に注目すべき安全性領域の評価は以下のとおりであった。

- ソマプシタン群で 2 件の副腎皮質機能不全の有害事象が報告され、それぞれ軽度又は中等度に分類され、いずれの事象もソマプシタンとの因果関係は「なし」と判定された。ノルディトロピン群の 1 件の副腎皮質機能不全の有害事象は重篤な有害事象として報告された。
- 52 週の投与期間において、注射部位反応を発現した被験者の割合は低く、ソマプシタン群（5.3%）とノルディトロピン群（5.9%）で同様であった。注射部位反応は、ソマプシタン群で 7 例 9 件、ノルディトロピン群で 4 例 4 件報告された。ソマプシタン群の 2 例（1.5%）は、「注射部位疼痛」を発現した。
- 脂肪組織萎縮症又は脂肪肥大症の有害事象は報告されなかった。ソマプシタン群で 1 件の軽度で非重篤の「後天性リポジストロフィー」が報告された。本事象は、治験薬投与を変更せずに回復し、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。
- 心電図に関連する有害事象の報告はなかった。
- 「2 型糖尿病」の報告はなかった。
- 2 件の良性新生物（「皮膚乳頭腫」及び「リンパ管腫」）がソマプシタン群で報告された。いずれの事象も軽度に分類され、非重篤であり、治験責任医師により治験薬との因果関係は「なし」と判定された。悪性新生物の報告はなかった。

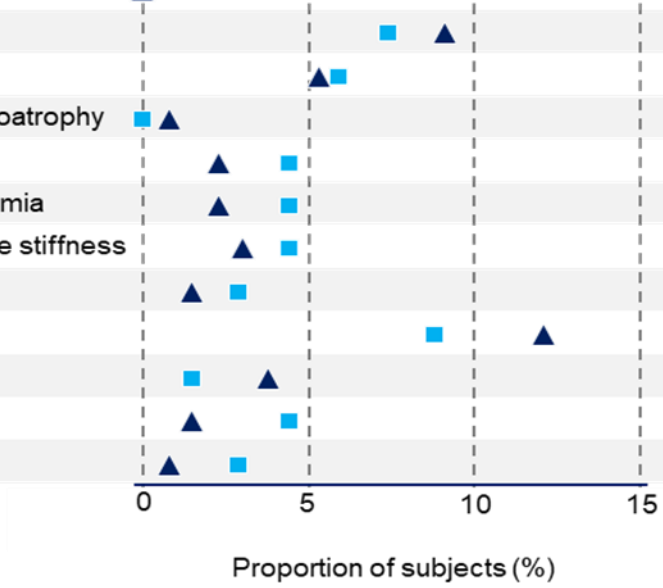
それぞれの特に注目すべき安全性領域の詳細は、器官別大分類別及び基本語別に 2.7.4.2.5.3～2.7.4.2.5.14 に示す。

さらに、特に注目すべき安全性領域は、第 2 相試験である 4172 試験〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.50～14.3.1.105。本臨床概要本文には、ソマプシタン 0.04/0.08/0.16 mg/kg/週併合群及びノルディトロピン群の結果を示す。〕及び安全性併合データ〔図 2.7.4.2-6（付録 2.7.4.7.1、Table 45～72 に基づく）〕について要約した。

この評価では新規の安全性の懸念はみられなかった。

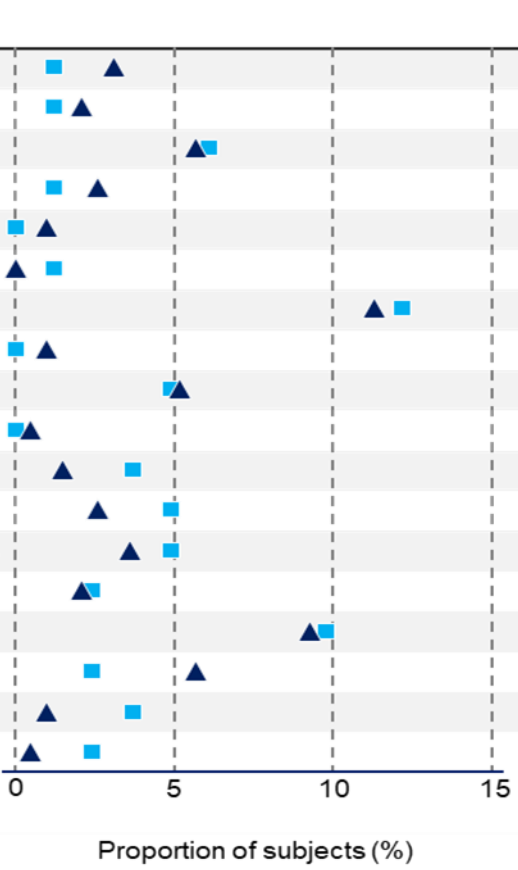
図 2.7.4.2-5　　特に注目すべき安全性領域に分類される有害事象の概要（4263 試験、主要期間）

Safety focus area	Norditropin®(N=68)				Somapacitan (N=132)			
	N	(%)	E	R	N	(%)	E	R
Hypothyroidism	1	(1.5)	1	1.4	6	(4.5)	6	4.5
Adrenocortical insufficiency	1	(1.5)	1	1.4	2	(1.5)	2	1.5
Vomiting	4	(5.9)	6	8.7	6	(4.5)	10	7.5
Peripheral oedema	1	(1.5)	1	1.4	4	(3.0)	5	3.7
Fatigue	0				2	(1.5)	4	3.0
Asthenia	1	(1.5)	1	1.4	0			
Allergic reactions	5	(7.4)	6	8.7	12	(9.1)	17	12.7
Injection site reactions	4	(5.9)	4	5.8	7	(5.3)	9	6.7
Lipohypertrophy/lipodystrophy/lipoatrophy	0				1	(0.8)	1	0.7
Covid-19	3	(4.4)	3	4.3	3	(2.3)	3	2.2
Type 2 diabetes incl. hyperglycaemia	3	(4.4)	3	4.3	3	(2.3)	3	2.2
Arthralgia, myalgia, joint or muscle stiffness	3	(4.4)	3	4.3	4	(3.0)	5	3.7
Neoplasms	2	(2.9)	2	2.9	2	(1.5)	2	1.5
Headache	6	(8.8)	11	15.9	16	(12.1)	22	16.5
Rare events	1	(1.5)	1	1.4	5	(3.8)	6	4.5
Medication errors	3	(4.4)	3	4.3	2	(1.5)	2	1.5
Overdose	2	(2.9)	2	2.9	1	(0.8)	1	0.7



Abbreviations: N: number of subjects with event(s), %: proportion of subjects with event(s), E: number of events, R: events per 100 patient years of exposure.

図 2.7.4.2-6　　特に注目すべき安全性領域に分類される有害事象の概要（安全性併合データ）



Safety focus area	Norditropin®(N=82)				Somapacitan (N=194)			
	N	(%)	E	R	N	(%)	E	R
Hypothyroidism	1	(1.2)	1	1.0	6	(3.1)	6	2.1
Adrenocortical insufficiency	1	(1.2)	1	1.0	4	(2.1)	4	1.4
Vomiting	5	(6.1)	10	9.6	11	(5.7)	15	5.3
Peripheral oedema	1	(1.2)	1	1.0	5	(2.6)	6	2.1
Fatigue	0				2	(1.0)	4	1.4
Asthenia	1	(1.2)	1	1.0	0			
Allergic reactions	10	(12.2)	13	12.4	22	(11.3)	41	14.5
Hypersensitivity (anaphylactic reactions)	0				2	(1.0)	2	0.7
Injection site reactions	4	(4.9)	4	3.8	10	(5.2)	17	6.0
Lipohypertrophy/lipodystrophy/lipoatrophy	0				1	(0.5)	1	0.4
Covid-19	3	(3.7)	3	2.9	3	(1.5)	3	1.1
Type 2 diabetes incl. Hyperglycaemia	4	(4.9)	4	3.8	5	(2.6)	5	1.8
Arthralgia, myalgia, joint or muscle stiffness	4	(4.9)	4	3.8	7	(3.6)	9	3.2
Neoplasms	2	(2.4)	2	1.9	4	(2.1)	4	1.4
Headache	8	(9.8)	13	12.4	18	(9.3)	26	9.2
Rare events	2	(2.4)	2	1.9	11	(5.7)	12	4.2
Medication errors	3	(3.7)	3	2.9	2	(1.0)	2	0.7
Overdose	2	(2.4)	2	1.9	1	(0.5)	1	0.4

Abbreviations: N: number of subjects with event(s), %: proportion of subjects with event(s), E: number of events, R: events per 100 patient years of exposure.

2.7.4.2.5.3 内分泌障害

2.7.4.2.5.3.1 甲状腺機能低下症

4263 試験（主要期間）で発現した甲状腺機能低下症の有害事象を表 2.7.4.2-15 に要約する。

甲状腺機能低下症の有害事象はノルディトロピン群（1.5%）と比較してソマプシタン群（4.5%）で多く発現した。大部分の有害事象は軽度に分類され、治験薬との因果関係は「なし」と判定された。「甲状腺機能低下症」は 52 週間の主要期間中に回復しなかった。

表 2.7.4.2-15　甲状腺機能低下症の有害事象の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin			somapacitan		
	N (%)	E	R	N (%)	E	R
Number of subjects	68			132		
Total patient years at risk	69.1			133.4		
内分泌障害	1 (1.5)	1	1.4	6 (4.5)	6	4.5
甲状腺機能低下症	1 (1.5)	1	1.4	4 (3.0)	4	3.0
続発性甲状腺機能低下症	0			2 (1.5)	2	1.5

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
MedDRA version 24.1.

4172 試験では、1 件の「甲状腺機能低下症」が発現した（ソマプシタン 0.04 mg/kg/週、主要期間）〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.50〕。

安全性併合データでは甲状腺機能低下症の有害事象のパターン（ソマプシタン群 3.1%、ノルディトロピン群 1.2%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 45）。

2.7.4.2.5.3.2 副腎皮質機能不全

4263 試験（主要期間）で発現した副腎皮質機能不全の有害事象を表 2.7.4.2-16 に要約する。

副腎皮質機能不全の有害事象を発現した被験者の割合はソマプシタン群（1.5%）とノルディトロピン群（1.5%）で同様であった。

ソマプシタン群では 2 件の副腎皮質機能不全の有害事象が発現し、それぞれ軽度及び中等度であり、いずれの事象も治験薬との因果関係は「なし」と判定された。ノルディトロピン群では 1 件の副腎皮質機能不全の有害事象が発現し、重篤な有害事象とされた。副腎皮質機能不全の有害事象別の詳細を表 2.7.4.2-17 に示す。

表 2.7.4.2-16　副腎皮質機能不全の有害事象の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin			somapacitan		
	N	(%)	E　R	N	(%)	E　R
Number of subjects	68			132		
Total patient years at risk	69.1			133.4		
内分泌障害	1	(1.5)	1　1.4	2	(1.5)	2　1.5
急性副腎皮質機能不全	1	(1.5)	1　1.4	0		
副腎皮質刺激ホルモン欠損症	0			1	(0.8)	1　0.7
続発性副腎皮質機能不全	0			1	(0.8)	1　0.7

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
MedDRA version 24.1.

表 2.7.4.2-17　副腎皮質機能不全の有害事象別の詳細（4263 試験、主要期間）

Treatment group/ Subject ID	Sex/Age/BMI	AE preferred term	Trial day/ Period/ Duration (days)	SAE	Severity/ Causality	Outcome	Action taken to trial product
Somapacitan [redacted]001	M/[redacted].5/17.2	副腎皮質刺激ホルモン欠損症	7/Main/	No	Moderate/ Unlikely	Not recovered	Not applicable[a]
Somapacitan [redacted]002	F/[redacted].3/15.6	続発性副腎皮質機能不全	370/Main/	No	Mild/ Unlikely	Not recovered	Dose not changed
Norditropin [redacted]002	F/[redacted].0/17.1	急性副腎皮質機能不全	26/Main/1	Yes	Moderate/ Unlikely	Recovered	Dose not changed

[a]The investigator had the option to choose “not applicable” as outcome.
Notes: Age in years.
Abbreviations: F: female; M: male; BMI: Body mass index (kg/m^2) at baseline. AE: adverse event; SAE: serious adverse event.

4172 試験では、ソマプシタン群で 3 件の副腎皮質機能不全の有害事象が発現した〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Section 12.3.4.1、Table 12-12 及び Table 14.3.1.52〕。

安全性併合データでは副腎皮質機能不全の有害事象のパターン（ソマプシタン群 2.1%、ノルディトロピン群 1.2%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 46）。

2.7.4.2.5.4 胃腸障害

2.7.4.2.5.4.1 膵炎

4263 試験（主要期間）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.26〕及び 4172 試験〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.54 及び 14.3.1.55〕の 2 つの試験では、「膵炎」の発現はなかった。したがって、安全性併合データでもみられていない（付録 2.7.4.7.1、Table 47）。

2.7.4.2.5.4.2 嘔吐

4263 試験（主要期間）で発現した有害事象「嘔吐」を表 2.7.4.2-18 に要約する。

「嘔吐」を発現した被験者の割合はソマプシタン群（4.5%）とノルディトロピン群（5.9%）で同様であった。

ソマプシタン群では 10 件の「嘔吐」が発現したが、いずれも軽度又は中等度に分類され、転帰は「回復」であった（大部分は 1～3 日後に回復）。1 件は重篤な有害事象と判定された（2.7.4.2.3.1 参照）。1 件の「嘔吐」は軽度に分類され、非重篤であり、持続期間は 113 日間であった（ソマプシタン群、被験者 ID：[redacted]002）。当該被験者は「嘔吐」発現の約 1.5 ヵ月前に頭部を損傷していた。

表 2.7.4.2-18　有害事象「嘔吐」の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin			somapacitan		
	N	(%)	E R	N	(%)	E R
Number of subjects	68			132		
Total patient years at risk	69.1			133.4		
胃腸障害						
嘔吐	4	(5.9)	6 8.7	6	(4.5)	10 7.5

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage.
MedDRA version 24.1.

ソマプシタン群で発現したそれぞれの有害事象「嘔吐」の詳細の一覧を治験総括報告書に示す〔4263 試験（52 週）（M 5.3.5.1）Table 12-11〕。

4172 試験では、「嘔吐」の単位時間あたりの発現件数はソマプシタン群（6 例）で 3.7 件/100 人・年、ノルディトロピン群（1 例）で 11.3 件/100 人・年であった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.56〕。

安全性併合データでは「嘔吐」のパターン（ソマプシタン群 5.7%、ノルディトロピン群 6.1%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 48）。

2.7.4.2.5.5 一般・全身障害

2.7.4.2.5.5.1 末梢性浮腫

4263 試験（主要期間）の解析では、末梢性浮腫の有害事象に多様な基本語（「末梢性浮腫」、「顔面腫脹」、「眼窩周囲浮腫」及び「顔面浮腫」）が含まれている（表 2.7.4.2-22）。

4263 試験で発現した末梢性浮腫の有害事象を表 2.7.4.2-19 に要約する。

ソマプシタン群では、「顔面腫脹」が 3 件、「顔面浮腫」が 1 件及び「眼窩周囲浮腫」が 1 件発現し（3.0%）、ノルディトロピン群では、「末梢性浮腫」が 1 件発現した（1.5%）。なお、ソマプシタン群とノルディトロピン群間の割り付け比率が 2：1 であることを考慮に入れる必要がある。6 件すべてが軽度に分類され、治験薬投与の変更はなく、完全に回復した（表 2.7.4.2-20）。

表 2.7.4.2-19　末梢性浮腫の有害事象の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin			somapacitan		
	N (%)	E	R	N (%)	E	R
Number of subjects	68			132		
Total patient years at risk	69.1			133.4		
Events	1 (1.5)	1	1.4	4 (3.0)	5	3.7
一般・全身障害および投与部位の状態	1 (1.5)	1	1.4	4 (3.0)	4	3.0
顔面腫脹	0			3 (2.3)	3	2.2
顔面浮腫	0			1 (0.8)	1	0.7
末梢性浮腫	1 (1.5)	1	1.4	0		
眼障害	0			1 (0.8)	1	0.7
眼窩周囲浮腫	0			1 (0.8)	1	0.7

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
MedDRA version 24.1.

表 2.7.4.2-20　末梢性浮腫の有害事象（顔面腫脹、顔面浮腫及び末梢性浮腫）別の詳細（4263 試験、主要期間）

Treatment group/ Subject ID	Sex/Age/ BMI	AE preferred term (reported term)	Trial day/ Period/ Duration (days)	SAE	Severity/ Causality	Outcome
Somapacitan [redacted]001	F/[redacted].0/14.4	顔面腫脹 (facial swelling for one hour)	19/Main/1	No	Mild/Unlikely	Recovered
Somapacitan [redacted]001	F/[redacted].1/13.8	顔面腫脹 (swelling face and eyes due to makeup)	138/Main/137	No	Mild/Unlikely	Recovered
Somapacitan [redacted]001	F/[redacted].4/14.8	眼窩周囲浮腫 (facial swelling)	3/Main/14	No	Mild/Possible	Recovered
		顔面腫脹 (intermittent facial swelling)	32/Main/155	No	Mild/Possible	Recovered
Somapacitan [redacted]001	M/[redacted].5/15.9	顔面浮腫 (face oedema)	85/Main/102	No	Mild/Possible	Recovered
Norditropin [redacted]001	M/1[redacted].0/16.4	末梢性浮腫 (mild peripheral oedema)	61/Main/30	No	Mild/Possible	Recovered

Notes: Age in years.
Abbreviations: F: female; M: male; BMI: Body mass index (kg/m^2) at baseline. AE: adverse event; SAE: serious adverse event.

4172 試験では「末梢性浮腫」の発現はなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.58 及び 14.3.1.59〕。4172 試験では、重篤な有害事象である「全身性浮腫」1 件が

報告された（発現日：Day 3、持続期間：9 日間）。当該事象の治験薬（ソマプシタン 0.16 mg/kg/週）との因果関係は「あり」と判定された。当該事象により治験薬投与が中断された。被験者は当該事象より完全に回復した。詳細は 2.7.4.2.4.2.2 に示す。1 件の「眼瞼腫脹」が発現し、下記の安全性併合データに含めている（付録 2.7.4.7.1、Table 52）。

安全性併合データでは末梢性浮腫の有害事象のパターン（ソマプシタン群 2.6%、ノルディトロピン群 1.2%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 49 及び 52）。

2.7.4.2.5.5.2 疲労

4263 試験（主要期間）で発現した有害事象「疲労」を表 2.7.4.2-21 に要約する。

ソマプシタン群では「疲労」が 2 例（1.5%）4 件で発現したが、ノルディトロピン群では発現はなかった。2 例で発現した「疲労」は非重篤で 2 件は軽度、2 件は重度に分類され、因果関係は「可能性あり」と判定された。これらの事象は治験薬投与を変更せずに回復した〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1〕。

表 2.7.4.2-21　有害事象「疲労」の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin			somapacitan		
	N	(%)	E　R	N	(%)	E　R
Number of subjects	68			132		
Total patient years at risk	69.1			133.4		
General disorders and administration site conditions						
疲労	0			2	(1.5)	4　3.0

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
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4172 試験では「疲労」の発現はなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.60 及び 14.3.1.61〕。

安全性併合データでは「疲労」のパターン（ソマプシタン群 1.0%、ノルディトロピン群 0.0%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 50）。

2.7.4.2.5.5.3 無力症

4263 試験（主要期間）では、ソマプシタン群では「無力症」の発現はなく、ノルディトロピン群では 1 例（1.5%）で発現した〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.30〕。

4172 試験では「無力症」の発現はなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.62 及び 14.3.1.63〕。

安全性併合データでは「無力症」のパターン（ソマプシタン群 0.0%、ノルディトロピン群 1.2%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 51）。

2.7.4.2.5.6 免疫系障害

2.7.4.2.5.6.1 アレルギー反応

4263 試験（主要期間）で発現したアレルギー反応の有害事象を表 2.7.4.2-22 に要約する。

アレルギー反応の有害事象を発現した被験者の割合はソマプシタン群（9.1%）とノルディトロピン群（7.4%）で同様であった。大部分の事象は蕁麻疹、発疹及び皮膚炎に関連するものであった。

アレルギー反応の有害事象の要約には顔面浮腫及び注射部位過敏反応に関連する基本語が含まれており、それぞれ表 2.7.4.2-19 及び表 2.7.4.2-23 にも記載する。

表 2.7.4.2-22　アレルギー反応の有害事象の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin				somapacitan				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	68				132				200			
Total patient years at risk	69.1				133.4				202.5			
Events	5	(7.4)	6	8.7	12	(9.1)	17	12.7	17	(8.5)	23	11.4
皮膚および皮下組織障害	4	(5.9)	5	7.2	7	(5.3)	10	7.5	11	(5.5)	15	7.4
蕁麻疹	2	(2.9)	2	2.9	2	(1.5)	5	3.7	4	(2.0)	7	3.5
発疹	1	(1.5)	2	2.9	1	(0.8)	1	0.7	2	(1.0)	3	1.5
アトピー性皮膚炎	0				2	(1.5)	2	1.5	2	(1.0)	2	1.0
皮膚炎	1	(1.5)	1	1.4	1	(0.8)	1	0.7	2	(1.0)	2	1.0
ヘノッホ・シェーンライン紫斑病	0				1	(0.8)	1	0.7	1	(0.5)	1	0.5
一般・全身障害および投与部位の状態	1	(1.5)	1	1.4	4	(3.0)	4	3.0	5	(2.5)	5	2.5
顔面腫脹	0				3	(2.3)	3	2.2	3	(1.5)	3	1.5
顔面浮腫	0				1	(0.8)	1	0.7	1	(0.5)	1	0.5
注射部位過敏反応	1	(1.5)	1	1.4	0				1	(0.5)	1	0.5
呼吸器、胸郭および縦隔障害	0				1	(0.8)	2	1.5	1	(0.5)	2	1.0
アレルギー性鼻炎	0				1	(0.8)	2	1.5	1	(0.5)	2	1.0
眼障害	0				1	(0.8)	1	0.7	1	(0.5)	1	0.5
眼窩周囲浮腫	0				1	(0.8)	1	0.7	1	(0.5)	1	0.5

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
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4172 試験では、アレルギー反応の有害事象の単位時間あたりの発現件数は、ソマプシタン 0.04/0.08/0.16 mg/kg/週併合群（14.8 件/100 人・年）及びソマプシタン 0.16 mg/kg/週併合群（16.7 件/100 人・年）とノルディトロピン群（19.7 件/100 人・年）で同様であった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.64〕。大部分の事象は皮膚炎及びアレルギー性鼻炎に関連するものであった。アレルギー反応の有害事象が認められた被験者の割合は 4263 試験と比較して 4172 試験で高い傾向がみられた（ソマプシタン 0.04/0.08/0.16 mg/kg/週併合群 22.2%、ソマプシタン 0.16 mg/kg/週併合群 19.2%及びノルディトロピン群 35.7%）。

安全性併合データではアレルギー反応の有害事象のパターン（ソマプシタン群 11.3%、ノルディトロピン群 12.2%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 52）。

2.7.4.2.5.6.2 アナフィラキシー反応

4263 試験（主要期間）ではアナフィラキシー反応の有害事象の発現はなかった〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.32〕。

4172 試験では、ソマプシタン群の 2 例において「アナフィラキシー反応」及び「アナフィラキシーショック」が認められた〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Listing 14.3.2.1〕。

- 被験者 ID：[redacted]001（症例番号：619784、ソマプシタン 0.04/0.16 mg/kg/週）：「アナフィラキシー反応」（発現日：Day 683）。当該被験者は食物アレルギー（チョコレート）を有することが確認されていた。
- 被験者 ID：[redacted]001（症例番号：682814、ソマプシタン 0.16 mg/kg/週）：「アナフィラキシーショック」（発現日：Day 861）。当該被験者は食物アレルギー（小麦及び卵）を有することが確認されていた。

いずれの事象も重篤な有害事象であったが、ソマプシタンとの因果関係は「なし」と判定された。いずれも遅発性であり、両被験者ともに治験薬投与を変更せずに完全に回復した〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 12-14〕。4172 試験で発現した 2 件のアナフィラキシー反応は安全性併合データに反映されている（付録 2.7.4.7.1、Table 53）。

2.7.4.2.5.7 傷害、処置及び投与部位の状態

注射部位反応の有害事象は、治験責任医師により評価され、注射部位の目視確認及び触診により評価された。注射部位反応が有害事象の定義に合致する場合、有害事象として報告された。治験責任医師が追加の調査が必要と判断した場合、症例報告書に含まれる Injection Site Reaction Form あるいは皮膚科専門医による画像評価（もしくは両方）により、追加の情報収集を実施した。

ソマプシタン投与を受けた小児 GHD 患者で、局所忍容性に関する問題はみられなかった。局所の注射部位反応は軽度又は中等度に分類され、一過性であった。

2.7.4.2.5.7.1 注射部位反応

4263 試験（主要期間）で発現した注射部位反応の有害事象を表 2.7.4.2-23 に要約する。

注射部位反応の有害事象（有害事象として報告）を発現した被験者の割合は、ソマプシタン群（5.3%）とノルディトロピン群（5.9%）で同様であった。ソマプシタン群では 7 例 9 件、ノルディトロピン群では 4 例 4 件発現した。いずれも軽度に分類され、ソマプシタン群では、9 件中 7 件の転帰は「回復」であり、ノルディトロピン群ではすべての事象の転帰は「回復」であった。

重篤な有害事象として報告された注射部位反応の有害事象はなかった。治験薬の投与中止に至った注射部位反応の有害事象は認められなかった。

表 2.7.4.2-23　注射部位反応の有害事象の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin				somapacitan				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	68				132				200			
Total patient years at risk	69.1				133.4				202.5			
Events	4	(5.9)	4	5.8	7	(5.3)	9	6.7	11	(5.5)	13	6.4
一般・全身障害および投与部位の状態	4	(5.9)	4	5.8	7	(5.3)	9	6.7	11	(5.5)	13	6.4
注射部位内出血	2	(2.9)	2	2.9	2	(1.5)	2	1.5	4	(2.0)	4	2.0
注射部位疼痛	1	(1.5)	1	1.4	2	(1.5)	2	1.5	3	(1.5)	3	1.5
注射部位血腫	0				2	(1.5)	4	3.0	2	(1.0)	4	2.0
注射部位過敏反応	1	(1.5)	1	1.4	0				1	(0.5)	1	0.5
注射部位腫脹	0				1	(0.8)	1	0.7	1	(0.5)	1	0.5

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
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4172 試験では、4 年間の試験期間中にソマプシタンを投与した被験者 4 例において 9 件の注射部位反応の有害事象が発現した（ソマプシタン 0.04/0.08/0.16 mg/kg/週併合群 8.9%、ソマプシタン 0.16 mg/kg/週併合群 5.8%、ノルディトロピン群 0.0%）〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.68〕。

安全性併合データでは注射部位反応の有害事象のパターン（ソマプシタン群 5.2%、ノルディトロピン群 4.9%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 54）。

臨床薬理試験である 4042 試験で認められた局所注射部位反応の要約を治験総括報告書〔4042 試験（M 5.3.3.2）Section 12.5.3〕に示す。4042 試験では、1 件の「注射部位疼痛」（軽度）が有害事象として報告された（ソマプシタン 0.16 mg/kg）。

2.7.4.2.5.7.2 脂肪肥大症／リポジストロフィー／脂肪組織萎縮症

4263 試験（主要期間）で発現した脂肪肥大症／リポジストロフィー／脂肪組織萎縮症の有害事象を表 2.7.4.2-24 に要約する。

4263 試験では脂肪肥大症又は脂肪組織萎縮症の有害事象の発現はなかった。ソマプシタン群で 1 件の「後天性リポジストロフィー」が発現した。当該事象は軽度に分類され、完全に回復した。当該事象の詳細を表 2.7.4.2-25 に、叙述を治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Section 14.3.3〕に示す。

表 2.7.4.2-24　脂肪肥大症／リポジストロフィー／脂肪組織萎縮症の有害事象の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin			somapacitan		
	N	(%)	E R	N	(%)	E R
Number of subjects	68			132		
Total patient years at risk	69.1			133.4		
皮膚および皮下組織障害						
後天性リポジストロフィー	0			1	(0.8)	1 0.7

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
MedDRA version 24.1.

4172 試験では、4 年間の試験期間中にソマプシタン 0.04 mg/kg/週を投与した被験者 2 例で 2 件の「脂肪組織萎縮症」が発現した〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.70〕。重篤な有害事象として報告されたものはなかった。いずれの事象も注射部位を変更することにより回復した。各事象の詳細を表 2.7.4.2-25 に、叙述を治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Section 12.3.4.5〕に示す。

安全性併合データでは脂肪肥大症／リポジストロフィー／脂肪組織萎縮症の有害事象のパターン（ソマプシタン群 0.5%、ノルディトロピン群 0.0%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 55）。

表 2.7.4.2-25　リポジストロフィー及び脂肪組織萎縮症の有害事象別の詳細〔4263 試験（主要期間）及び 4172 試験〕

Trial/ Trial product/ Subject ID	Sex/Age/ BMI	AE preferred term	Onset day/ Trial phase/ Duration (days)	Severity	Causality	SAE	Recovered (yes/no)	Comment
Trial 4263								
Somapacitan 0.16 mg/kg [redacted]002	F/[redacted].2/13.8	後天性リポジストロフィー	332/ Main/ 217	Mild	Unlikely	No	Yes	Reported term: Lipodystrophy of the upper extremities No change in dose
Trial 4172								
Somapacitan 0.04/0.16 mg/kg [redacted]001	F/[redacted].0/15.0	脂肪組織萎縮症	274/ Ext/ 275	Severe	Probable	No	Yes	The lipoatrophy was transient and disappeared after change of injection site. No change in dose (somapacitan 0.04 mg/kg).
Somapacitan 0.04/0.16 mg/kg [redacted]002	M/[redacted].0/15.6	脂肪組織萎縮症	171/ Main/ 210	Severe	Probable	No	Yes	The lipoatrophy reported by the parents could not be verified neither by the investigator, nor the dermatologist. Recovering after change of injection site. No change in dose (somapacitan 0.04 mg/kg).

Notes: Age in years.
Abbreviations: F: female; BMI: Body mass index (kg/m^2) at baseline; NA: Not applicable/Not available.

2.7.4.2.5.8 感染症及び寄生虫症

2.7.4.2.5.8.1 新型コロナウイルス感染症（COVID-19）

4263 試験（主要期間）で認められた有害事象「COVID-19」を表 2.7.4.2-26 に要約する。

「COVID-19」を発現した被験者の割合はソマプシタン群で 2.3%、ノルディトロピン群で 4.4%であった。

5 件は軽度に分類され、非重篤であり、完全に回復した。1 件は重篤な有害事象として報告され、持続期間は 17 日間であり、本事象によりノルディトロピンの投与を中断した（因果関係は「なし」）。当該被験者は完全に回復した。

表 2.7.4.2-26　有害事象「COVID-19」の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin			somapacitan		
	N (%)	E	R	N (%)	E	R
Number of subjects	68			132		
Total patient years at risk	69.1			133.4		
感染症および寄生虫症						
COVID-19	3 (4.4)	3	4.3	3 (2.3)	3	2.2

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
MedDRA version 24.1.

4172 試験では COVID-19 に関連する有害事象の報告はなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.72 及び 14.3.1.73〕。

安全性併合データでは COVID-19 に関連する有害事象を発現した被験者の割合（ソマプシタン群 1.5%、ノルディトロピン群 3.7%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 56）。

2.7.4.2.5.9 臨床検査

2.7.4.2.5.9.1 血中アルカリホスファターゼ増加

4263 試験（主要期間）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.36〕及び 4172 試験〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.74 及び 14.3.1.75〕の 2 つの試験では、「血中アルカリホスファターゼ増加」の発現はなかった。したがって、安全性併合データでもみられていない（付録 2.7.4.7.1、Table 57）。

2.7.4.2.5.9.2 薬物特異性抗体陽性

抗体については 2.7.4.3.1 に記載する。有害事象として報告された抗体は認められなかった〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.37、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.76 及び 14.3.1.77、付録 2.7.4.7.1、Table 58（安全性併合データ）〕。

2.7.4.2.5.9.3 潜在的な心不整脈作用（心電図に関連する有害事象）

潜在的な心不整脈作用を示す有害事象（心電図に関連する有害事象）を特定するため、高位グループ語「不整脈」を用いて検索を行った。

4263 試験（主要期間）では、心不整脈作用に関連する有害事象の発現はなかった〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.38〕。心電図の評価を 2.7.4.4.5 に要約する。

4172 試験では、ソマプシタン群において 2 件の心不整脈作用に関連する軽度の非重篤な有害事象が発現した〔コホート I：「心電図異常」、治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.10、コホート III：「心電図 QT 延長」、治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.12〕。「心電図 QT 延長」は QT 延長を引き起こすことが確認されている併用薬剤の投与を受けていた被験者で報告された。2 件の事象の詳細を表 2.7.4.2-27 に示す。

表 2.7.4.2-27　心電図に関連する有害事象別の詳細（4172 試験）

Trial product/ Subject ID	Sex/Age/ BMI	AE Preferred term	Trial day/ Phase/ Duration (days)	Severity/ Causality	SAE	Recovered (yes/no)	Comment
Somapacitan 0.08/0.16 mg/kg/week Cohort I: [redacted]004	F/[redacted].1/15.0	心電図異常	1108/ Long-term safety ext	Mild/ Possible	No	Not recovered	No change in dose
Somapacitan 0.16 mg/kg/week Cohort III: [redacted]005	M/1[redacted].7/30.9	心電図 QT 延長	380/ Long-term safety ext	Mild/ Unlikely	No	Not recovered	No change in dose. Concomitant medication: SSRI (Fluoxetine for depression) known to cause QT prolongation.

Notes: Age in years.
Abbreviations: F: female; M: male; BMI: body mass index (kg/m^2) at baseline. AE: adverse event; SAE: serious adverse event.

4172 試験で認められた心電図に関連する有害事象はいずれも心不整脈作用に関する SMQ では特定されなかったため、心不整脈作用に関連する有害事象は安全性併合データに含まれていない（付録 2.7.4.7.1、Table 59）。

2.7.4.2.5.10　代謝系障害

2.7.4.2.5.10.1 高血糖／2 型糖尿病

4263 試験（主要期間）で発現した糖代謝障害に関連する有害事象（高血糖の有害事象）を表 2.7.4.2-28 に要約する。

糖代謝障害に関連する有害事象が認められた被験者の割合は、ソマプシタン群（2.3%）及びノルディトロピン群（4.4%）のいずれにおいても低かった。報告された有害事象 6 件はいずれも非重篤であ

り、軽度に分類され、6 件中 5 件は治験薬投与の変更に至るものではなかった。ソマプシタン群の 1 件の軽度の「空腹時血中ブドウ糖不良」により用量の減量に至った（2.7.4.2.4.2.1）。6 件中 5 件の有害事象の転帰は「回復」であったが、ノルディトロピン群で報告された「グリコヘモグロビン増加」は「未回復」と報告された。

4263 試験の 52 週間の主要期間中、2 型糖尿病の有害事象の発現はなかった。

表 2.7.4.2-28　高血糖を含む 2 型糖尿病の有害事象の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin			somapacitan		
	N	(%)	E　R	N	(%)	E　R
Number of subjects	68			132		
Total patient years at risk	69.1			133.4		
Events	3	(4.4)	3　4.3	3	(2.3)	3　2.2
代謝および栄養障害	2	(2.9)	2　2.9	2	(1.5)	2　1.5
高血糖	2	(2.9)	2　2.9	1	(0.8)	1　0.7
空腹時血中ブドウ糖不良	0			1	(0.8)	1　0.7
臨床検査	1	(1.5)	1　1.4	1	(0.8)	1　0.7
血中ブドウ糖増加	0			1	(0.8)	1　0.7
グリコヘモグロビン増加	1	(1.5)	1　1.4	0		

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
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4172 試験では、ソマプシタン 0.16 mg/kg/週群で 2 件（「高血糖」及び「血中ブドウ糖増加」）及びノルディトロピン群で 1 件（「空腹時血中ブドウ糖不良」）の糖代謝障害に関連する有害事象が発現した〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.80〕。

安全性併合データでは高血糖の有害事象のパターン（ソマプシタン群 2.6%、ノルディトロピン群 4.9%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 60）。

2.7.4.2.5.11　筋骨格系障害

2.7.4.2.5.11.1 関節痛、筋肉痛、関節硬直及び筋肉硬直

4263 試験（主要期間）で発現した有害事象「関節痛」、「筋肉痛」、「関節硬直」及び筋肉硬直（「筋骨格硬直」）を表 2.7.4.2-29 に要約する。

筋骨格系障害の有害事象を発現した被験者の割合はソマプシタン群（3.0%）とノルディトロピン群（4.4%）で同様であった。

表 2.7.4.2-29　有害事象「関節痛」、「筋肉痛」、「関節硬直」及び「筋骨格硬直」の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin			somapacitan		
	N (%)	E	R	N (%)	E	R
Number of subjects	68			132		
Total patient years at risk	69.1			133.4		
筋骨格系および結合組織障害	3 (4.4)	3	4.3	4 (3.0)	5	3.7
関節痛	2 (2.9)	2	2.9	2 (1.5)	3	2.2
筋肉痛	0			2 (1.5)	2	1.5
関節硬直	0			0		
筋骨格硬直	1 (1.5)	1	1.4	0		

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
MedDRA version 24.1.

4172 試験では、「関節痛」（ソマプシタン群 3 件、ノルディトロピン群 1 件）及び「筋肉痛」（ソマプシタン群 1 件）の発現は少なく、「関節硬直」又は筋肉硬直の有害事象の発現はなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.82～14.3.1.89〕。

安全性併合データでは筋骨格系障害の有害事象のパターン（ソマプシタン群 3.6%、ノルディトロピン群 4.9%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 61～64）。

2.7.4.2.5.11.2側弯症

4263 試験（主要期間）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.44〕及び 4172 試験〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.90 及び 14.3.1.91〕の 2 つの試験では、「側弯症」の発現はなかった。したがって、安全性併合データでもみられていない（付録 2.7.4.7.1、Table 65）。

2.7.4.2.5.12　新生物

2.7.4.2.5.12.1新生物

4263 試験（主要期間）で発現した新生物の有害事象を表 2.7.4.2-30 に要約する。

良性新生物の有害事象を発現した被験者の割合は、ソマプシタン群（1.5%）及びノルディトロピン群（2.9%）のいずれにおいても低かった。悪性新生物の有害事象の発現はなかった〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1〕。

ソマプシタン群では 2 件の良性新生物の有害事象〔「皮膚乳頭腫」（報告された事象名：verruca vulgaris）及び「リンパ管腫」（報告された事象名：sclerotherapy of lymphangioma）〕が発現した。いずれも軽度に分類され、非重篤であり、治験責任医師により治験薬との因果関係は「なし」と判定された。「皮膚乳頭腫」の転帰は「未回復」であった。

ノルディトロピン群では2件の良性新生物の有害事象（「皮膚乳頭腫」及び「脂肪腫」）が発現した。いずれも軽度に分類され、非重篤であり、転帰は「回復」で、治験責任医師により治験薬との因果関係は「なし」と判定された。

表 2.7.4.2-30　新生物の有害事象の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin			somapacitan		
	N	(%)	E　R	N	(%)	E　R
Number of subjects	68			132		
Total patient years at risk	69.1			133.4		
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）	2	(2.9)	2　2.9	2	(1.5)	2　1.5
皮膚乳頭腫	1	(1.5)	1　1.4	1	(0.8)	1　0.7
脂肪腫	1	(1.5)	1　1.4	0		
リンパ管腫	0			1	(0.8)	1　0.7

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
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4172 試験では、ソマプシタン群において 2 例 3 件の良性新生物の有害事象（「皮膚乳頭腫」）が発現した〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.92〕。いずれも軽度に分類され、非重篤であり、転帰は「回復」で、治験責任医師により治験薬との因果関係は「なし」と判定された〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1〕。ノルディトロピン群では新生物の有害事象の発現はなかった。4172 試験では悪性新生物の有害事象の発現はなかった。

安全性併合データでは良性新生物の有害事象のパターン（ソマプシタン群 2.1%、ノルディトロピン群 2.4%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 66）。

2.7.4.2.5.13　神経系障害

2.7.4.2.5.13.1 頭痛

4263 試験（主要期間）で発現した有害事象「頭痛」を表 2.7.4.2-31 に要約する。

「頭痛」を発現した被験者の割合はソマプシタン群（12.1%）とノルディトロピン群（8.8%）で同様であった。ほとんどの事象が軽度に分類され、大部分の事象の転帰が「回復」であった。

表 2.7.4.2-31　有害事象「頭痛」の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin			somapacitan		
	N (%)	E	R	N (%)	E	R
Number of subjects	68			132		
Total patient years at risk	69.1			133.4		
神経系障害						
頭痛	6 (8.8)	11	15.9	16 (12.1)	22	16.5

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
MedDRA version 24.1.

ソマプシタン群では、2 件の「頭痛」が重度に分類された〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 12-3〕。4 例で発現した 4 件の「頭痛」の転帰は「未回復」であった。3 例では再発性の頭痛であることを示す事象名（occasional headaches 又は intermittent headaches）で報告され、そのうちの 1 例で報告された事象は重度と分類された（眼底検査は正常）。各事象の詳細は、治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1〕に示す。

4172 試験では、「頭痛」の発現は少なかった（コホート I：ソマプシタン群 1 例 3 件、ノルディトロピン群 2 例 2 件、コホート III：1 例 1 件）〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.94 及び 14.3.1.95〕。

安全性併合データでは有害事象「頭痛」のパターン（ソマプシタン群 9.3%、ノルディトロピン群 9.8%）は、4263 試験と概ね同様であった（付録 2.7.4.7.1、Table 67）。

2.7.4.2.5.13.2 錯感覚

4263 試験（主要期間）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.47〕及び 4172 試験〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.96 及び 14.3.1.97〕の 2 つの試験では、「錯感覚」の発現はなかった。したがって、安全性併合データでもみられていない（付録 2.7.4.7.1、Table 68）。

2.7.4.2.5.13.3 脳卒中

4263 試験（主要期間）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.48〕及び 4172 試験〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.98 及び 14.3.1.99〕の 2 つの試験では、「脳卒中」の発現はなかった。したがって、安全性併合データでもみられていない（付録 2.7.4.7.1、Table 69）。

2.7.4.2.5.13.4 手根管症候群

4263 試験（主要期間）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.49〕及び 4172 試験〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.100 及び 14.3.1.101〕の 2 つ

の試験では、「手根管症候群」の発現はなかった。したがって、安全性併合データでもみられていない（付録 2.7.4.7.1、Table 70）。

2.7.4.2.5.13.5 良性頭蓋内圧亢進

4263 試験（主要期間）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.50〕及び 4172 試験〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.102 及び 14.3.1.103〕の 2 つの試験では、「良性頭蓋内圧亢進」の発現はなかった。したがって、安全性併合データでもみられていない（付録 2.7.4.7.1、Table 71）。

2.7.4.2.5.14 その他の事象

2.7.4.2.5.14.1 稀な事象

他の MedDRA 検索で特定されなかった稀な事象を特定するため、追加の MedDRA 検索を実施した。

稀な事象を表 2.7.4.2-32 に要約する。

稀な事象の MedDRA 検索により、ソマプシタン群で 5 例 6 件、ノルディトロピン群で 1 例 1 件の事象が特定された。いずれも軽度又は中等度に分類され、治験薬投与の変更はなく、完全に回復した。

ソマプシタン群では、稀な事象の検索により末梢性浮腫の有害事象 5 件（2.7.4.2.5.5.1 に示す）及び「停留精巣」1 件（両側精巣固定術のために入院を必要としたため重篤な有害事象と判断された）が特定された（詳細は表 2.7.4.2-8 に示す）。

ノルディトロピン群では 1 件の「肺臓炎」が発現した。

表 2.7.4.2-32　稀な有害事象の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin				somapacitan				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	68				132				200			
Total patient years at risk	69.1				133.4				202.5			
Events	1	(1.5)	1	1.4	5	(3.8)	6	4.5	6	(3.0)	7	3.5
一般・全身障害および投与部位の状態	0				4	(3.0)	4	3.0	4	(2.0)	4	2.0
顔面腫脹	0				3	(2.3)	3	2.2	3	(1.5)	3	1.5
顔面浮腫	0				1	(0.8)	1	0.7	1	(0.5)	1	0.5
眼障害	0				1	(0.8)	1	0.7	1	(0.5)	1	0.5
眼窩周囲浮腫	0				1	(0.8)	1	0.7	1	(0.5)	1	0.5
呼吸器、胸郭および縦隔障害	1	(1.5)	1	1.4	0				1	(0.5)	1	0.5
肺臓炎	1	(1.5)	1	1.4	0				1	(0.5)	1	0.5
先天性、家族性および遺伝性障害	0				1	(0.8)	1	0.7	1	(0.5)	1	0.5
停留精巣	0				1	(0.8)	1	0.7	1	(0.5)	1	0.5

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
MedDRA version 24.1.

4172 試験では、稀な事象の発現は少なく、ノルディトロピン/ソマプシタン群で「非アルコール性脂肪性肝疾患」が 1 件、ノルディトロピン群で「ネフローゼ症候群」が 1 件報告された〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.104〕。この 2 件の詳細を表 2.7.4.2-33 に示す。ソマプシタン群で認められた「アナフィラキシー反応」及び「アナフィラキシーショック」各 1 件を 2.7.4.2.5.6.2 に、「心電図 QT 延長」1 件を 2.7.4.2.5.9.3 に記載する。ソマプシタン群では、稀な事象として「眼瞼腫脹」1 件（2.7.4.2.5.5.1 の安全性併合データに含まれる）及び「血小板減少症」も報告された。

表 2.7.4.2-33　稀な有害事象別の詳細（4172 試験）

Trial product Subject ID	Sex/Age/ BMI	AE Preferred term	Trial day/ Phase/ Duration (days)	Severity/ Causality Norditropin/ somapacitan	SAE	Recovered (yes/no)	Action taken/ comments
Norditropin 0.034 mg/kg/day/ Somapacitan 0.16 mg/kg/week [redacted]004	M/[redacted].5/18.6	非アルコール性脂肪性肝疾患	1098/ Long-term safety ext/ 53	Moderate/ Possible/ Unlikely	No	Yes	Reported at 156 weeks which was end of Norditropin treatment. There was no confirmation of the diagnosis by a liver biopsy.
Norditropin 0.034 mg/kg/day [redacted]002	M/[redacted].1/15.6	ネフローゼ症候群	366/Ext	Moderate/ Unlikely/ Not applicable	Yes	No	Drug withdrawn

Notes: Age in years.
Abbreviations: M: male; BMI: body mass index (kg/m^2) at baseline. AE: adverse event; SAE: serious adverse event.

安全性併合データの稀な事象の要約を付録 2.7.4.7.1、Table 72 に示す。

2.7.4.2.5.14.2 投薬過誤

4263 試験（主要期間）で認められた投薬過誤を表 2.7.4.2-34 に要約する。

52 週間の試験期間中に投薬過誤が 5 件報告された。ソマプシタン群の 1 例（被験者 ID：[redacted]002）及びノルディトロピン群の 2 例（被験者 ID：[redacted]001 及び[redacted]001）で「偶発的過量投与」が報告された。投薬過誤による有害事象の報告はなかった〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.21〕。

表 2.7.4.2-34　投与過誤の要約（器官別大分類別及び基本語別）（4263 試験、主要期間）

	Norditropin			somapacitan		
	N (%)	E	R	N (%)	E	R
Number of subjects	68			132		
Total patient years at risk	69.1			133.4		
傷害、中毒および処置合併症	3 (4.4)	3	4.3	2 (1.5)	2	1.5
偶発的過量投与	2 (2.9)	2	2.9	1 (0.8)	1	0.7
偶発的過少量投与	0			1 (0.8)	1	0.7
投薬過誤	1 (1.5)	1	1.4	0		

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage
MedDRA version 24.1.

4172 試験では投薬過誤の報告はなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.106 及び 14.3.1.107〕。

安全性併合データで投薬過誤を報告した被験者の割合（ソマプシタン群 1.0%、ノルディトロピン群 3.7%）を付録 2.7.4.7.1、Table 73 に示す。

2.7.4.2.5.14.3 乱用又は誤用

4263 試験（主要期間）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.53〕及び 4172 試験〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.108 及び 14.3.1.109〕では乱用又は誤用の報告はなかった。したがって、安全性併合データでもみられていない（付録 2.7.4.7.1、Table 74）。

2.7.4.2.5.14.4 過量投与

4263 試験（主要期間）では「偶発的過量投与」が 3 件報告された（ソマプシタン群 1 件、ノルディトロピン群 2 件）（表 2.7.4.2-34 参照）。

4172 試験では「偶発的過量投与」の報告はなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.110 及び 14.3.1.111〕。

安全性併合データで「偶発的過量投与」を報告した被験者の割合（ソマプシタン群 0.5%、ノルディトロピン群 2.4%）を付録 2.7.4.7.1、Table 75 に示す。

2.7.4.2.5.14.5 製品を介する感染因子の伝播の疑い

4263 試験（主要期間）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.55〕及び 4172 試験〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.112 及び 14.3.1.113〕の 2 つの試験では、製品を介する感染因子の伝播の疑いの報告はなかった。したがって、安全性併合データでもみられていない（付録 2.7.4.7.1、Table 76）。

2.7.4.2.5.15　連続 2 回以上の来院で IGF-I SD スコアが+2 超となった被験者における有害事象

4263 試験（主要期間）では、IGF-I SD スコアの平均はいずれの群でも 52 週まで+2 を超えなかった。IGF-I SD スコアの平均については、Module 2.7.3.3.2.2.1、図 2.7.3.3-5 に示す。

連続 2 回以上の来院で IGF-I SD スコアが+2 超となった被験者では（ソマプシタン群 5 例、3.8%、ノルディトロピン群 2 例、2.9%）、それぞれの群のその他の被験者と比較して、報告された有害事象の発現頻度又は種類に特定の傾向はみられなかった〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.23〕。連続 2 回以上の来院で IGF-I SD スコアが+2 超となった被験者 7 例では、重篤な有害事象は認められず（2.7.4.3.3.2.1）、用量の減量に至った有害事象も認められなかった。個々の有害事象の詳細は治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.12〕に示す。

4172 試験では、IGF-I SD スコアの平均はいずれの群でも 208 週まで+2 を超えなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Section 11.3.4〕。

連続 2 回以上の来院で IGF-I SD スコアが+2 超となった被験者では、それぞれの群のその他の被験者と比較して、報告された有害事象の発現頻度又は種類に特定の傾向はみられなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.6（ノルディトロピン）及び 14.3.1.7（ソマプシタン）及び Appendix 16.2.7、Listing 16.2.7.23〕。コホート II 及び III では IGF-I SD スコアが+2 超となった被験者はいなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.8 及び 14.3.1.9〕。

2.7.4.2.6　Adverse drug reaction

ノボ ノルディスク社は集積したデータに基づき、すべての有害事象とソマプシタンとの潜在的な因果関係を評価した。ソマプシタンの企業中核データシート（CCDS）に記載予定の adverse drug reaction の評価は、その生物学的妥当性及び詳細な医学的評価等に基づいて行った。

CCDS に提示する、小児 GHD 患者において特定されたソマプシタンの adverse drug reaction を表 2.7.4.2-35 に示す。Adverse drug reaction は、進行中の主要な第 3 相試験（4263 試験、52 週間の主要期間）で収集された安全性データ及び hGH 製剤のクラスエフェクトと考えられる adverse drug reaction に基づく。主要な第 3 相試験の発現頻度に基づき、adverse drug reaction の発現頻度を算出した。概して、adverse drug reaction は非重篤であり、軽度であった。

Adverse drug reaction を発現頻度が極めて高頻度（Very common、10%以上）、高頻度（Common、1%以上 10%未満）、低頻度（Uncommon、0.1%以上 1%未満）、まれ（0.01%以上 0.1%未満）、及び極めてまれ（0.01%未満）で分類し、MedDRA 器官別大分類別に一覧で示した。

表 2.7.4.2-35　CCDS に提示する、ソマプシタンの adverse drug reaction（小児 GHD 患者）

MedDRA System organ class	Very common (≥1/10)	Common (≥1/100 to <1/10)
内分泌障害		甲状腺機能低下症 副腎皮質機能不全
代謝および栄養障害		高血糖
神経系障害	頭痛	
筋骨格系および結合組織障害		関節痛
一般・全身障害および投与部位の状態		末梢性浮腫 注射部位反応 疲労

Notes: There were no uncommon, rare, or very rare ADRs for somapacitan in children with GHD.

2.7.4.2.7　4263 試験の安全性延長期間（104 週）の有害事象の評価

4263 試験での 104 週までの安全性データが得られた。全体として、104 週までのソマプシタンの安全性プロファイルは 1 日 1 回投与の hGH 製剤のよく知られた安全性プロファイルと同様であった。新規の安全性又は局所忍容性に関する所見は認められなかった。得られたデータから、0 週からソマプシタンの投与を受けていた被験者と 52 週でノルディトロピンからソマプシタンに切り替えた被験者間で安全性パラメータについて違いは認められなかった。

104 週間を通じてソマプシタンを投与した被験者（ソマプシタン/ソマプシタン群）の有害事象の単位時間あたりの発現件数は 206.9 件／100 人・年であった。大部分の有害事象（104 週までのソマプシタン/ソマプシタン群で 98.5%）は、軽度又は中等度に分類された。52 週間の主要期間において、有害事象の単位時間あたりの発現件数は、ソマプシタン群とノルディトロピン群で概ね同様であった。ソマプシタン/ソマプシタン群及び 52 週でノルディトロピンからソマプシタン投与に切り替えた被験者のいずれにおいても、有害事象の単位時間あたりの発現件数は 1 年目と比較して 2 年目（52～104 週）で少なかった（表 2.7.4.2-36）。

最も高頻度で報告された有害事象〔ソマプシタン/ソマプシタン群（0～104 週）で 5%以上〕は、「上咽頭炎」、「頭痛」、「四肢痛」及び「発熱」（有害事象を発現した被験者の割合順）を含む、小児でよくみられる事象であった〔治験総括報告書、4263 試験（104 週）Table 14.3.1.7〕。ソマプシタン/ソマプシタン群（0～104 週）で最も高頻度で報告された治験薬との因果関係が「可能性あり」又は「あり」と判定された有害事象（2%以上）は、「頭痛」、「四肢痛」、「嘔吐」及び「注射部位内出血」であった〔治験総括報告書、4263 試験（104 週）Table 14.3.1.15〕。治験薬との因果関係が「可能性あり」又は「あり」と判定されたその他のすべての有害事象は、1～2 例の被験者で報告され、異なる器官別大分類及び基本語にわたって報告された。

104 週までに死亡の報告はなかった。

ソマプシタン/ソマプシタン群では、104 週までに 9 例 12 件の重篤な有害事象が報告された（0～52 週では 6 例 8 件、52～104 週では 3 例 4 件）。ソマプシタン/ソマプシタン群で 52～104 週に報告された

重篤な有害事象は、「気管支炎」、「COVID-19」、「胃腸炎」及び「インフルエンザ」であった。ノルディトロピン/ソマプシタン群では、52～104 週で重篤な有害事象の報告はなかった。すべての重篤な有害事象の転帰は回復であり、治験責任医師により治験薬との因果関係は「なし」と判定された〔治験総括報告書、4263 試験（104 週）（M 5.3.5.1）Section 12.2.2〕。0～52 週に報告された重篤な有害事象は 2.7.4.2.3.1 に示す。

有害事象により治験薬投与の中止に至った被験者はいなかった。有害事象又は連続 2 回以上の来院で IGF-I SD スコアが+2.5 超となった場合、治験薬の用量減量が可能であった〔治験総括報告書、4263 試験（104 週）（M 5.3.5.1）Section 12.3.3 及び 12.3.5〕。52 週間の主要期間において、ソマプシタン群の 1 例（被験者 ID：[redacted]002）及びノルディトロピン群の 2 例（被験者 ID：[redacted]001 及び[redacted]001）が、有害事象により治験薬の用量減量に至った（2.7.4.2.4.2.1）。主要期間で治験薬の用量減量に至ったソマプシタン群の 1 例の被験者（被験者 ID：[redacted]002）では、52～104 週の間に治験薬の用量が再度減量された。この被験者で用量減量に至った 2 件の有害事象は、軽度の「空腹時血中ブドウ糖不良」2 件〔369 日（主要期間）に発現（転帰：回復）及び 638 日（延長期間）に発現（転帰：未回復）〕であった。この被験者で報告されたその他の有害事象は、「頭痛」及び「貧血」であった。0～104 週間で連続 2 回以上の来院で IGF-I SD スコアが+2.5 超となったために治験薬の用量減量に至った被験者は 3 例であった〔ソマプシタン/ソマプシタン群の 2 例の被験者及びノルディトロピン/ソマプシタン群の 1 例の被験者（ノルディトロピン投与中）〕。この 3 例において、IGF-I SD スコアが+2.5 超となったことに関連する安全性の問題は認められなかった。

104 週間で、連続 2 回以上の来院で IGF-I SD スコアが+2 超となった被験者では、それぞれの群のその他の被験者と比較して、報告された有害事象の発現頻度又は種類に特定の傾向はみられなかった。これらの被験者のうち、有害事象により治験薬の用量減量に至った被験者はいなかった〔治験総括報告書、4263 試験（104 週）（M 5.3.5.1）Section 12.3.5〕。

104 週間で、注射部位反応の発現頻度は両群とも低かった〔治験総括報告書、4263 試験（104 週）（M 5.3.5.1）Table 14.3.1.35〕。

安全性延長期間において、糖代謝障害に関連する有害事象を報告した被験者の割合は低かった（ソマプシタン/ソマプシタン群：0.8%、ノルディトロピン/ソマプシタン群：1.5%）。いずれの群においても、2 型糖尿病と診断された小児はいなかった〔治験総括報告書、4263 試験（104 週）（M 5.3.5.1）Table 14.3.1.41〕。

104 週までのソマプシタンの安全性プロファイルは、日本人小児 GHD 患者及び全集団で同様であった。詳細は M 5.3.5.4 に示す。

4263 試験の 104 週までの有害事象のさらなる詳細は治験総括報告書に示す〔4263 試験（104 週）（M 5.3.5.1）〕。

表 2.7.4.2-36　有害事象の概要〔On-treatment 観察期間、安全性解析対象集団、4263 試験、安全性延長期間（104 週まで）〕

	somapacitan week 0-52			Norditropin week 0-52			somapacitan/ somapacitan week 52-104			Norditropin/ somapacitan week 52-104			somapacitan/ somapacitan week 0-104		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	132			68			131			68			132		
Total patient years at risk (on treatment)	133.4			69.1			126.1			67.1			259.5		
All adverse events (on treatment)	96	(72.7)	327 245.0	41	(60.3)	150 217.1	82	(62.6)	210 166.6	39	(57.4)	84 125.3	114	(86.4)	537 206.9
Serious adverse events															
Yes (on treatment)	6	(4.5)	8 6.0	2	(2.9)	3 4.3	3	(2.3)	4 3.2	0			9	(6.8)	12 4.6
No (on treatment)	95	(72.0)	319 239.0	41	(60.3)	147 212.8	82	(62.6)	206 163.4	39	(57.4)	84 125.3	113	(85.6)	525 202.3
Severity															
Mild (on treatment)	89	(67.4)	270 202.3	35	(51.5)	122 176.6	77	(58.8)	174 138.0	34	(50.0)	64 95.4	108	(81.8)	444 171.1
Moderate (on treatment)	27	(20.5)	50 37.5	12	(17.6)	27 39.1	23	(17.6)	35 27.8	9	(13.2)	18 26.8	42	(31.8)	85 32.8
Severe (on treatment)	4	(3.0)	7 5.2	1	(1.5)	1 1.4	1	(0.8)	1 0.8	2	(2.9)	2 3.0	5	(3.8)	8 3.1
Causality (Norditropin)															
Probable (on treatment)	0			4	(5.9)	5 7.2	0			1	(1.5)	1 1.5	0		
Possible (on treatment)	0			9	(13.2)	21 30.4	0			4	(5.9)	4 6.0	0		
Unlikely (on treatment)	3	(2.3)	10 7.5	38	(55.9)	124 179.5	10	(7.6)	15 11.9	32	(47.1)	66 98.4	12	(9.1)	25 9.6
Missing (on treatment)	95	(72.0)	317 237.5	0			79	(60.3)	195 154.7	8	(11.8)	13 19.4	113	(85.6)	512 197.3
Causality (somapacitan)															
Probable (on treatment)	12	(9.1)	17 12.7	0			6	(4.6)	11 8.7	1	(1.5)	1 1.5	16	(12.1)	28 10.8
Possible (on treatment)	22	(16.7)	47 35.2	0			6	(4.6)	8 6.3	9	(13.2)	12 17.9	23	(17.4)	55 21.2
Unlikely (on treatment)	91	(68.9)	263 197.1	0			81	(61.8)	191 151.5	38	(55.9)	71 105.9	112	(84.8)	454 174.9
Missing (on treatment)	0			41	(60.3)	150 217.1	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
AE causality is based on judgement of investigators.
On treatment: Measurement after first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until week 104 or 14 days after last trial drug administration, whichever comes first, for all other subjects.

Summary of adverse events - overview - safety analysis set

	somapacitan week 0-52			Norditropin week 0-52			somapacitan/ somapacitan week 52-104			Norditropin/ somapacitan week 52-104			somapacitan/ somapacitan week 0-104		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Action taken to trial product due to AE (Norditropin)															
Drug interrupted (on treatment)	0			5	(7.4)	5 7.2	0			0			0		
Drug withdrawn (on treatment)	0			0			0			0			0		
Dose reduced (on treatment)	0			2	(2.9)	6 8.7	0			0			0		
Dose increased (on treatment)	0			0			0			0			0		
Dose not changed (on treatment)	0			40	(58.8)	137 198.3	4	(3.1)	5 4.0	1	(1.5)	1 1.5	4	(3.0)	5 1.9
Not applicable (on treatment)	4	(3.0)	11 8.2	1	(1.5)	2 2.9	9	(6.9)	13 10.3	33	(48.5)	70 104.4	12	(9.1)	24 9.2
Unknown (on treatment)	0			0			0			0			0		
Missing (on treatment)	95	(72.0)	316 236.8	0			78	(59.5)	192 152.3	8	(11.8)	13 19.4	112	(84.8)	508 195.7
Action taken to trial product due to AE (somapacitan)															
Drug interrupted (on treatment)	2	(1.5)	2 1.5	0			2	(1.5)	2 1.6	0			4	(3.0)	4 1.5
Drug withdrawn (on treatment)	0			0			0			0			0		
Dose reduced (on treatment)	1	(0.8)	1 0.7	0			1	(0.8)	1 0.8	0			1	(0.8)	2 0.8
Dose increased (on treatment)	1	(0.8)	1 0.7	0			1	(0.8)	1 0.8	1	(1.5)	1 1.5	2	(1.5)	2 0.8
Dose not changed (on treatment)	94	(71.2)	321 240.5	0			82	(62.6)	203 161.0	38	(55.9)	81 120.8	112	(84.8)	524 201.9
Not applicable (on treatment)	0			0			2	(1.5)	3 2.4	1	(1.5)	2 3.0	2	(1.5)	3 1.2
Unknown (on treatment)	2	(1.5)	2 1.5	0			0			0			2	(1.5)	2 0.8
Missing (on treatment)	0			41	(60.3)	150 217.1	0			0			0		
Outcome															
Recovered/resolved (on treatment)	89	(67.4)	255 191.1	40	(58.8)	135 195.4	73	(55.7)	174 138.0	36	(52.9)	67 99.9	108	(81.8)	429 165.3
Recovering/resolving (on treatment)	6	(4.5)	10 7.5	1	(1.5)	1 1.4	4	(3.1)	4 3.2	2	(2.9)	2 3.0	10	(7.6)	14 5.4
Recovered/resolved with sequelae (on treatment)	1	(0.8)	1 0.7	1	(1.5)	1 1.4	0			1	(1.5)	1 1.5	1	(0.8)	1 0.4
Not recovered/not resolved (on treatment)	33	(25.0)	58 43.5	10	(14.7)	13 18.8	25	(19.1)	32 25.4	10	(14.7)	12 17.9	50	(37.9)	90 34.7
Fatal (on treatment)	0			0			0			0			0		
Unknown (on treatment)	1	(0.8)	3 2.2	0			0			2	(2.9)	2 3.0	1	(0.8)	3 1.2
Missing (on treatment)	0			0			0			0			0		
Treatment discontinuations due to adverse events (on treatment)	0			0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
AE causality is based on judgement of investigators.
On treatment: Measurement after first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until week 104 or 14 days after last trial drug administration, whichever comes first, for all other subjects.

2.7.4.2.8　有害事象の要約

臨床試験に基づくと、ソマプシタン週 1 回投与の安全性プロファイル（小児 GHD 患者に対する 208 週までの皮下投与）は既存の 1 日 1 回投与の hGH 製剤（ノルディトロピン等）の安全性プロファイルと同様であった。臨床的に問題となる安全性又は局所忍容性の所見は認められなかった。報告された有害事象は 1 日 1 回投与の hGH 製剤の臨床試験で認められた有害事象と全体的に同様であり、小児 GHD における hGH 製剤のクラスエフェクトとしてよく知られているものであった（頭痛等）。

ノルディトロピンと比較してソマプシタンにより糖代謝障害のリスクが増大することは示されなかった。4263 試験（主要期間）における高血糖の有害事象の単位時間あたりの発現件数はソマプシタン群（2.2 件/100 人・年）、ノルディトロピン群（4.3 件/100 人・年）のいずれにおいても少なかった。ソマプシタン群又はノルディトロピン群において新たに 2 型糖尿病と診断された被験者はいなかった。

2.7.4.3　臨床検査値の評価

2.7.4.3.1　免疫原性

4263 試験（52 週間の主要期間）及び 4172 試験（208 週まで）の完了部分の免疫原性の評価を以下に要約し、さらなる詳細は Integrated Summary of Immunogenicity（M 5.3.5.3）に示す。

試験期間中のいずれの時点においても、抗ソマプシタン抗体が陽性となった被験者数は少なかった。4263 試験及び 4172 試験のいずれにおいても、抗ソマプシタン抗体は、薬物動態、薬力学的作用、有効性及び有害事象（注射部位反応及びアレルギー反応を含む）の発現に影響を与えることはなかった〔Integrated Summary of Immunogenicity（M 5.3.5.3）Section 4〕。

第 3 相試験（4263 試験、主要期間）の結果

ソマプシタン群の 20 例（15.2%）及びノルディトロピン群の 7 例（10.3%）で、低力価かつ中和作用のない抗体が認められた。ソマプシタン群の 20 例には、ベースラインで抗体陽性であったが、hGH 製剤による治療歴がなかったため偽陽性である可能性が高い 4 例が含まれている。低力価かつ中和作用のない抗体が認められた被験者のうち、ソマプシタン群の 2 例（1.5%）及びノルディトロピン群の 1 例（1.5%）で、少なくとも 2 回連続して抗体が陽性となった。抗ソマプシタン抗体の要約を来院別に表 2.7.4.3-1 に示す。

表 2.7.4.3-1　　抗 GH 抗体の要約（来院別）（安全性解析対象集団、4263 試験、主要期間）

	Norditropin N (%)	somapacitan N (%)
Safety analysis set	68	132
Visit 2 (Week 0)		
N	68 (100.0)	132 (100.0)
Positive antibodies	0	4 (3.0)
Cross reacting	NA	0
Neutralizing	0	0
Visit 4 (Week 13)		
N	64 (100.0)	123 (100.0)
Positive antibodies	5 (7.8)	10 (8.1)
Cross reacting	NA	2 (1.6)
Neutralizing	0	0
Visit 7 (Week 52)		
N	67 (100.0)	132 (100.0)
Positive antibodies	3 (4.5)	8 (6.1)
Cross reacting	NA	4 (3.0)
Neutralizing	0	0
Subjects with a positive antibody sample	7 (10.3)	20 (15.2)
Subjects with two consecutive positive antibody samples	1 (1.5)	2 (1.5)

N: Number of subjects, %: Percentage, NA: Not applicable

Notes: The 4 subjects with positive antibodies at baseline are most likely false positive findings as the subjects were naïve to GH treatment and did not have positive antibodies at the following visit.

抗体に関する個々のデータは治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Listing 14.3.4.3（抗ソマプシタン抗体）及び 14.3.4.2（抗 hGH 抗体）〕に示す。詳細は Antibody Analytical Report〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Appendix 16.2.9〕及び Integrated Summary of Immunogenicity（M 5.3.5.3）に示す。

第 2 相試験（4172 試験、208 週まで）の結果

ソマプシタンを投与した 10 例及びノルディトロピンを投与した 1 例で、低力価かつ中和作用のない抗体が認められた（表 2.7.4.3-2）。このうち、ソマプシタン群 3 例（6.7%）及びノルディトロピン/ソマプシタン群 1 例（7.1%）で、少なくとも 2 回連続して抗体が陽性となった。抗ソマプシタン抗体の来院別の要約を治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Table 14.3.5.61〕に示す。

コホート II 及び III の 10 例の被験者では、抗ソマプシタン抗体が検出された被験者はいなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.5.62〕。10 例のうち 2 例の被験者で、52 週の抗薬物抗体の検体を採取している。

表 2.7.4.3-2　　抗 GH 抗体の要約（安全性解析対象集団、4172 試験）

Cohort I Treatment group.	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week) N (%)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled N (%)
Safety Analysis Set	14	45
Visit 2 (Week 0)		
N	14 (100.0)	45 (100.0)
Positive antibodies	0	0
Cross reacting	NA	0
Neutralizing	0	0
Visit 20 (Week 208)		
N	11 (100.0)	37 (100.0)
Positive antibodies	0	3 (8.1)
Cross reacting	NA	1 (2.7)
Neutralizing	0	0
Subjects with a positive antibody sample	1 (7.1)	10[a] (22.2)
Subjects with two consecutive positive antibody samples	1 (7.1)	3 (6.7)

N: Number of subjects, %: Percentage, NA: Not applicable

[a] Only 9 subjects were positive for anti-somapacitan antibodies in trial 4172 as 1 subject ([redacted]002) only received somapacitan treatment for 3 weeks and was withdrawn from the trial after the first extension (52 weeks). The subject was included in the trial in violation of the inclusion/exclusion criteria. The subject initiated treatment with somatropin after the 3 weeks of treatment with somapacitan. The low titre cross-reacting antibodies measured at week 52 (49 weeks after end of somapacitan treatment) were therefore anti-hGH antibodies.

Notes: Neutralising refers to in vitro neutralising effect against both somapacitan and hGH.
After 156 weeks all children on Norditropin were switched to somapacitan 0.16 mg/kg/week.

抗体に関する個々のデータは治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Listing 14.3.4.4 及び 14.3.4.6（コホート I）ならびに Listing 14.3.4.5（コホート II 及び III）〕に示す。詳細は Antibody Analytical Report〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Appendix 16.2.9〕に示す。

4042 試験では、抗ソマプシタン抗体又は抗 GH 抗体が検出された被験者はいなかった。

免疫原性の詳細については、Integrated summary of immunogenicity（M 5.3.5.3）に示す。

2.7.4.3.2　血糖コントロール

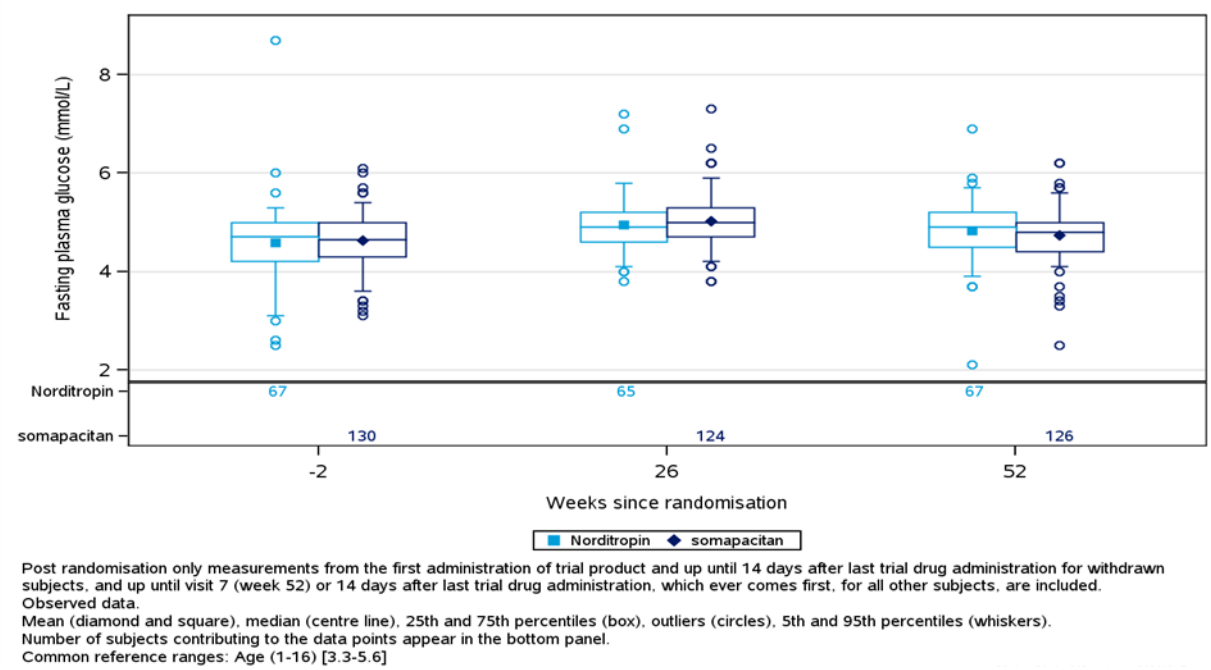
2.7.4.3.2.1 主要な第 3 相試験（4263 試験、主要期間）の結果

空腹時血糖値の平均はいずれの群でも基準範囲内であった。ベースラインから 52 週のソマプシタン投与において、空腹時血糖値及び HbA1c の平均に臨床的に問題となる変化はみられなかった（図 2.7.4.3-1 及び図 2.7.4.3-2）。ノルディトロピン投与後も臨床的に問題となる変化はみられなかった。ベースライン及び 52 週の空腹時血糖値の平均は、いずれの群においても 4.6～5.0 mmol/L の範囲内であった〔治験総括報告書 4263 試験（52 週）（M 5.3.5.1）Table 14.3.5.26〕。ベースライン及び 52 週の HbA1c の平均は、両群で同様であった（52 週：ソマプシタン 5.31%、ノルディトロピン 5.31%）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.5.26〕。

空腹時インスリンの平均は基準範囲内であった（図 2.7.4.3-3 及び治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.5.27）。空腹時インスリンにみられた変化は、hGH 製剤を投与した時に予想される範囲内であり、ソマプシタン群とノルディトロピン群で同様であった（図 2.7.4.3-3）。

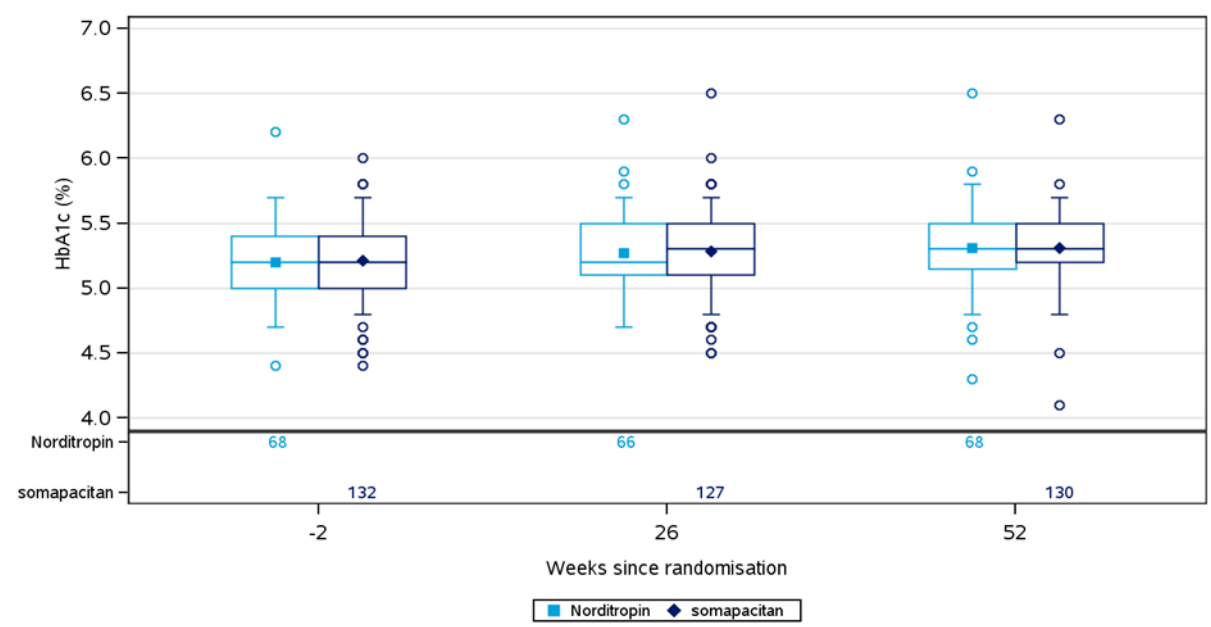
試験期間中、2 型糖尿病と診断された被験者はいなかった。

図 2.7.4.3-1　　空腹時血糖値（mmol/L）の平均（4263 試験、主要期間）



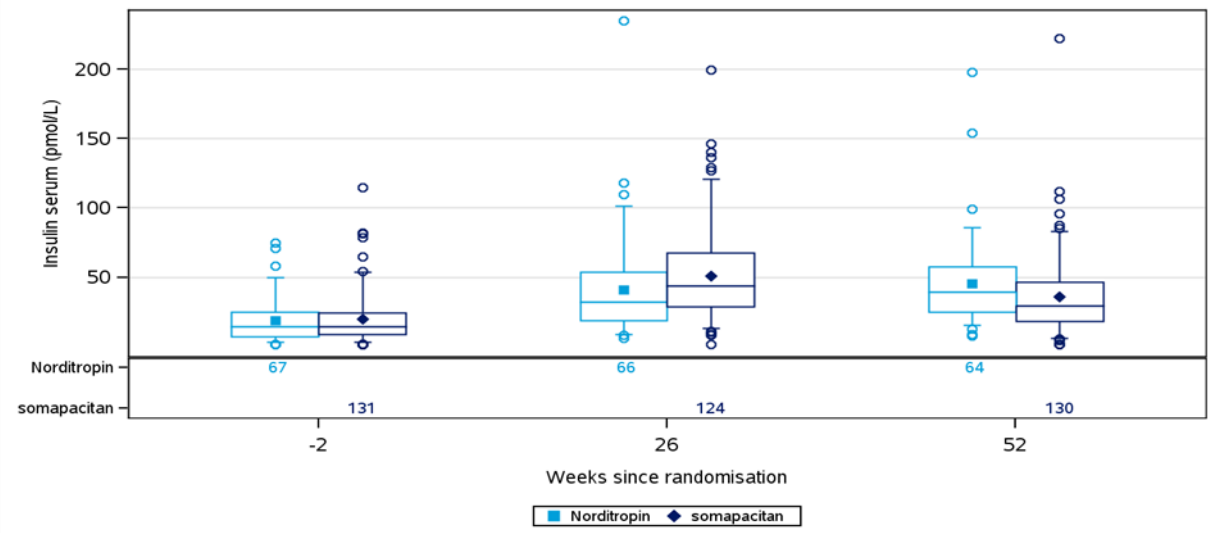
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
Observed data.
Mean (diamond and square), median (centre line), 25th and 75th percentiles (box), outliers (circles), 5th and 95th percentiles (whiskers).
Number of subjects contributing to the data points appear in the bottom panel.
Common reference ranges: Age (1-16) [3.3-5.6]

図 2.7.4.3-2　　HbA1c（%）の平均（4263 試験、主要期間）



Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
Observed data.
Mean (diamond and square), median (centre line), 25th and 75th percentiles (box), outliers (circles), 5th and 95th percentiles (whiskers).
Number of subjects contributing to the data points appear in the bottom panel.
Common reference ranges: Age (0-111) [0-6.4]

図 2.7.4.3-3　　空腹時インスリン（pmol/L）の平均（4263 試験、主要期間）



Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
Observed data.
Mean (diamond and square), median (centre line), 25th and 75th percentiles (box), outliers (circles), 5th and 95th percentiles (whiskers).
Number of subjects contributing to the data points appear in the bottom panel.
Common reference ranges: Age (1-5) [0-262.521]
Male reference ranges: Age (5-18) [11.8065-378.5025]
Female reference ranges: Age (5-18) [11.112-786.8685]

糖代謝パラメータをさらに治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Table 14.3.5.26～14.3.5.28 及び Figure 14.3.5.29～14.3.5.48〕に要約する。

ADA（Diabetes Care vol.39, suppl.1, Jan 2016）の糖尿病診断基準（空腹時血糖値が 7.0 mmol/L 以上又は HbA1c が 6.5%以上）を上回った被験者について、空腹時血糖値及び HbA1c の推移を群別に示す。

ソマプシタン群の 1 例（被験者 ID：[redacted]002）及びノルディトロピン群の 3 例で空腹時血糖値が 7 mmol/L 以上となった（4263 試験、52 週間の主要期間）（付録 2.7.4.7.1、Figure 35 及び 36）。ソマプシタン群の 1 例では、有害事象の発現はなかった〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1〕。

試験期間中、ベースラインを含む 1 回以上の来院でソマプシタン群の 1 例（被験者 ID：[redacted]002）及びノルディトロピン群の 1 例で HbA1c が 6.5%以上となった（付録 2.7.4.7.1、Figure 39 及び 40）。ソマプシタン群の 1 例では、Day 369 に用量の減量に至る軽度の「空腹時血中ブドウ糖不良」が認められた（2.7.4.2.4.2.1）。

糖代謝に関連する有害事象の要約を群別に表 2.7.4.2-28 に示す。

2.7.4.3.2.2 補足的な情報

2.7.4.3.2.2.1 第 2 相試験（4172 試験、208 週まで）の結果

空腹時血糖値、空腹時インスリン又は HbA1c の平均に臨床的に問題となるベースラインからの変化はみられず、ソマプシタン群とノルディトロピン群で同様であった。

208 週の HbA1c の平均（SD）は両群で同様であった〔ソマプシタン 0.04/0.08/0.16 mg/kg/週併合群：5.28（0.29）%、ノルディトロピン/ソマプシタン群：5.46（0.24）%〕。空腹時インスリンのベースラインからの増加は小児 GHD 患者に hGH 製剤を投与した時に予想される範囲内であり、ソマプシタン投与を受けた被験者とノルディトロピン投与を受けた被験者で同様であった。試験期間中、糖尿病と診断された被験者はいなかった。詳細は治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Section 12.4.2〕に示す。

試験期間中、1 回以上の来院でソマプシタン群の 4 例（被験者 ID：[redacted]001、[redacted]005、[redacted]005 及び [redacted]003）で空腹時血糖値が 7.0 mmol/L 以上となったが、208 週にはすべての被験者で空腹時血糖値が基準範囲内に復した（付録 2.7.4.7.1、Listing 32 ならびに Figure 33 及び 34）。試験期間中に HbA1c が 6.5%以上となった被験者はいなかった（付録 2.7.4.7.1、Figure 37 及び 38）。

本試験で報告された血糖値に関連する有害事象は 2.7.4.2.5.10.1 に示す。

2.7.4.3.2.2.2 臨床薬理試験（4042 試験）の結果

試験期間中（単回投与、1 週間）に臨床的に意味のある変化はみられなかった。ソマプシタン投与による空腹時血糖値及び空腹時インスリンに対する明らかな影響がみられたが、hGH 製剤を投与した時に予想される範囲内のものであった。詳細を治験総括報告書〔4042 試験（M 5.3.3.2）Section 12.6.1.2〕に示す。

2.7.4.3.3 その他の血液学的検査及び血液生化学的検査

2.7.4.3.3.1 臨床試験を通じた標準的な血液学的検査及び血液生化学的検査

小児 GHD 患者を対象として評価した血液学的及び血液生化学的パラメータについて、いずれの試験及び群でも、臨床的に問題となるスクリーニング時からの変化はみられなかった。個々の試験の詳細については、各試験の治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）、4172 試験（208 週）（M

5.3.5.1）及び 4042 試験（M 5.3.3.2）〕に示す。なお、治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）〕の血液生化学的検査の表の eGFR の値が、誤りにより提示されていなかったため、修正した表を付録 2.7.4.7.1、Table 78～81 に含めた。eGFR について、臨床的に問題となる変化はみられなかった。

臨床検査項目について、臨床的に問題のある変化は有害事象として報告され、すべての有害事象の要約の器官別大分類「臨床検査」及び「代謝および栄養障害」に含められている〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Table 14.3.1.4、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.10（コホート I）及び 14.3.1.12（コホート II 及び III）〕。したがって、これらの有害事象の評価は 2.7.4.2（有害事象の解析）に含められている。

2.7.4.3.3.2 IGF-I 及び標準化された IGF-I（IGF-I SD スコア）

2.7.4.3.3.2.1 主要な第 3 相試験（4263 試験、主要期間）の結果

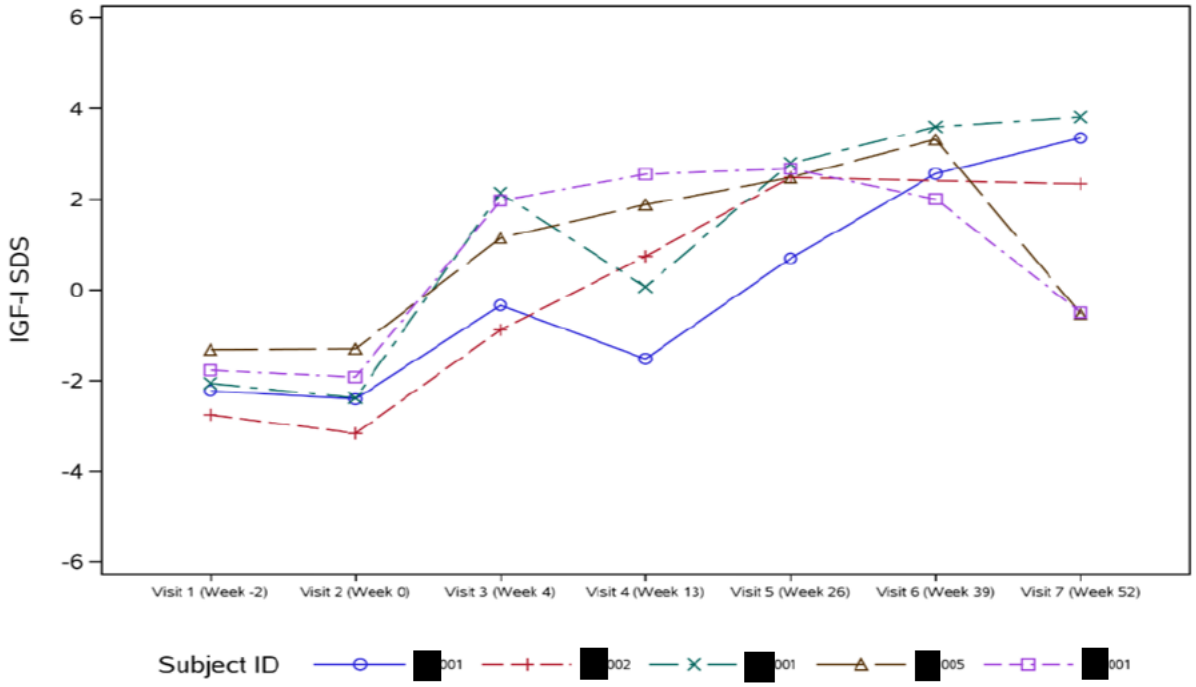
IGF-I SD スコアの平均は 52 週間の投与期間中+2 を下回っており、IGF-I SD スコアはソマプシタン群とノルディトロピン群で同様であった。IGF-I SD スコアの平均の詳細は、Module 2.7.3.3.2.2.1 に示す。

52 週間の投与期間中に、連続 2 回以上の来院で IGF-I SD スコアが+2 超となった被験者について、各被験者における IGF-I SD スコアの推移を群別に示す（図 2.7.4.3-4 及び図 2.7.4.3-5）。

IGF-I SD スコアが+2 超となった被験者はいずれの群でも少なく、これらの被験者における IGF-I SD スコアの推移はソマプシタン群及びノルディトロピン群で同様であった。52 週間の投与期間中、ソマプシタン群では 5 例（3.8%）が連続 2 回以上の来院で IGF-I SD スコアが+2 を超えた（図 2.7.4.3-4）。5 例のうち 3 例では、52 週の IGF-I SD スコアは+2 以下に復したか、わずかに+2 を超えた値であった（被験者 ID [redacted]002：2.33、被験者 ID [redacted]005：-0.53、被験者 ID [redacted]001：-0.50）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Listing 16.2.6.1〕。52 週間の投与期間中、ノルディトロピン群では 2 例（2.9%）が 52 週においても IGF-I SD スコアがわずかに+2 を超えた値となった（図 2.7.4.3-5）。

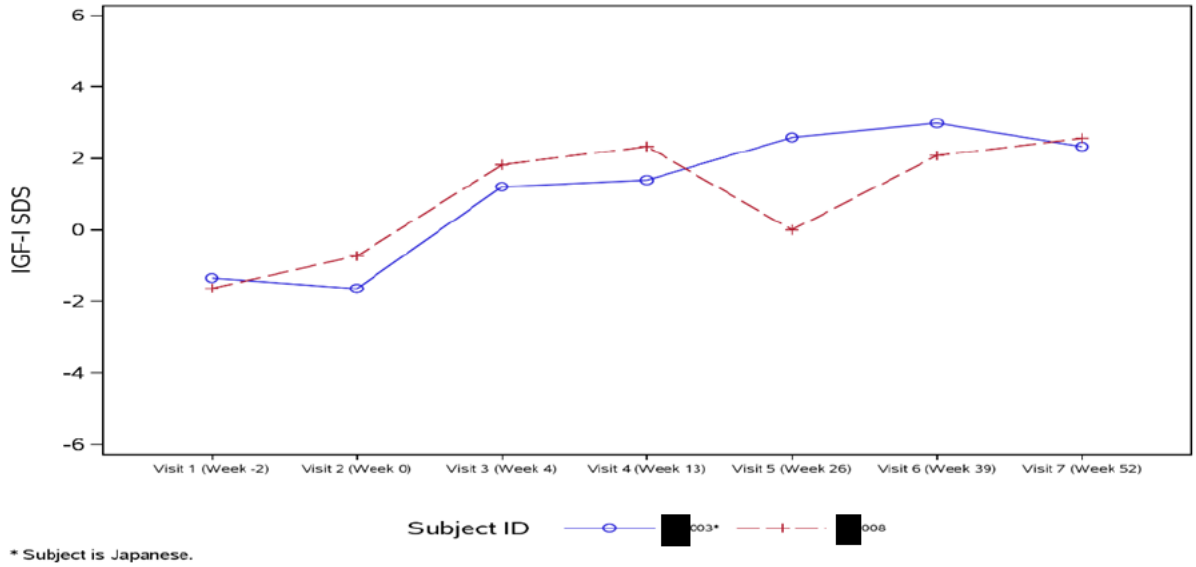
IGF-I 濃度のピーク値が生理的範囲を一時的に超えたことが、安全性への懸念に関連しないことを確認するため、IGF-I SD スコア（ピーク値）が+2 を超えた 7 例の有害事象を評価した（2.7.4.2.5.15 参照）。

図 2.7.4.3-4　　連続 2 回以上の来院で IGF-I SD スコアが+2 超となった被験者（ソマプシタン群）（4263 試験、主要期間）



Notes: Reference range IGF-I SDS from -2 to +2.

図 2.7.4.3-5　　連続 2 回以上の来院で IGF-I SD スコアが+2 超となった被験者（ノルディトロピン群）（4263 試験、主要期間）



* Subject is Japanese.

Notes: Reference range IGF-I SDS from -2 to +2.

各群の 1 例が、連続 2 回の来院で IGF-I SD スコアが+2.5 を超えたため用量を減量した。この 2 例において IGF-I SD スコアが+2.5 超となったことに関連する安全性の懸念は認められなかった。

- 被験者 ID[redacted]001（ソマプシタン群）：52 週間の主要期間中 4 件の有害事象が認められたが、いずれも軽度に分類され、治験薬との因果関係は「なし」と判定された（「SARS-CoV-2 抗体検査陽性」、「筋肉痛」、「紅斑」及び「四肢痛」）〔治験総括報告書、4263 試験（52 週）（M

5.3.5.1）Listing 16.2.7.1〕。IGF-I SD スコア：13 週で 2.54、26 週で 2.67、39 週で 2.00、52 週で-0.50〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Listing 16.2.6.1〕。来院 5 から来院 6 までの間にソマプシタンの投与量を 3.1 mg から 2.3 mg に減量した。来院 6 まで 2.3 mg を維持し、その後来院 7 までに 2.4 mg に増量し、来院 7 以降 2.5 mg に増量した。

- 被験者 ID[redacted]003（ノルディトロピン群）：52 週間の主要期間中 5 件の有害事象が認められたが、いずれも軽度に分類され、治験薬との因果関係は「なし」と判定された（「喘息」2 件及び「上咽頭炎」3 件）〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Listing 16.2.7.1〕。IGF-I SD スコア：26 週で 2.58、39 週で 2.98、52 週で 2.33〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Listing 16.2.6.1〕。来院 6 から来院 7 までの間にノルディトロピンの投与量を 0.5 mg から 0.4 mg に減量し、その後 0.4 mg を維持した。

2.7.4.3.3.2.2 補足的な情報

2.7.4.3.3.2.2.1 第 2 相試験（4172 試験）の結果

IGF-I SD スコアの平均はいずれの群でも 208 週まで+2 を超えなかった。IGF-I SD スコアの平均の詳細は、Module 2.7.3.3.2.2.2 を参照のこと。

208 週間の投与期間中、ソマプシタン投与を受けた被験者では 4 例が連続 2 回以上の来院で IGF-I SD スコアが+2 を超えた（付録 2.7.4.7.1、Figure 42）。4 例のうち 3 例では、208 週の IGF-I SD スコアは+2 以下に復したか、わずかに+2 を超えた値であり（被験者 ID[redacted]003：2.07、被験者 ID[redacted]002：2.19（156 週）、被験者 ID[redacted]003：0.40）、1 例（被験者 ID：[redacted]003）では、208 週の IGF-I SD スコアは 2.7 であった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Listing 16.2.6.5〕。ノルディトロピン及びソマプシタン投与を受けた被験者では 2 例が連続 2 回以上の来院で IGF-I SD スコアが+2 を超えた（付録 2.7.4.7.1、Figure 41）。いずれの被験者においても、208 週の IGF-I SD スコアは+2 以下に復した（被験者 ID[redacted]001：1.40、被験者 ID [redacted]001：0.67）〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Listing 16.2.6.5〕。

連続 2 回以上の来院で IGF-I SD スコアが+2 超となった被験者（コホート I）では、各群のその他の被験者と比較して、報告された有害事象の発現頻度又は種類に特定の傾向はみられなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.6 及び 14.3.1.7〕。連続 2 回以上の来院で IGF-I SD スコアが+2 超となった被験者では、重篤な有害事象又は臨床的に問題となる有害事象は認められず、用量の変更に至った有害事象も認められなかった。被験者別の有害事象の一覧を治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.23〕に示す。

コホート II 又は III では連続 2 回以上の来院で IGF-I SD スコアが+2 超となった被験者はいなかった〔治験総括報告書、4172 試験（208 週）（M 5.3.5.1）Table 14.3.1.8 及び 14.3.1.9〕。

2.7.4.3.3.2.2.2 臨床薬理試験（4042 試験）の結果

4042 試験（単回投与、1 週間）では、用量依存的な IGF-I 反応がみられた。4042 試験の結果の詳細は、総括報告書〔4042 試験（M 5.3.3.2）Section 11.3.1〕に示す。

2.7.4.3.4　4263 試験の安全性延長期間（104 週）の臨床検査値の評価

いずれの群においても、ベースラインから 104 週までの臨床検査について、臨床的に問題となる変化はみられなかった。

52 週間の主要期間で、ソマプシタン投与を受けた被験者の 20 例（15.2%）で抗体が認められた。0～104 週で、ソマプシタン/ソマプシタン群の 25 例（18.9%）で、抗体が認められた（ベースラインで抗体陽性であったが、hGH 製剤による治療歴がなかったため偽陽性である可能性が高い 4 例が含まれている）。これらの被験者のうち 4 例（3.0%）で、少なくとも 2 回連続して抗体が陽性となった。陽性となった被験者で中和活性を有する抗体は認められなかった。

ノルディトロピン/ソマプシタン群では、0～52 週において、7 例（10.3%）で、ノルディトロピンに対する抗体が陽性となった。これらの被験者のうち 1 例（1.5%）で、ノルディトロピン投与中に少なくとも 2 回連続して抗体が陽性となった。52～104 週において、ノルディトロピン/ソマプシタン群の 5 例（7.4%）で、抗ソマプシタン抗体が認められた。これらの被験者のうち 3 例（4.4%）で、ソマプシタン投与中に少なくとも 2 回連続して抗体が陽性となった。なお、ノルディトロピン/ソマプシタン群の 52～104 週のデータは、抗ノルディトロピン抗体がソマプシタンに結合する可能性による交絡があるため注意が必要である。陽性となった被験者で中和活性を有する抗体は認められなかった。

104 週までに、空腹時血糖値及び HbA1c の平均の推移について、投与群間で明らかな違いはなかった。104 週間を通じて、IGF-I SD スコアの平均は基準範囲内（-2～+2）であり、IGF-I SD スコア+2 超と関連する有害事象はみられなかった。

4263 試験の 104 週までの結果に関するさらなる詳細は治験総括報告書に示す〔4263 試験（104 週）（M 5.3.5.1）〕。

2.7.4.3.5　臨床検査値の評価の要約

小児 GHD 患者において、抗薬物抗体産生又はアレルギー／過敏症反応のリスクが、ノルディトロピンと比較してソマプシタンで増大することは示唆されなかった。小児 GHD 患者を対象とした 3 つの完了した臨床試験では、ソマプシタン投与後に抗ソマプシタン中和抗体は認められなかった。

小児 GHD 患者（日本人健康被験者を含む）において、その他の血液学的検査及び血液生化学的検査の値について、臨床的に問題となる変化又は問題となる群間の差はみられなかった。小児 GHD 患者を対象とする完了した臨床試験では、ソマプシタンの投与後に、臨床的に問題となる臨床検査値又は臨床検査値異常はみられなかった（有害事象として報告されたものは除く）。

小児 GHD 患者を対象とした臨床試験では、空腹時血糖値及び HbA1c の平均は基準範囲内であり、臨床的に問題となる明らかな変化はみられなかった。空腹時インスリンの平均は、ほぼ基準範囲内であった（第 3 相試験の結果）。

小児 GHD 患者を対象とした臨床試験において、IGF-I 濃度のピーク値が一時的に生理的範囲を超えた被験者がみられたが、安全性への懸念との関連はなかった。

2.7.4.4　バイタルサイン、身体的所見及び安全性に関連する他の観察項目

2.7.4.4.1　バイタルサイン

試験ごとに群及び来院時期が異なることから、結果を試験別に示す。

2.7.4.4.1.1 主要な第 3 相試験（4263 試験、主要期間）の結果

小児 GHD 患者へのソマプシタン反復投与後にバイタルサイン（収縮期／拡張期血圧及び脈拍数の平均）に臨床的に問題となるベースラインからの変化はみられなかった。バイタルサインの平均は、ソマプシタン群とノルディトロピン群で同様であった。

第 3 相試験では、血圧の軽微な変化が認められた。収縮期／拡張期血圧のベースラインからの変化量の平均（SD）を表 2.7.4.4-1 に要約する。

なお、SD が大きいことに反映されているように、血圧の自然変動（時間の影響、活動レベル、ストレスへの反応等）を考慮する必要がある。

バイタルサインの詳細は、治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Section 12.5.1〕に示す。

表 2.7.4.4-1　　拡張期及び収縮期血圧（mmHg）のベースラインからの変化量（4263 試験、主要期間）

Trial ID	**Trial duration**	**Somapacitan**		**Norditropin**	
	Weeks	Change in systolic blood pressure	Change in diastolic blood pressure	Change in systolic blood pressure	Change in diastolic blood pressure
		Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Trial 4263	52	0.3 (10.9)	0.4 (10.0)	3.9 (10.6)	3.4 (8.4)

2.7.4.4.1.2 補足的な情報

2.7.4.4.1.2.1 第 2 相試験（4172 試験、208 週まで）の結果

4172 試験（208 週まで）では、ソマプシタン投与を受けた被験者で、バイタルサイン（収縮期／拡張期血圧及び脈拍数の平均）に臨床的に問題となるベースラインからの変化はみられなかった。バイタルサインの平均は、ソマプシタン群とノルディトロピン群で同様であった。詳細を治験総括報告書に示す〔4172 試験（208 週）（M 5.3.5.1）Section 12.5.1〕。

2.7.4.4.1.2.2 臨床薬理試験（4042 試験）の結果

4042 試験では、バイタルサインに臨床的に問題となるベースラインからの変化はみられなかった。詳細を治験総括報告書に示す〔4042 試験（M 5.3.3.1）Section 12.7.1〕。

2.7.4.4.2　　体重

2.7.4.4.2.1 第 3 相試験（4263 試験、主要期間）の結果

成長期の小児で予想されるとおり、52 週間の期間中にいずれの群でも体重の着実な増加が認められた〔治験総括報告書、4263 試験（52 週）（M 5.3.5.1）Section 11.3.1〕。体重の変化に関連する有害事象は認められなかった。

2.7.4.4.2.2 補足的な情報

2.7.4.4.2.2.1 第 2 相試験（4172 試験、208 週まで）の結果

成長期の小児で予想されるとおり、すべての群でベースラインから 208 週までに体重の平均の増加がみられた。体重の変化に関連する有害事象は認められなかった。

体重の詳細は、治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Section 11.3.9〕に示す。

2.7.4.4.2.2.2 臨床薬理試験（4042 試験）の結果

体重の平均にはいずれの群でも大きな変化はみられなかった。評価期間が短く（1 週間、単回投与）、各用量群の評価対象の被験者数が少なかったことを考慮する必要がある。

体重の詳細は、治験総括報告書〔4042 試験（M 5.3.3.1）Section 12.7.1〕に示す。

2.7.4.4.3　骨年齢

いずれの試験（4263 試験及び 4172 試験）でも、骨年齢は暦年齢に近づいていた。52 週及び 208 週での各被験者の骨年齢／暦年齢比は、大部分の被験者で 1 を下回っていた。骨年齢のベースラインからの変化量にソマプシタン群とノルディトロピン群で臨床的に意味のある違いはみられなかった。いずれの試験でも骨年齢に関連する有害事象は認められなかった。

骨年齢の詳細は、治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Section 11.2.1.3 及び 4172 試験（208 週）（M 5.3.5.1）Section 11.3.6〕に示す。

2.7.4.4.4　　身体所見

2.7.4.4.4.1 主要な第 3 相試験（4263 試験、主要期間）の結果

スクリーニング時及び試験期間中、「臨床的に問題となる身体所見」として報告された所見を有していた被験者は 15 例であった〔ソマプシタン群 12 例（うち 6 例はスクリーニング時）、ノルディトロピン群 3 例（すべてスクリーニング時）〕。このうちソマプシタン群の 4 つの所見が特に注目すべきものであり〔リンパ節症（有害事象は「発熱」及び「鼻炎」）、発疹（有害事象は「発疹」）、アトピー性皮膚炎（有害事象は「アトピー性皮膚炎」）及び皮膚病変（有害事象は「伝染性軟属腫」）〕、4 件すべてが有害事象として報告された。

身体所見の詳細は、治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Section 12.5.2〕に示す。

2.7.4.4.4.2 補足的な情報

2.7.4.4.4.2.1 第 2 相試験（4172 試験、208 週まで）の結果

すべての群を通じて、「臨床的に問題となる身体所見」として報告された所見は 20 件であった。このうちソマプシタン群の 3 つの所見が特に注目すべきものであり（左大腿部血腫、脂肪組織萎縮症及び皮膚萎縮）、3 件すべてが有害事象として報告された。

身体所見の詳細は、治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Section 12.5.2〕に示す。

2.7.4.4.5　心電図

小児を対象とした臨床試験において、小児 GHD 患者へのソマプシタン投与後に、心電図に臨床的に意味のある変化はみられなかった。

2.7.4.4.5.1 主要な第 3 相試験（4263 試験、主要期間）の結果

治験責任医師により心電図が「異常／臨床的に問題あり」と判定されたものはなかった。すべての心電図が治験責任医師により「正常」又は「異常／臨床的に問題なし」と判定された（スクリーニング時及び 52 週に評価）。治験責任医師の判定による心電図結果のカテゴリー（「正常」、「異常／臨床的に問題なし」又は「異常／臨床的に問題あり」）別の要約を治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Table 12-26〕に示す。

心電図の評価に関する詳細は治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Section 12.5.3〕に示す。

心不整脈作用に関連する有害事象は認められなかった（2.7.4.2.5.9.3）。

2.7.4.4.5.2 補足的な情報

2.7.4.4.5.2.1 第 2 相試験（4172 試験、208 週まで）の結果

4172 試験（208 週まで）では、いずれの群においても心電図に臨床的に問題となる変化はみられず、試験中又は群間で臨床的に意味のある違いはみられなかった。

4172 試験では、ソマプシタン群において 2 件の心不整脈作用に関連する有害事象が発現した（コホート I：「心電図異常」、コホート III：「心電図 QT 延長」）。2.7.4.2.5.9.3 を参照のこと。

心電図の評価の詳細については、治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Section 12.5.3〕に示す。

2.7.4.4.5.2.2 臨床薬理試験（4042 試験）の結果

心電図結果の総合的な評価で「異常／臨床的に問題あり」に分類された結果はなかった〔治験総括報告書、4042 試験（M 5.3.5.1）Listing 14.3.7.5〕。心不整脈作用に関連する有害事象は報告されなかった。

心電図の評価の詳細については、治験総括報告書〔4042 試験（M 5.3.3.2）Section 12.7.3〕に示す。

2.7.4.4.6　二次性徴

2.7.4.4.6.1 主要な第 3 相試験（4263 試験、主要期間）の結果

二次性徴発来の有無を来院別に治験総括報告書〔4263 試験（52 週）（M 5.3.5.1）Table 14.2.110〕に要約する。大部分の被験者は試験期間を通して Tanner stage 1 であり、52 週間の間にほとんど変化はみられなかった。

2.7.4.4.6.2 補足的な情報

2.7.4.4.6.2.1 第 2 相試験（4172 試験）の結果

コホート I で無作為割り付けされた被験者ならびにコホート II 及び III のすべての被験者の Tanner stage を来院別に治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Appendix 16.2.4、Listing 16.2.4.9〕に示す。大部分の被験者は 208 週間を通じて Tanner stage 1 であった。

2.7.4.4.7　4263 試験の安全性延長期間（104 週）のバイタルサイン、身体的所見及び安全性に関連する他の観察項目の評価

いずれの群においても、ベースラインから 104 週までの身体所見、バイタルサイン及び心電図について、臨床的に問題となる変化はみられなかった。

4263 試験の 104 週までの結果に関するさらなる詳細は治験総括報告書に示す〔4263 試験（104 週）（M 5.3.5.1）〕。

2.7.4.4.8　バイタルサイン、身体的所見及び安全性に関連する他の観察項目の要約

小児を対象とした臨床試験において、小児 GHD 患者へのソマプシタン反復投与後に、バイタルサイン（収縮期／拡張期血圧及び脈拍数の平均）に臨床的に意味のあるベースラインからの変化はみられなかった。バイタルサインの平均は、ソマプシタン群とノルディトロピン群で同様であった。

成長期の小児で予想されるとおり、すべての群で体重の平均の増加がみられた。

小児を対象とした臨床試験において、小児 GHD 患者へのソマプシタン投与後に、心電図に臨床的に意味のある変化はみられなかった。

2.7.4.5　特別な患者集団及び状況下における安全性

2.7.4.5.1　内因性民族的要因

2.7.4.5.1.1 男女別の安全性（第 3 相試験、4263 試験）

ソマプシタンの安全性は、性別に関わらず一貫していると考えられた（表 2.7.4.5-1）。男女別の結果は、国際共同第 3 相試験（4263 試験、主要期間）と同様であった。国際共同第 3 相試験に基づく男女別の有害事象のプロファイルに特記すべき安全性の懸念は認められなかった。男女別の有害事象の概要及び有害事象の要約表を付録 2.7.4.7.1、Table 24～27 に示す。

2.7.4.5.1.2 年齢群別の安全性（第 3 相試験、4263 試験）

ソマプシタンの安全性は、すべての年齢群で一貫していると考えられた（表 2.7.4.5-2）。年齢群別の結果は、国際共同第 3 相試験（4263 試験、主要期間）と同様であった。国際共同第 3 相試験に基づく年齢群別の有害事象のプロファイルに特記すべき安全性の懸念は認められなかった。年齢群別（6 歳未満及び 6 歳以上）の有害事象の概要及び有害事象の要約表を付録 2.7.4.7.1、Table 28～31 に示す。

表 2.7.4.5-1　男女別の有害事象の概要（第 3 相試験、4263 試験、主要期間）

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Male									
Number of subjects	50			99			149		
Total patient years at risk	50.8			99.9			150.7		
All adverse events	26	(52.0)	94 184.9	69	(69.7)	224 224.3	95	(63.8)	318 211.0
Serious adverse events	0			5	(5.1)	7 7.0	5	(3.4)	7 4.6
Causality									
Probable	3	(6.0)	4 7.9	9	(9.1)	13 13.0	12	(8.1)	17 11.3
Possible	5	(10.0)	12 23.6	11	(11.1)	23 23.0	16	(10.7)	35 23.2
Treatment discont due to AEs	0			0			0		
Female									
Number of subjects	18			33			51		
Total patient years at risk	18.3			33.6			51.9		
All adverse events	15	(83.3)	53 290.3	25	(75.8)	86 256.0	40	(78.4)	139 268.1
Serious adverse events	2	(11.1)	3 16.4	1	(3.0)	1 3.0	3	(5.9)	4 7.7
Causality									
Probable	1	(5.6)	1 5.5	3	(9.1)	3 8.9	4	(7.8)	4 7.7
Possible	4	(22.2)	9 49.3	9	(27.3)	22 65.5	13	(25.5)	31 59.8
Treatment discont due to AEs	0			0			0		

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage, AE: Adverse event
AE causality is based on judgement of investigators.

表 2.7.4.5-2　年齢群別の有害事象の概要（第 3 相試験、4263 試験、主要期間）

	Norditropin			somapacitan			Total		
	N	(%)	E　R	N	(%)	E　R	N	(%)	E　R
Age < 6 yrs									
Number of subjects	33			64			97		
Total patient years at risk	33.5			64.1			97.5		
All adverse events	20	(60.6)	80　239.2	46	(71.9)	181　282.4	66	(68.0)	261　267.6
Serious adverse events	1	(3.0)	2　6.0	3	(4.7)	4　6.2	4	(4.1)	6　6.2
Causality									
Probable	0			6	(9.4)	9　14.0	6	(6.2)	9　9.2
Possible	3	(9.1)	4　12.0	14	(21.9)	32　49.9	17	(17.5)	36　36.9
Treatment discont due to AEs	0			0			0		
Age ≥ 6 yrs									
Number of subjects	35			68			103		
Total patient years at risk	35.6			69.4			105.0		
All adverse events	21	(60.0)	67　188.0	48	(70.6)	129　186.0	69	(67.0)	196　186.7
Serious adverse events	1	(2.9)	1　2.8	3	(4.4)	4　5.8	4	(3.9)	5　4.8
Causality									
Probable	4	(11.4)	5　14.0	6	(8.8)	7　10.1	10	(9.7)	12　11.4
Possible	6	(17.1)	17　47.7	6	(8.8)	13　18.7	12	(11.7)	30　28.6
Treatment discont due to AEs	0			0			0		

N: Number of subjects, E: Number of events, R: Event rate per 100 patient years at risk, %: Percentage, AE: Adverse event
AE causality is based on judgement of investigators.

2.7.4.5.1.3 内因性民族的要因が日本人集団と全集団間の安全性に与える影響

4263 試験では、全集団と日本人集団の被験者背景及びベースライン特性の違いの有無について、内因性民族的要因（年齢及び性別）を検討することにより評価した。4263 試験では、被験者背景及びベースライン特性について日本人集団と全集団との間に明らかな違いは認められなかった（Module 2.7.3.3.1.2.1）。

2.7.4.5.2　外因性民族的要因

外因性民族的要因がソマプシタンの安全性プロファイルに与える影響の有無を評価するための解析は行わなかった。

2.7.4.5.2.1 1 日 1 回投与の hGH 製剤から切り替える患者（4172 試験）

1 日 1 回投与のノルディトロピンから週 1 回投与のソマプシタンに切り替えた被験者における安全性（有害事象及び重篤な有害事象）も検討した。この評価は、第 2 相試験である 4172 試験におけるノルディトロピン（0 週から 156 週まで）からソマプシタン（156 週から 208 週まで）に切り替えた被験者の安全性のデータに基づいて行った。

1 日 1 回投与のノルディトロピンから週 1 回投与のソマプシタンに切り替えた被験者の安全性プロファイルは、投与期間を通してノルディトロピン（0～156 週）又はソマプシタンの投与を受けた被験者の安全性プロファイルと同様であった。4172 試験における有害事象の概要（群別）を治験総括報告書〔4172 試験（208 週）（M 5.3.5.1）Table 12-3〕に示す。

2.7.4.5.3　薬物相互作用

臨床的に関連する可能性がある、ソマプシタンの CCDS に提示する薬物相互作用の一覧を表 2.7.4.5-3 に示す。また、糖質コルチコイドと hGH 製剤との相互作用は、表 2.7.4.5-4 に示す CCDS に提示する警告及び使用上の注意としてさらに詳細に示した。

これらの薬物相互作用は、ソマプシタンの薬力学的作用及び薬物動態の特性に基づいており、1 日 1 回投与の hGH 製剤の相互作用としてよく知られているものである。

表 2.7.4.5-3　CCDS に提示した薬物相互作用

Topic	**Descriptive text**
Cytochrome P450 metabolised drugs	Data from an interaction trial performed in AGHD patients suggests that GH administration may increase the clearance of compounds known to be metabolised by cytochrome P450 isoenzymes. The clearance of compounds metabolised by cytochrome P450 3A4 (e.g., sex steroids, corticosteroids, anticonvulsants, and cyclosporine) may be especially increased resulting in lower plasma levels of these compounds. The clinical significance of this is unknown.
Glucocorticoids	GH decreases the conversion of cortisone to cortisol and may unmask previously undiscovered central hypoadrenalism or render low glucocorticoid replacement doses ineffective.
Antihyperglycaemic products	Antihyperglycaemic treatment, including insulin, may require dose adjustment in case of somapacitan co-administration, since somapacitan may decrease insulin sensitivity.

Topic	Descriptive text
Other	The metabolic effects of GH can also be influenced by concomitant treatment with other hormones, e.g., testosterone and thyroid hormones.
In adults	
Oral estrogen replacement	In women on oral estrogen replacement, a higher dose of GH may be required to achieve the treatment goal.

表 2.7.4.5-4　CCDS に提示したソマプシタンの警告及び使用上の注意

Topic	Proposed text
Traceability	In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.
Adrenocortical insufficiency	Patients receiving GH treatment who have or are at risk for pituitary hormone deficiency(s) may be at risk for reduced serum cortisol levels and/or unmasking of central (secondary) hypoadrenalism. In addition, patients treated with glucocorticoid replacement for previously diagnosed hypoadrenalism may require an increase in their maintenance or stress doses following initiation of GH treatment. Monitor patients for reduced serum cortisol levels and/or need for glucocorticoid dose increases in those with known hypoadrenalism.
Thyroid function	GH increases the extrathyroidal conversion of T4 to T3 and may as such unmask incipient hypothyroidism. As hypothyroidism interferes with the response to GH treatment, patients should have their thyroid function tested regularly, and should receive replacement treatment with thyroid hormone when indicated.
Glucose metabolism impairment	Treatment with GH may decrease insulin sensitivity, particularly at higher doses in susceptible patients. Consequently, hyperglycaemia may occur in patients with inadequate insulin secretory capacity. As a result, previously undiagnosed impaired glucose tolerance and overt diabetes mellitus may be unmasked during GH treatment. Therefore, glucose levels should be monitored periodically in all patients treated with GH, especially in those with risk factors for diabetes mellitus, such as obesity, or a family history of diabetes mellitus. Patients with pre-existing type 1 or type 2 diabetes mellitus or impaired glucose tolerance should be monitored closely during GH treatment. The doses of antihyperglycemic drugs (i.e., insulin or oral agents) may require adjustment when GH treatment is instituted in these patients.
Neoplasms	There is no evidence for increased risk of new primary cancers in patients, treated with GH. In patients in complete remission from malignant disease or pituitary tumour, GH treatment has not been associated with an increased relapse rate. Patients who have achieved complete remission of malignant disease or pituitary tumour should be followed closely for relapse after commencement of GH treatment. GH treatment should be interrupted in case of any development or reoccurrence of malignant disease. An overall slight increase in second neoplasms has been observed in childhood cancer survivors treated with GH, with the most frequent being intracranial tumors. The dominant risk factor for second neoplasms seems to be prior exposure to radiation.
Benign intracranial hypertension	In the event of severe or recurrent headache, visual symptoms, nausea, and/or vomiting, a funduscopy for papilloedema is recommended. If papilloedema is confirmed, a diagnosis of benign intracranial hypertension should be considered and if appropriate the GH treatment should be discontinued. At present there is insufficient evidence to guide clinical decision making in patients with resolved intracranial hypertension. If GH treatment is restarted, careful monitoring for symptoms of intracranial hypertension is necessary.
Lipohypertrophy	When somapacitan is administered at the same site over a long period of time, lipohypertrophy may occur. The injection site should be rotated to reduce the risk.
Adults	
Oral oestrogen replacement	Oral oestrogen influences the IGF-I response to GH including somapacitan. Women taking any form of oral oestrogen replacement should consider changing the route of oestrogen administration (e.g., transdermal-, vaginal hormone products). If a woman on oral oestrogen replacement is starting somapacitan treatment, higher starting doses and a longer titration period may be required.

Topic	Proposed text
	If a woman taking somapacitan begins oral oestrogen replacement, the dose of somapacitan may need to be increased to maintain the serum IGF-I levels within the normal age-appropriate range. Conversely, if a woman on somapacitan discontinues oral oestrogen replacement, the dose of somapacitan may need to be reduced to avoid excess of somapacitan and/or undesirable effects.
Long-term treatment	GHD is a lifelong disease and needs to be treated accordingly.

2.7.4.5.4　妊娠及び授乳時の使用

受胎能

ソマプシタンの使用及びソマプシタンが受胎能に与える潜在的な影響に関する臨床経験はない。

雌雄ラットにソマプシタンを投与した際、受胎能に有害な影響はみられなかった。

妊娠

妊娠中のソマプシタンの使用に関する臨床経験はない。

非臨床試験では生殖毒性が示されている。したがって、妊娠中の女性及び避妊法を用いていない妊娠の可能性がある女性には、ソマプシタンの使用は推奨されない。

授乳

ソマプシタン及びその代謝物がヒト母乳中に移行するか否かは不明である。

これまでに得られた動物における薬力学的作用／毒性データからソマプシタンが母乳中に移行することが示されている。授乳された新生児／乳児へのリスクは否定できない。授乳を中止するかソマプシタン投与を中止するかは授乳と治療の有益性を考慮して判断すること。

2.7.4.5.5　過量投与

ソマプシタンの過量投与に関する臨床経験は限られている。

4263 試験のソマプシタン群において 1 件の「偶発的過量投与」が報告された（2.7.4.2.5.14.4 参照）。

2.7.4.5.6　薬物乱用

ソマプシタンの薬物乱用及び依存に関する臨床経験はない。

2.7.4.5.7　離脱症状及び反跳現象

ソマプシタン投与後の離脱症状及び反跳作用の可能性については、ソマプシタンの臨床試験で検討していない。ソマプシタンの作用機序を考慮すると、離脱症状及び反跳作用の可能性はないと考えられる。他の hGH 製剤でもそのような作用はみられていない。

2.7.4.5.8　自動車運転及び機械操作に対する影響又は精神機能の障害

自動車運転及び機械操作に対する影響に関するソマプシタンの臨床経験はない。

2.7.4.5.9　特別な患者集団及び状況下における安全性の要約

小児の部分集団別（年齢群別及び男女別）の有害事象プロファイルに安全性に問題となる特定の所見は認められなかった。

1 日 1 回投与のノルディトロピンから週 1 回投与のソマプシタンに切り替えた被験者の安全性プロファイルは、投与期間を通してノルディトロピン又はソマプシタンの投与を受けた被験者の安全性プロファイルと同様であった。

腎機能障害又は肝機能障害を有する小児におけるソマプシタンの使用に関する臨床経験はない。

ソマプシタンの潜在的な薬物相互作用は、ソマプシタンの薬力学的作用及び薬物動態の特性に基づいており、1 日 1 回投与の hGH 製剤の相互作用としてよく知られているものである。

ソマプシタンの使用及びソマプシタンが受胎能、妊娠及び授乳に与える潜在的な影響に関する臨床経験はない。

特別な状況下（過量投与又は薬物乱用及び依存）におけるソマプシタンの使用に関する臨床経験はない。

2.7.4.6 市販後データ

2.7.4.6.1　　小児 GHD における市販後データ

ソマプシタンは小児患者に対する適応を取得していないため、小児における市販後データは得られていない。

2.7.4.6.2　　AGHD における市販後データ

2022 年 3 月 6 日時点のソマプシタンの市販後における自発報告の集積データによると、2 例 3 件の非重篤な有害事象が認められている（基本語で「異常感」、「血中アルカリホスファターゼ増加」及び「γ－グルタミルトランスフェラーゼ増加」）。転帰は「軽快」と報告されており、ソマプシタンの投与に変更はない。

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ソグルーヤ皮下注 5mg
ソグルーヤ皮下注 10mg
ソグルーヤ皮下注 15mg

成長ホルモン分泌不全性低身長症及び
15 mg 製剤剤形追加

2.7.4.7 付録
1. 解析帳票

ノボ ノルディスク ファーマ株式会社

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Clinical Summary of Safety

1: Summary of adherence (%) - full analysis set

	Norditropin N (%)	somapacitan (0.16mg/kg/week) safety pooled N (%)
Number of subjects	82	194
Number of reported dosings	36448	15622
Number of dosings in adherence	34938	15581
Number of planned dosings	39860	16519
Number of planned dosings until treatment discontinuation**	38085	16239
Adherence according to diary*		
<80%	10 (12.2)	20 (10.3)
80 - 95%	19 (23.2)	26 (13.4)
>95%	53 (64.6)	148 (76.3)
Adherence according to diary until treatment discontinuation**		
<80%	8 (9.8)	17 (8.8)
80 - 95%	19 (23.2)	27 (13.9)
>95%	55 (67.1)	150 (77.3)

N: Number of subjects, %: Percentage
* Number of reported dosings from diary in adherence divided by number of planned dosings multiplied by 100.
** For subjects discontinuing treatment, the planned number of dosings will be counted up until last day on treatment.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.
Dosings in adherence: 4263: All injections recorded between visit 2 and visit 7 in the diary with a dose above 0. A dose for Norditropin® will be counted in adherence if taken at or after 3 pm and before 3 am the following day. A dose of somapacitan will be counted in adherence if taken within 1 day before to 2 days after planned date of dosing. 4172: All injections recorded between visit 2 and visit 20 in the diary with a dose above 0. A dose for Norditropin® will be counted in adherence if taken at or after 3 am and before 3 am the following day. A dose of somapacitan will be counted in adherence if taken within 2 days before or 2 days after planned date of dosing.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:06:20 - tsladhergroupsumfas.sas/tsladhergroupsumfaspool.txt

2: Summary of exposure - safety analysis set

	Norditropin	somapacitan (0.16mg/kg/week) safety pooled
Number of exposed subject	82	194
Days of exposure*		
Mean (SD)	464.32 (255.79)	533.38 (360.98)
Median	369.0	371.0
Min ; Max	45 ; 1196	7 ; 1484
Treatment dose** (mg)		
Mean (SD)	2.79 (1.23)	3.90 (1.26)
Median	2.88	3.80
Min ; Max	0.40 ; 5.20	2.00 ; 9.90
Treatment dose** (mg/kg)		
Mean (SD)	0.03 (0.0007)	0.16 (0.0011)
Median	0.03	0.16
Min ; Max	0.03 ; 0.04	0.16 ; 0.16
Total patient years at risk (on treatment)	104.54	282.75

N: Number of subjects, SD: Standard deviation
*Exposure days in the treatment period are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan or to visit 20 (week 208 for cohort I and week 52 for cohort II and III) for 4172 and for 4263 to visit 7 (week 52), which ever comes first.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.
**Last prescribed dose.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:06:35 - tslexposumsaspool.sas/tslexposumsaspool.txt

3: Subject exposure by 3 month periods - summary - full analysis set

	Norditropin N (%)	somapacitan (0.16mg/kg/week) safety pooled N (%)
Number of Subjects	82	194
Exposure period		
>0 months	82 (100.0)	194 (100.0)
>3 months	81 (98.8)	192 (99.0)
>6 months	81 (98.8)	188 (96.9)
>9 months	81 (98.8)	186 (95.9)
>12 months	81 (98.8)	183 (94.3)
>15 months	11 (13.4)	41 (21.1)
>18 months	11 (13.4)	39 (20.1)
>21 months	11 (13.4)	39 (20.1)

N: Number of subjects, %: Percentage
Month = 30 days.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:06:28 - tslexpo3monthsumsaspool.sas/tslexpo3monthsumsas.txt

4: Summary of demographics - full analysis set

	Norditropin	somapacitan (0.16mg/kg/week) safety pooled	Total
Number of subjects	82	194	265
Age group			
N	82 (100.0)	194 (100.0)	265 (100.0)
<6 years	40 (48.8)	94 (48.5)	129 (48.7)
>=6 years	42 (51.2)	100 (51.5)	136 (51.3)
Sex			
N	82 (100.0)	194 (100.0)	265 (100.0)
Female	23 (28.0)	56 (28.9)	75 (28.3)
Male	59 (72.0)	138 (71.1)	190 (71.7)
Country			
N	82 (100.0)	194 (100.0)	265 (100.0)
Austria	0	3 (1.5)	3 (1.1)
Brazil	1 (1.2)	0	1 (0.4)
Canada	0	1 (0.5)	1 (0.4)
France	1 (1.2)	6 (3.1)	7 (2.6)
Germany	2 (2.4)	4 (2.1)	6 (2.3)
India	12 (14.6)	25 (12.9)	34 (12.8)
Israel	1 (1.2)	9 (4.6)	10 (3.8)
Italy	1 (1.2)	3 (1.5)	4 (1.5)
Japan	14 (17.1)	32 (16.5)	44 (16.6)
Korea	4 (4.9)	12 (6.2)	16 (6.0)
Latvia	0	2 (1.0)	2 (0.8)
Poland	1 (1.2)	0	1 (0.4)
Russia	4 (4.9)	17 (8.8)	21 (7.9)
Serbia	2 (2.4)	3 (1.5)	5 (1.9)
Slovenia	1 (1.2)	5 (2.6)	5 (1.9)
Spain	2 (2.4)	0	2 (0.8)
Sweden	0	2 (1.0)	2 (0.8)
Switzerland	1 (1.2)	1 (0.5)	2 (0.8)
Thailand	2 (2.4)	3 (1.5)	5 (1.9)
Turkey	1 (1.2)	1 (0.5)	2 (0.8)
Ukraine	10 (12.2)	15 (7.7)	21 (7.9)
United Kingdom	3 (3.7)	4 (2.1)	7 (2.6)
United States	19 (23.2)	46 (23.7)	64 (24.2)
Ethnicity			

N: Number of subjects, %: Percentage, GHD: Growth hormone deficiency
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

Summary of demographics - full analysis set

	Norditropin	somapacitan (0.16mg/kg/week) safety pooled	Total
N	82 (100.0)	194 (100.0)	265 (100.0)
Hispanic or Latino	1 (1.2)	6 (3.1)	7 (2.6)
Not Hispanic or Latino	77 (93.9)	179 (92.3)	245 (92.5)
Not reported	4 (4.9)	9 (4.6)	13 (4.9)
Race			
N	82 (100.0)	194 (100.0)	265 (100.0)
White	43 (52.4)	111 (57.2)	148 (55.8)
Asian	34 (41.5)	75 (38.7)	104 (39.2)
Black or African American	2 (2.4)	0	2 (0.8)
Other	0	1 (0.5)	1 (0.4)
Not reported	3 (3.7)	7 (3.6)	10 (3.8)
GHD cause			
N	82 (100.0)	194 (100.0)	265 (100.0)
Idiopathic	73 (89.0)	172 (88.7)	235 (88.7)
Organic	9 (11.0)	22 (11.3)	30 (11.3)

N: Number of subjects, %: Percentage, GHD: Growth hormone deficiency
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

5: Summary of baseline characteristics - full analysis set

	Norditropin	somapacitan (0.16mg/kg/week) safety pooled	Total
Number of subjects	82	194	265
Age (yrs)			
N	82	194	265
Mean (SD)	6.33 (2.35)	6.53 (2.65)	6.47 (2.56)
Median	6.15	6.10	6.10
Min ; Max	2.7 ; 11.0	[redacted].5 ; 16.1	[redacted].5 ; 16.1
Height (cm)			
N	82	194	265
Mean (SD)	99.9 (14.7)	102.7 (16.6)	101.9 (16.1)
Median	97.9	100.5	100.1
Min ; Max	58.2 ; 128.6	63.5 ; 182.9	58.2 ; 182.9
Body weight (kg)			
N	82	194	265
Mean (SD)	15.92 (4.94)	17.40 (8.61)	16.96 (7.72)
Median	14.70	15.00	15.00
Min ; Max	5.2 ; 27.4	6.0 ; 81.1	5.2 ; 81.1
BMI (kg/m^2)			
N	82	194	265
Mean (SD)	15.59 (1.38)	15.76 (2.05)	15.71 (1.88)
Median	15.41	15.30	15.35
Min ; Max	12.6 ; 18.8	12.8 ; 30.9	12.6 ; 30.9
GH peak (ug/L)			
N	82	193	264
Mean (SD)	4.08 (2.64)	4.54 (2.50)	4.40 (2.54)
Median	4.10	4.90	4.70
Min ; Max	0.00 ; 9.50	0.03 ; 9.80	0.00 ; 9.80
Mothers height (cm)			
N	77	175	242
Mean (SD)	157.7 (7.38)	158.5 (7.68)	158.3 (7.59)
Median	157.5	158.4	158.0
Min ; Max	140.0 ; 173.8	124.5 ; 180.0	124.5 ; 180.0
Fathers height (cm)			

N: Number of subjects, BMI: Body mass index, GH: Growth hormone, SD: Standard deviation, yrs: Years
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

Summary of baseline characteristics - full analysis set

	Norditropin	somapacitan (0.16mg/kg/week) safety pooled	Total
N	76	175	241
Mean (SD)	170.2 (8.02)	171.1 (8.53)	170.8 (8.37)
Median	170.1	171.0	170.4
Min ; Max	151.7 ; 192.0	135.0 ; 191.0	135.0 ; 192.0

N: Number of subjects, BMI: Body mass index, GH: Growth hormone, SD: Standard deviation, yrs: Years
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

6: Summary of adverse events - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	82			194			265		
Total patient years at risk	104.5			282.7			387.3		
All adverse events	55	(67.1)	243 232.4	142	(73.2)	653 230.9	189	(71.3)	896 231.4
Serious adverse events									
Yes	4	(4.9)	6 5.7	10	(5.2)	14 5.0	14	(5.3)	20 5.2
No	55	(67.1)	237 226.7	141	(72.7)	639 226.0	188	(70.9)	876 226.2
Severity									
Mild	49	(59.8)	204 195.1	132	(68.0)	556 196.6	174	(65.7)	760 196.2
Moderate	17	(20.7)	37 35.4	46	(23.7)	89 31.5	62	(23.4)	126 32.5
Severe	2	(2.4)	2 1.9	5	(2.6)	8 2.8	7	(2.6)	10 2.6
Causality (Norditropin)									
Probable	6	(7.3)	7 6.7	0			6	(2.3)	7 1.8
Possible	11	(13.4)	26 24.9	1	(0.5)	1 0.4	12	(4.5)	27 7.0
Unlikely	52	(63.4)	205 196.1	7	(3.6)	11 3.9	52	(19.6)	216 55.8
Missing	1	(1.2)	5 4.8	134	(69.1)	641 226.7	135	(50.9)	646 166.8
Causality (somapacitan)									
Probable	0			17	(8.8)	31 11.0	17	(6.4)	31 8.0
Possible	0			27	(13.9)	53 18.7	27	(10.2)	53 13.7
Unlikely	1	(1.2)	5 4.8	137	(70.6)	569 201.2	138	(52.1)	574 148.2
Missing	55	(67.1)	238 227.7	0			55	(20.8)	238 61.5
Action taken to trial product due to AE (Norditropin)									
Drug interrupted	7	(8.5)	8 7.7	0			7	(2.6)	8 2.1

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1 , AE: Adverse event, On treatment: Measurement after first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects,and up until visit 20 (week 208 for cohort I and week 52 for cohort II and III) for 4172 and for 4263 until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects.
AE causality is based on judgement of investigators.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

Summary of adverse events - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Drug withdrawn	2	(2.4)	2 1.9	0			2	(0.8)	2 0.5
Dose reduced	2	(2.4)	6 5.7	0			2	(0.8)	6 1.5
Dose increased	0			0			0		
Dose not changed	54	(65.9)	222 212.4	0			54	(20.4)	222 57.3
Unknown	0			0			0		
Not Applicable	0			8	(4.1)	12 4.2	8	(3.0)	12 3.1
Missing	1	(1.2)	5 4.8	134	(69.1)	641 226.7	135	(50.9)	646 166.8
Action taken to trial product due to AE (somapcitan)									
Drug interrupted	0			6	(3.1)	7 2.5	6	(2.3)	7 1.8
Drug withdrawn	0			0			0		
Dose reduced	0			1	(0.5)	1 0.4	1	(0.4)	1 0.3
Dose increased	0			1	(0.5)	1 0.4	1	(0.4)	1 0.3
Dose not changed	1	(1.2)	5 4.8	135	(69.6)	626 221.4	136	(51.3)	631 162.9
Unknown	0			3	(1.5)	3 1.1	3	(1.1)	3 0.8
Not Applicable	0			9	(4.6)	15 5.3	9	(3.4)	15 3.9
Missing	55	(67.1)	238 227.7	0			55	(20.8)	238 61.5
Related to technical complaint (Norditropin)									
Yes	1	(1.2)	1 1.0	0			1	(0.4)	1 0.3
No	55	(67.1)	237 226.7	8	(4.1)	12 4.2	55	(20.8)	249 64.3
Missing	1	(1.2)	5 4.8	134	(69.1)	641 226.7	135	(50.9)	646 166.8
Related to technical complaint (somapacitan)									
Yes	0			1	(0.5)	3 1.1	1	(0.4)	3 0.8
No	1	(1.2)	5 4.8	142	(73.2)	650 229.9	143	(54.0)	655 169.1
Missing	55	(67.1)	238 227.7	0			55	(20.8)	238 61.5
Outcome									
Recovered/resolved	54	(65.9)	213 203.7	133	(68.6)	557 197.0	180	(67.9)	770 198.8

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1 , AE: Adverse event, On treatment: Measurement after first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects,and up until visit 20 (week 208 for cohort I and week 52 for cohort II and III) for 4172 and for 4263 until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects.
AE causality is based on judgement of investigators.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

Summary of adverse events - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Recovering/resolving	1	(1.2)	1 1.0	5	(2.6)	9 3.2	6	(2.3)	10 2.6
Recovered/resolved with sequelae	1	(1.2)	1 1.0	2	(1.0)	2 0.7	3	(1.1)	3 0.8
Not recovered/not resolved	18	(22.0)	28 26.8	51	(26.3)	82 29.0	68	(25.7)	110 28.4
Fatal	0			0			0		
Unknown	0			1	(0.5)	3 1.1	1	(0.4)	3 0.8
Missing	0			0			0		
Treatment (Norditropin)									
Treatment discontinuations due to adverse events	2	(2.4)	2 1.9	0			2	(0.8)	2 0.5
Treatment (somapacitan)									
Treatment discontinuations due to adverse events	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1 , AE: Adverse event, On treatment: Measurement after first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects,and up until visit 20 (week 208 for cohort I and week 52 for cohort II and III) for 4172 and for 4263 until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects.
AE causality is based on judgement of investigators.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

7: Serious adverse events - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	82			194			265		
Total patient years at risk	104.5			282.7			387.3		
All adverse events	4	(4.9)	6 5.7	10	(5.2)	14 5.0	14	(5.3)	20 5.2
Severity									
Mild	1	(1.2)	1 1.0	2	(1.0)	2 0.7	3	(1.1)	3 0.8
Moderate	2	(2.4)	4 3.8	7	(3.6)	10 3.5	9	(3.4)	14 3.6
Severe	1	(1.2)	1 1.0	2	(1.0)	2 0.7	3	(1.1)	3 0.8
Causality (Norditropin)									
Probable	0			0			0		
Possible	0			0			0		
Unlikely	4	(4.9)	6 5.7	0			4	(1.5)	6 1.5
Missing	0			10	(5.2)	14 5.0	10	(3.8)	14 3.6
Causality (somapacitan)									
Probable	0			1	(0.5)	2 0.7	1	(0.4)	2 0.5
Possible	0			0			0		
Unlikely	0			10	(5.2)	12 4.2	10	(3.8)	12 3.1
Missing	4	(4.9)	6 5.7	0			4	(1.5)	6 1.5
Action taken to trial product due to AE (Norditropin)									
Drug interrupted	1	(1.2)	1 1.0	0			1	(0.4)	1 0.3
Drug withdrawn	1	(1.2)	1 1.0	0			1	(0.4)	1 0.3
Dose reduced	0			0			0		
Dose increased	0			0			0		
Dose not changed	3	(3.7)	4 3.8	0			3	(1.1)	4 1.0
Unknown	0			0			0		
Not Applicable	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1 , AE: Adverse event
AE causality is based on judgement of investigators.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

Serious adverse events - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Missing	0			10	(5.2)	14 5.0	10	(3.8)	14 3.6
Action taken to trial product due to AE (somapcitan)									
Drug interrupted	0			3	(1.5)	4 1.4	3	(1.1)	4 1.0
Drug withdrawn	0			0			0		
Dose reduced	0			0			0		
Dose increased	0			0			0		
Dose not changed	0			8	(4.1)	10 3.5	8	(3.0)	10 2.6
Unknown	0			0			0		
Not Applicable	0			0			0		
Missing	4	(4.9)	6 5.7	0			4	(1.5)	6 1.5
Related to technical complaint (Norditropin)									
Yes	0			0			0		
No	4	(4.9)	6 5.7	0			4	(1.5)	6 1.5
Missing	0			10	(5.2)	14 5.0	10	(3.8)	14 3.6
Related to technical complaint (somapacitan)									
Yes	0			0			0		
No	0			10	(5.2)	14 5.0	10	(3.8)	14 3.6
Missing	4	(4.9)	6 5.7	0			4	(1.5)	6 1.5
Outcome									
Recovered/resolved	4	(4.9)	5 4.8	10	(5.2)	14 5.0	14	(5.3)	19 4.9
Recovering/resolving	0			0			0		
Recovered/resolved with sequelae	0			0			0		
Not recovered/not resolved	1	(1.2)	1 1.0	0			1	(0.4)	1 0.3
Fatal	0			0			0		
Unknown	0			0			0		
Missing	0			0			0		
Treatment (Norditropin)									

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1 , AE: Adverse event
AE causality is based on judgement of investigators.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

Serious adverse events - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Treatment discontinuations due to adverse events	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Treatment (somapacitan)												
Treatment discontinuations due to adverse events	0				0				0			

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1 , AE: Adverse event
AE causality is based on judgement of investigators.
The somapacitan (0.16mg/kg/week) safety pooled arm contains all subjects from 4263 and 4172 from the day they receive somapacitan 0.16mg/kg/week.

8: Summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	82			194			265		
Total patient years at risk	104.5			282.7			387.3		
Events	55	(67.1)	243 232.4	142	(73.2)	653 230.9	189	(71.3)	896 231.4
Infections and infestations	38	(46.3)	90 86.1	81	(41.8)	234 82.8	115	(43.4)	324 83.7
Nasopharyngitis	10	(12.2)	25 23.9	23	(11.9)	71 25.1	32	(12.1)	96 24.8
Influenza	5	(6.1)	6 5.7	11	(5.7)	15 5.3	16	(6.0)	21 5.4
Bronchitis	7	(8.5)	8 7.7	7	(3.6)	9 3.2	14	(5.3)	17 4.4
Rhinitis	6	(7.3)	7 6.7	8	(4.1)	10 3.5	14	(5.3)	17 4.4
Respiratory tract infection	4	(4.9)	5 4.8	7	(3.6)	12 4.2	11	(4.2)	17 4.4
Upper respiratory tract infection	3	(3.7)	4 3.8	7	(3.6)	11 3.9	10	(3.8)	15 3.9
Otitis media	3	(3.7)	3 2.9	7	(3.6)	10 3.5	10	(3.8)	13 3.4
Gastroenteritis	3	(3.7)	3 2.9	6	(3.1)	6 2.1	9	(3.4)	9 2.3
COVID-19	3	(3.7)	3 2.9	3	(1.5)	3 1.1	6	(2.3)	6 1.5
Gastroenteritis viral	0			5	(2.6)	8 2.8	5	(1.9)	8 2.1
Viral infection	1	(1.2)	1 1.0	4	(2.1)	6 2.1	5	(1.9)	7 1.8
Otitis media acute	1	(1.2)	1 1.0	4	(2.1)	5 1.8	5	(1.9)	6 1.5
Molluscum contagiosum	3	(3.7)	3 2.9	2	(1.0)	2 0.7	5	(1.9)	5 1.3
Tonsillitis	1	(1.2)	1 1.0	4	(2.1)	4 1.4	5	(1.9)	5 1.3
Ear infection	2	(2.4)	2 1.9	2	(1.0)	2 0.7	4	(1.5)	4 1.0
Tooth abscess	3	(3.7)	3 2.9	1	(0.5)	1 0.4	4	(1.5)	4 1.0
Pharyngitis streptococcal	1	(1.2)	2 1.9	2	(1.0)	5 1.8	3	(1.1)	7 1.8
Pharyngitis	0			3	(1.5)	6 2.1	3	(1.1)	6 1.5
Sinusitis	0			3	(1.5)	4 1.4	3	(1.1)	4 1.0
Impetigo	0			3	(1.5)	3 1.1	3	(1.1)	3 0.8
Paronychia	1	(1.2)	1 1.0	2	(1.0)	2 0.7	3	(1.1)	3 0.8
Varicella	1	(1.2)	1 1.0	2	(1.0)	2 0.7	3	(1.1)	3 0.8
Respiratory tract infection viral	1	(1.2)	3 2.9	2	(1.0)	2 0.7	2	(0.8)	5 1.3
Urinary tract infection	0			2	(1.0)	4 1.4	2	(0.8)	4 1.0
Conjunctivitis	0			2	(1.0)	2 0.7	2	(0.8)	2 0.5

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
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Summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Hand-foot-and-mouth disease	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Hordeolum	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Pneumonia	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Acute sinusitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Bacterial infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Conjunctivitis bacterial	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Cystitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Dermatitis infected	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Dientamoeba infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Enteritis infectious	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Eye infection	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Fungal infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Furuncle	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Gastrointestinal viral infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Herpangina	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Herpes dermatitis	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Infection parasitic	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Laryngitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Latent tuberculosis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Mumps	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Oral herpes	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Otitis externa	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Parotitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Pharyngotonsillitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Respiratory syncytial virus bronchitis	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Scarlet fever	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Streptococcal infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Tinea infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Tonsillitis streptococcal	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Tooth infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Tracheitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
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Summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Upper respiratory tract infection bacterial	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Viral upper respiratory tract infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
General disorders and administration site conditions	14 (17.1)	26	24.9	40 (20.6)	63	22.3	53 (20.0)	89	23.0
Pyrexia	9 (11.0)	17	16.3	24 (12.4)	30	10.6	32 (12.1)	47	12.1
Injection site bruising	2 (2.4)	2	1.9	3 (1.5)	5	1.8	5 (1.9)	7	1.8
Injection site pain	1 (1.2)	1	1.0	3 (1.5)	5	1.8	4 (1.5)	6	1.5
Swelling face	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Fatigue	0			2 (1.0)	4	1.4	2 (0.8)	4	1.0
Injection site haematoma	0			2 (1.0)	4	1.4	2 (0.8)	4	1.0
Pain	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Asthenia	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Chest discomfort	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Face oedema	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Generalised oedema	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Hyperthermia	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Influenza like illness	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Injection site discomfort	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Injection site hypersensitivity	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Injection site reaction	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Injection site swelling	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Local reaction	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Malaise	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Oedema peripheral	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
PFAPA syndrome	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Peripheral swelling	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Swelling	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Gastrointestinal disorders	9 (11.0)	19	18.2	30 (15.5)	71	25.1	39 (14.7)	90	23.2
Vomiting	5 (6.1)	10	9.6	11 (5.7)	15	5.3	16 (6.0)	25	6.5

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Constipation	1 (1.2)	1	1.0	9 (4.6)	12	4.2	10 (3.8)	13	3.4
Diarrhoea	2 (2.4)	3	2.9	6 (3.1)	10	3.5	8 (3.0)	13	3.4
Nausea	1 (1.2)	1	1.0	5 (2.6)	6	2.1	6 (2.3)	7	1.8
Abdominal pain	1 (1.2)	1	1.0	4 (2.1)	5	1.8	5 (1.9)	6	1.5
Abdominal pain upper	1 (1.2)	1	1.0	3 (1.5)	5	1.8	4 (1.5)	6	1.5
Stomatitis	0			2 (1.0)	12	4.2	2 (0.8)	12	3.1
Toothache	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Aphthous ulcer	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Enterocolitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Gastritis	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Gastrooesophageal reflux disease	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Haematochezia	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Umbilical hernia	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Respiratory, thoracic and mediastinal disorders	11 (13.4)	15	14.3	25 (12.9)	37	13.1	36 (13.6)	52	13.4
Cough	4 (4.9)	4	3.8	9 (4.6)	10	3.5	13 (4.9)	14	3.6
Rhinitis allergic	3 (3.7)	3	2.9	6 (3.1)	8	2.8	9 (3.4)	11	2.8
Oropharyngeal pain	1 (1.2)	2	1.9	4 (2.1)	4	1.4	5 (1.9)	6	1.5
Asthma	1 (1.2)	2	1.9	3 (1.5)	4	1.4	4 (1.5)	6	1.5
Adenoidal hypertrophy	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Epistaxis	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Respiratory disorder	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Rhinorrhoea	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Upper respiratory tract inflammation	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Bronchial hyperreactivity	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Nasal congestion	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Pneumonitis	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Tonsillar hypertrophy	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Wheezing	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3

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Summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Skin and subcutaneous tissue disorders	9 (11.0)	11	10.5	28 (14.4)	43	15.2	35 (13.2)	54	13.9
Urticaria	3 (3.7)	3	2.9	2 (1.0)	5	1.8	5 (1.9)	8	2.1
Dermatitis	2 (2.4)	2	1.9	3 (1.5)	3	1.1	5 (1.9)	5	1.3
Rash	1 (1.2)	2	1.9	3 (1.5)	4	1.4	4 (1.5)	6	1.5
Eczema	1 (1.2)	1	1.0	3 (1.5)	4	1.4	4 (1.5)	5	1.3
Dermatitis atopic	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Pruritus	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Miliaria	0			2 (1.0)	4	1.4	2 (0.8)	4	1.0
Erythema	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Skin lesion	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Acanthosis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Alopecia	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Dermatitis allergic	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Dermatosis	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Dry skin	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Eczema asteatotic	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Haemorrhage subcutaneous	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Henoch-Schonlein purpura	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Keratosis pilaris	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Leukoderma	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Lipodystrophy acquired	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Poikiloderma	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Psoriasis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Skin atrophy	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Skin fissures	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Skin hyperpigmentation	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Nervous system disorders	11 (13.4)	21	20.1	23 (11.9)	33	11.7	34 (12.8)	54	13.9
Headache	8 (9.8)	13	12.4	18 (9.3)	26	9.2	26 (9.8)	39	10.1
Dizziness	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Autonomic nervous system imbalance	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3

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Summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

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	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Cognitive disorder	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Disturbance in attention	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Epilepsy	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Febrile convulsion	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Fine motor skill dysfunction	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Intellectual disability	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Migraine	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Nystagmus	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Presyncope	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Somnolence	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Speech disorder	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Speech disorder developmental	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Musculoskeletal and connective tissue disorders	6	(7.3)	11	10.5	26	(13.4)	38	13.4	32	(12.1)	49	12.7
Pain in extremity	3	(3.7)	5	4.8	14	(7.2)	19	6.7	17	(6.4)	24	6.2
Arthralgia	3	(3.7)	3	2.9	4	(2.1)	6	2.1	7	(2.6)	9	2.3
Growing pains	0				4	(2.1)	5	1.8	4	(1.5)	5	1.3
Myalgia	0				3	(1.5)	3	1.1	3	(1.1)	3	0.8
Arthritis reactive	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Foot deformity	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Groin pain	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Hip deformity	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Muscle hypertrophy	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Musculoskeletal stiffness	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Neck pain	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Soft tissue swelling	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Injury, poisoning and procedural complications	4	(4.9)	5	4.8	25	(12.9)	37	13.1	29	(10.9)	42	10.8
Contusion	1	(1.2)	1	1.0	3	(1.5)	5	1.8	4	(1.5)	6	1.5
Accidental overdose	2	(2.4)	2	1.9	1	(0.5)	1	0.4	3	(1.1)	3	0.8
Arthropod sting	0				3	(1.5)	3	1.1	3	(1.1)	3	0.8

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	N (%)	E	R	N (%)	E	R	N (%)	E	R
Skin laceration	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Hand fracture	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Head injury	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Joint dislocation	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Accidental underdose	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Animal bite	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Arthropod bite	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Concussion	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Eye contusion	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Fall	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Foot fracture	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Foreign body	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Heat stroke	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Ligament sprain	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Lip injury	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Lower limb fracture	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Medication error	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Nasal injury	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Procedural pain	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Radius fracture	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Road traffic accident	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Skin abrasion	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Thermal burn	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Upper limb fracture	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Venomous sting	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Investigations	5 (6.1)	8	7.7	15 (7.7)	19	6.7	20 (7.5)	27	7.0
Blood glucose increased	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Blood thyroid stimulating hormone increased	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Cortisol decreased	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Haematology test abnormal	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Low density lipoprotein increased	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5

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	N (%)	E	R	N (%)	E	R	N (%)	E	R
Alanine aminotransferase increased	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Aspartate aminotransferase increased	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Aspiration joint	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Blood cholesterol abnormal	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Blood creatine phosphokinase increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Blood glucose abnormal	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Blood phosphorus increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Electrocardiogram QT prolonged	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Electrocardiogram abnormal	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Glycosylated haemoglobin increased	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Haematocrit increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Haemoglobin increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Platelet count increased	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
SARS-CoV-2 test positive	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Thyroxine decreased	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Thyroxine free decreased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Tri-iodothyronine increased	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Metabolism and nutrition disorders	6 (7.3)	6	5.7	10 (5.2)	12	4.2	16 (6.0)	18	4.6
Hypercholesterolaemia	1 (1.2)	1	1.0	3 (1.5)	3	1.1	4 (1.5)	4	1.0
Hyperglycaemia	2 (2.4)	2	1.9	2 (1.0)	2	0.7	4 (1.5)	4	1.0
Dyslipidaemia	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Impaired fasting glucose	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Dehydration	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Hyperlipidaemia	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Hyperphosphataemia	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Iodine deficiency	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Iron deficiency	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Zinc deficiency	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3

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	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Eye disorders	4	(4.9)	8	7.7	10	(5.2)	12	4.2	14	(5.3)	20	5.2
Conjunctivitis allergic	0				3	(1.5)	3	1.1	3	(1.1)	3	0.8
Strabismus	2	(2.4)	3	2.9	0				2	(0.8)	3	0.8
Eye irritation	0				1	(0.5)	2	0.7	1	(0.4)	2	0.5
Anisometropia	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Dry eye	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Eye pain	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Eye pruritus	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Eyelid cyst	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Hypermetropia	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Myopia	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Optic nerve cupping	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Periorbital oedema	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Swelling of eyelid	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Vision blurred	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Visual impairment	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Blood and lymphatic system disorders	6	(7.3)	6	5.7	7	(3.6)	7	2.5	13	(4.9)	13	3.4
Anaemia	2	(2.4)	2	1.9	3	(1.5)	3	1.1	5	(1.9)	5	1.3
Iron deficiency anaemia	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Lymphadenopathy	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
Eosinophilia	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Hypochromic anaemia	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Monocytosis	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Thrombocytopenia	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Immune system disorders	3	(3.7)	5	4.8	10	(5.2)	11	3.9	12	(4.5)	16	4.1
Seasonal allergy	2	(2.4)	3	2.9	5	(2.6)	6	2.1	6	(2.3)	9	2.3
Food allergy	1	(1.2)	1	1.0	2	(1.0)	2	0.7	3	(1.1)	3	0.8
Allergy to metals	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Anaphylactic reaction	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3

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	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Anaphylactic shock	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Drug hypersensitivity	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Endocrine disorders	2	(2.4)	2	1.9	10	(5.2)	10	3.5	12	(4.5)	12	3.1
Hypothyroidism	1	(1.2)	1	1.0	4	(2.1)	4	1.4	5	(1.9)	5	1.3
Secondary hypothyroidism	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
Adrenal insufficiency	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Adrenocortical insufficiency acute	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Adrenocorticotropic hormone deficiency	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Glucocorticoid deficiency	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Secondary adrenocortical insufficiency	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Psychiatric disorders	3	(3.7)	3	2.9	6	(3.1)	6	2.1	9	(3.4)	9	2.3
Attention deficit hyperactivity disorder	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Tic	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Anxiety	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Enuresis	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Generalised anxiety disorder	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Nightmare	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Sleep disorder	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2	(2.4)	2	1.9	4	(2.1)	4	1.4	6	(2.3)	6	1.5
Skin papilloma	1	(1.2)	1	1.0	3	(1.5)	3	1.1	4	(1.5)	4	1.0
Lipoma	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Lymphangioma	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Ear and labyrinth disorders	1	(1.2)	1	1.0	3	(1.5)	4	1.4	4	(1.5)	5	1.3
Cerumen impaction	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5

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	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Ear pain	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Tinnitus	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Reproductive system and breast disorders	0				3	(1.5)	5	1.8	3	(1.1)	5	1.3
Balanoposthitis	0				3	(1.5)	5	1.8	3	(1.1)	5	1.3
Vascular disorders	1	(1.2)	1	1.0	2	(1.0)	4	1.4	3	(1.1)	5	1.3
Haematoma	0				1	(0.5)	3	1.1	1	(0.4)	3	0.8
Hot flush	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Vein disorder	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Hepatobiliary disorders	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Gallbladder disorder	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Nonalcoholic fatty liver disease	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Surgical and medical procedures	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Adenoidectomy	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Open reduction of fracture	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Congenital, familial and genetic disorders	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Cryptorchism	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Renal and urinary disorders	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Nephrotic syndrome	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

9: Summary of serious adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	4	(4.9)	6	5.7	10	(5.2)	14	5.0	14	(5.3)	20	5.2
Infections and infestations	3	(3.7)	3	2.9	3	(1.5)	3	1.1	6	(2.3)	6	1.5
Gastroenteritis	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
COVID-19	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Otitis media	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Respiratory syncytial virus bronchitis	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Tonsillitis	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Gastrointestinal disorders	0				3	(1.5)	3	1.1	3	(1.1)	3	0.8
Vomiting	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
Umbilical hernia	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Immune system disorders	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
Anaphylactic reaction	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Anaphylactic shock	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Respiratory, thoracic and mediastinal disorders	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
Adenoidal hypertrophy	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Asthma	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Congenital, familial and genetic disorders	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Cryptorchism	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Endocrine disorders	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3

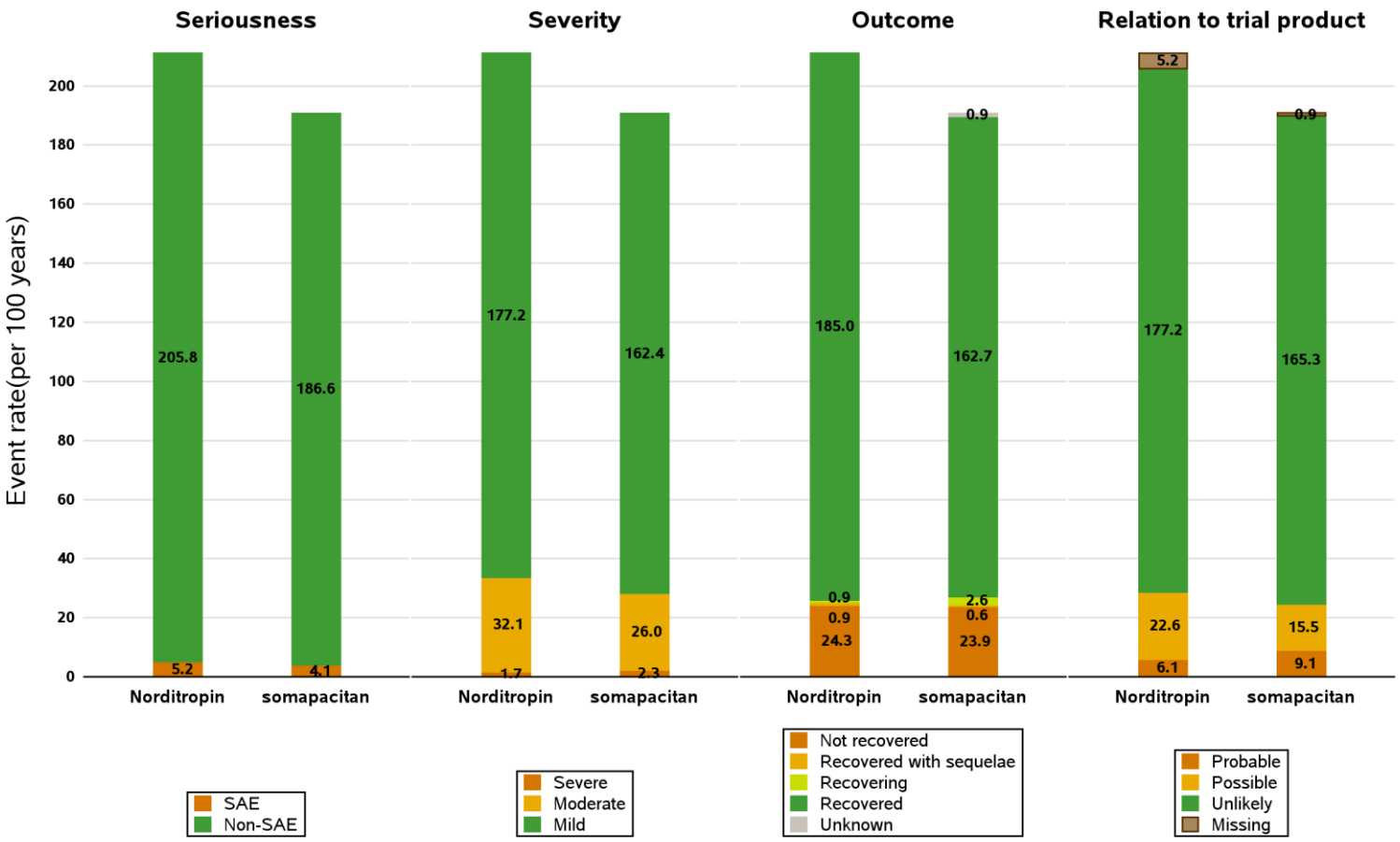
N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of serious adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Adrenocortical insufficiency acute	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
General disorders and administration site conditions	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Generalised oedema	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Metabolism and nutrition disorders	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Dehydration	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Nervous system disorders	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Headache	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Renal and urinary disorders	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Nephrotic syndrome	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Surgical and medical procedures	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Adenoidectomy	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

10: Adverse events by seriousness, severity, outcome and relation to trial product - on-treatment - safety analysis set



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11: Summary of severe adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	82			194			265		
Total patient years at risk	104.5			282.7			387.3		
Events	2	(2.4)	2 1.9	5	(2.6)	8 2.8	7	(2.6)	10 2.6
Nervous system disorders	1	(1.2)	1 1.0	2	(1.0)	2 0.7	3	(1.1)	3 0.8
Headache	1	(1.2)	1 1.0	2	(1.0)	2 0.7	3	(1.1)	3 0.8
Surgical and medical procedures	1	(1.2)	1 1.0	1	(0.5)	1 0.4	2	(0.8)	2 0.5
Adenoidectomy	1	(1.2)	1 1.0	0			1	(0.4)	1 0.3
Open reduction of fracture	0			1	(0.5)	1 0.4	1	(0.4)	1 0.3
General disorders and administration site conditions	0			1	(0.5)	2 0.7	1	(0.4)	2 0.5
Fatigue	0			1	(0.5)	2 0.7	1	(0.4)	2 0.5
Musculoskeletal and connective tissue disorders	0			1	(0.5)	2 0.7	1	(0.4)	2 0.5
Pain in extremity	0			1	(0.5)	2 0.7	1	(0.4)	2 0.5
Respiratory, thoracic and mediastinal disorders	0			1	(0.5)	1 0.4	1	(0.4)	1 0.3
Asthma	0			1	(0.5)	1 0.4	1	(0.4)	1 0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

12: Summary of moderate adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	17	(20.7)	37	35.4	46	(23.7)	89	31.5	62	(23.4)	126	32.5
Infections and infestations	11	(13.4)	16	15.3	19	(9.8)	29	10.3	29	(10.9)	45	11.6
Bronchitis	3	(3.7)	3	2.9	3	(1.5)	3	1.1	6	(2.3)	6	1.5
Influenza	1	(1.2)	1	1.0	3	(1.5)	3	1.1	4	(1.5)	4	1.0
Respiratory tract infection	1	(1.2)	1	1.0	3	(1.5)	3	1.1	4	(1.5)	4	1.0
Gastroenteritis	1	(1.2)	1	1.0	2	(1.0)	2	0.7	3	(1.1)	3	0.8
Pharyngitis streptococcal	0				2	(1.0)	5	1.8	2	(0.8)	5	1.3
Nasopharyngitis	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Otitis media acute	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Tonsillitis	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Tooth abscess	2	(2.4)	2	1.9	0				2	(0.8)	2	0.5
COVID-19	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Eye infection	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Gastrointestinal viral infection	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Herpangina	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Molluscum contagiosum	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Otitis media	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Paronychia	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Pharyngotonsillitis	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Pneumonia	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Respiratory syncytial virus bronchitis	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Scarlet fever	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Streptococcal infection	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Upper respiratory tract infection	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Urinary tract infection	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Viral infection	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of moderate adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Respiratory, thoracic and mediastinal disorders	1 (1.2)	1	1.0	9 (4.6)	11	3.9	10 (3.8)	12	3.1
Oropharyngeal pain	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Asthma	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Cough	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Rhinitis allergic	0			1 (0.5)	2	0.7	1 (0.4)	2	0.5
Adenoidal hypertrophy	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Bronchial hyperreactivity	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Pneumonitis	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Gastrointestinal disorders	3 (3.7)	4	3.8	6 (3.1)	8	2.8	9 (3.4)	12	3.1
Vomiting	2 (2.4)	2	1.9	2 (1.0)	3	1.1	4 (1.5)	5	1.3
Diarrhoea	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Abdominal pain upper	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Constipation	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Gastritis	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
General disorders and administration site conditions	0			8 (4.1)	12	4.2	8 (3.0)	12	3.1
Pyrexia	0			8 (4.1)	11	3.9	8 (3.0)	11	2.8
Generalised oedema	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Injury, poisoning and procedural complications	1 (1.2)	1	1.0	6 (3.1)	6	2.1	7 (2.6)	7	1.8
Hand fracture	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Head injury	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Joint dislocation	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Lower limb fracture	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Radius fracture	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Road traffic accident	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Upper limb fracture	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of moderate adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Nervous system disorders	4 (4.9)	4	3.8	2 (1.0)	2	0.7	6 (2.3)	6	1.5
Headache	3 (3.7)	3	2.9	1 (0.5)	1	0.4	4 (1.5)	4	1.0
Cognitive disorder	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Febrile convulsion	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Metabolism and nutrition disorders	1 (1.2)	1	1.0	4 (2.1)	4	1.4	5 (1.9)	5	1.3
Hypercholesterolaemia	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Dehydration	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Hyperglycaemia	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Zinc deficiency	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Skin and subcutaneous tissue disorders	1 (1.2)	2	1.9	3 (1.5)	3	1.1	4 (1.5)	5	1.3
Dermatitis atopic	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Rash	1 (1.2)	2	1.9	0			1 (0.4)	2	0.5
Urticaria	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Endocrine disorders	1 (1.2)	1	1.0	3 (1.5)	3	1.1	4 (1.5)	4	1.0
Adrenal insufficiency	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Adrenocortical insufficiency acute	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Adrenocorticotropic hormone deficiency	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Secondary hypothyroidism	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Musculoskeletal and connective tissue disorders	2 (2.4)	2	1.9	2 (1.0)	2	0.7	4 (1.5)	4	1.0
Arthritis reactive	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Foot deformity	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Pain in extremity	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Soft tissue swelling	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Immune system disorders	1 (1.2)	1	1.0	2 (1.0)	2	0.7	3 (1.1)	3	0.8

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of moderate adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Anaphylactic reaction	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Anaphylactic shock	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Seasonal allergy	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Investigations	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Blood creatine phosphokinase increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Low density lipoprotein increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Psychiatric disorders	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Nightmare	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Sleep disorder	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Eye disorders	1 (1.2)	2	1.9	0			1 (0.4)	2	0.5
Eye pain	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Vision blurred	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Blood and lymphatic system disorders	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Hypochromic anaemia	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Congenital, familial and genetic disorders	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Cryptorchism	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Hepatobiliary disorders	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Nonalcoholic fatty liver disease	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Renal and urinary disorders	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Nephrotic syndrome	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Reproductive system and breast disorders	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of moderate adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Balanoposthitis	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

13: Summary of mild adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	82			194			265		
Total patient years at risk	104.5			282.7			387.3		
Events	49	(59.8)	204 195.1	132	(68.0)	556 196.6	174	(65.7)	760 196.2
Infections and infestations	32	(39.0)	74 70.8	73	(37.6)	205 72.5	101	(38.1)	279 72.0
Nasopharyngitis	9	(11.0)	24 23.0	22	(11.3)	70 24.8	30	(11.3)	94 24.3
Rhinitis	6	(7.3)	7 6.7	8	(4.1)	10 3.5	14	(5.3)	17 4.4
Influenza	4	(4.9)	5 4.8	8	(4.1)	12 4.2	12	(4.5)	17 4.4
Bronchitis	5	(6.1)	5 4.8	5	(2.6)	6 2.1	10	(3.8)	11 2.8
Upper respiratory tract infection	3	(3.7)	4 3.8	6	(3.1)	10 3.5	9	(3.4)	14 3.6
Respiratory tract infection	3	(3.7)	4 3.8	6	(3.1)	9 3.2	9	(3.4)	13 3.4
Otitis media	3	(3.7)	3 2.9	6	(3.1)	9 3.2	9	(3.4)	12 3.1
Gastroenteritis	2	(2.4)	2 1.9	4	(2.1)	4 1.4	6	(2.3)	6 1.5
Gastroenteritis viral	0			5	(2.6)	8 2.8	5	(1.9)	8 2.1
COVID-19	3	(3.7)	3 2.9	2	(1.0)	2 0.7	5	(1.9)	5 1.3
Viral infection	1	(1.2)	1 1.0	3	(1.5)	5 1.8	4	(1.5)	6 1.5
Ear infection	2	(2.4)	2 1.9	2	(1.0)	2 0.7	4	(1.5)	4 1.0
Molluscum contagiosum	2	(2.4)	2 1.9	2	(1.0)	2 0.7	4	(1.5)	4 1.0
Pharyngitis	0			3	(1.5)	6 2.1	3	(1.1)	6 1.5
Otitis media acute	0			3	(1.5)	4 1.4	3	(1.1)	4 1.0
Sinusitis	0			3	(1.5)	4 1.4	3	(1.1)	4 1.0
Impetigo	0			3	(1.5)	3 1.1	3	(1.1)	3 0.8
Tonsillitis	0			3	(1.5)	3 1.1	3	(1.1)	3 0.8
Varicella	1	(1.2)	1 1.0	2	(1.0)	2 0.7	3	(1.1)	3 0.8
Respiratory tract infection viral	1	(1.2)	3 2.9	2	(1.0)	2 0.7	2	(0.8)	5 1.3
Conjunctivitis	0			2	(1.0)	2 0.7	2	(0.8)	2 0.5
Hand-foot-and-mouth disease	0			2	(1.0)	2 0.7	2	(0.8)	2 0.5
Hordeolum	1	(1.2)	1 1.0	1	(0.5)	1 0.4	2	(0.8)	2 0.5
Paronychia	0			2	(1.0)	2 0.7	2	(0.8)	2 0.5
Tooth abscess	1	(1.2)	1 1.0	1	(0.5)	1 0.4	2	(0.8)	2 0.5

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Summary of mild adverse events by system organ class and preferred term - on-treatment - safety analysis set

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	N (%)	E	R	N (%)	E	R	N (%)	E	R
Urinary tract infection	0			1 (0.5)	3	1.1	1 (0.4)	3	0.8
Pharyngitis streptococcal	1 (1.2)	2	1.9	0			1 (0.4)	2	0.5
Acute sinusitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Bacterial infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Conjunctivitis bacterial	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Cystitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Dermatitis infected	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Dientamoeba infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Enteritis infectious	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Fungal infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Furuncle	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Herpes dermatitis	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Infection parasitic	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Laryngitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Latent tuberculosis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Mumps	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Oral herpes	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Otitis externa	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Parotitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Pneumonia	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Tinea infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Tonsillitis streptococcal	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Tooth infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Tracheitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Upper respiratory tract infection bacterial	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Viral upper respiratory tract infection	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
General disorders and administration site conditions	14 (17.1)	26	24.9	34 (17.5)	49	17.3	47 (17.7)	75	19.4
Pyrexia	9 (11.0)	17	16.3	17 (8.8)	19	6.7	25 (9.4)	36	9.3

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	N (%)	E	R	N (%)	E	R	N (%)	E	R
Injection site bruising	2 (2.4)	2	1.9	3 (1.5)	5	1.8	5 (1.9)	7	1.8
Injection site pain	1 (1.2)	1	1.0	3 (1.5)	5	1.8	4 (1.5)	6	1.5
Swelling face	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Injection site haematoma	0			2 (1.0)	4	1.4	2 (0.8)	4	1.0
Fatigue	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Pain	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Asthenia	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Chest discomfort	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Face oedema	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Hyperthermia	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Influenza like illness	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Injection site discomfort	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Injection site hypersensitivity	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Injection site reaction	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Injection site swelling	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Local reaction	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Malaise	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Oedema peripheral	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
PFAPA syndrome	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Peripheral swelling	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Swelling	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Gastrointestinal disorders	7 (8.5)	15	14.3	27 (13.9)	63	22.3	34 (12.8)	78	20.1
Vomiting	4 (4.9)	8	7.7	10 (5.2)	12	4.2	14 (5.3)	20	5.2
Constipation	1 (1.2)	1	1.0	8 (4.1)	11	3.9	9 (3.4)	12	3.1
Nausea	1 (1.2)	1	1.0	5 (2.6)	6	2.1	6 (2.3)	7	1.8
Diarrhoea	2 (2.4)	3	2.9	3 (1.5)	7	2.5	5 (1.9)	10	2.6
Abdominal pain	1 (1.2)	1	1.0	4 (2.1)	5	1.8	5 (1.9)	6	1.5
Abdominal pain upper	0			3 (1.5)	4	1.4	3 (1.1)	4	1.0
Stomatitis	0			2 (1.0)	12	4.2	2 (0.8)	12	3.1
Toothache	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Aphthous ulcer	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Enterocolitis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3

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Summary of mild adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gastrooesophageal reflux disease	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Haematochezia	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Umbilical hernia	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Skin and subcutaneous tissue disorders	8 (9.8)	9	8.6	25 (12.9)	40	14.1	32 (12.1)	49	12.7
Dermatitis	2 (2.4)	2	1.9	3 (1.5)	3	1.1	5 (1.9)	5	1.3
Urticaria	3 (3.7)	3	2.9	1 (0.5)	4	1.4	4 (1.5)	7	1.8
Eczema	1 (1.2)	1	1.0	3 (1.5)	4	1.4	4 (1.5)	5	1.3
Rash	0			3 (1.5)	4	1.4	3 (1.1)	4	1.0
Pruritus	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Miliaria	0			2 (1.0)	4	1.4	2 (0.8)	4	1.0
Erythema	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Skin lesion	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Acanthosis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Alopecia	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Dermatitis allergic	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Dermatitis atopic	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Dermatosis	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Dry skin	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Eczema asteatotic	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Haemorrhage subcutaneous	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Henoch-Schonlein purpura	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Keratosis pilaris	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Leukoderma	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Lipodystrophy acquired	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Poikiloderma	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Psoriasis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Skin atrophy	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Skin fissures	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Skin hyperpigmentation	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3

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	N (%)	E	R	N (%)	E	R	N (%)	E	R
Musculoskeletal and connective tissue disorders	6 (7.3)	9	8.6	24 (12.4)	34	12.0	30 (11.3)	43	11.1
Pain in extremity	3 (3.7)	4	3.8	14 (7.2)	17	6.0	17 (6.4)	21	5.4
Arthralgia	3 (3.7)	3	2.9	4 (2.1)	6	2.1	7 (2.6)	9	2.3
Growing pains	0			4 (2.1)	5	1.8	4 (1.5)	5	1.3
Myalgia	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Groin pain	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Hip deformity	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Muscle hypertrophy	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Musculoskeletal stiffness	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Neck pain	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Respiratory, thoracic and mediastinal disorders	10 (12.2)	14	13.4	20 (10.3)	25	8.8	30 (11.3)	39	10.1
Cough	4 (4.9)	4	3.8	8 (4.1)	8	2.8	12 (4.5)	12	3.1
Rhinitis allergic	3 (3.7)	3	2.9	5 (2.6)	6	2.1	8 (3.0)	9	2.3
Asthma	1 (1.2)	2	1.9	1 (0.5)	1	0.4	2 (0.8)	3	0.8
Oropharyngeal pain	1 (1.2)	2	1.9	1 (0.5)	1	0.4	2 (0.8)	3	0.8
Epistaxis	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Respiratory disorder	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Rhinorrhoea	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Upper respiratory tract inflammation	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Adenoidal hypertrophy	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Nasal congestion	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Tonsillar hypertrophy	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Wheezing	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Nervous system disorders	7 (8.5)	16	15.3	22 (11.3)	29	10.3	29 (10.9)	45	11.6
Headache	4 (4.9)	9	8.6	17 (8.8)	23	8.1	21 (7.9)	32	8.3
Dizziness	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Autonomic nervous system imbalance	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3

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	N (%)	E	R	N (%)	E	R	N (%)	E	R
Disturbance in attention	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Epilepsy	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Fine motor skill dysfunction	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Intellectual disability	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Migraine	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Nystagmus	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Presyncope	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Somnolence	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Speech disorder	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Speech disorder developmental	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Injury, poisoning and procedural complications	3 (3.7)	4	3.8	23 (11.9)	31	11.0	26 (9.8)	35	9.0
Contusion	1 (1.2)	1	1.0	3 (1.5)	5	1.8	4 (1.5)	6	1.5
Accidental overdose	2 (2.4)	2	1.9	1 (0.5)	1	0.4	3 (1.1)	3	0.8
Arthropod sting	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Skin laceration	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Accidental underdose	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Animal bite	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Arthropod bite	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Concussion	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Eye contusion	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Fall	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Foot fracture	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Foreign body	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Hand fracture	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Head injury	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Heat stroke	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Joint dislocation	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Ligament sprain	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Lip injury	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Medication error	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Nasal injury	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3

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	N (%)	E	R	N (%)	E	R	N (%)	E	R
Procedural pain	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Skin abrasion	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Thermal burn	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Venomous sting	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Investigations	5 (6.1)	8	7.7	13 (6.7)	17	6.0	18 (6.8)	25	6.5
Blood glucose increased	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Blood thyroid stimulating hormone increased	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Cortisol decreased	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Haematology test abnormal	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Alanine aminotransferase increased	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Aspartate aminotransferase increased	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Aspiration joint	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Blood cholesterol abnormal	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Blood glucose abnormal	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Blood phosphorus increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Electrocardiogram QT prolonged	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Electrocardiogram abnormal	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Glycosylated haemoglobin increased	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Haematocrit increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Haemoglobin increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Low density lipoprotein increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Platelet count increased	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
SARS-CoV-2 test positive	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Thyroxine decreased	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Thyroxine free decreased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Tri-iodothyronine increased	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Eye disorders	3 (3.7)	6	5.7	10 (5.2)	12	4.2	13 (4.9)	18	4.6

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of mild adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Conjunctivitis allergic	0				3	(1.5)	3	1.1	3	(1.1)	3	0.8
Strabismus	2	(2.4)	3	2.9	0				2	(0.8)	3	0.8
Eye irritation	0				1	(0.5)	2	0.7	1	(0.4)	2	0.5
Anisometropia	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Dry eye	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Eye pruritus	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Eyelid cyst	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Hypermetropia	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Myopia	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Optic nerve cupping	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Periorbital oedema	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Swelling of eyelid	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Visual impairment	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Metabolism and nutrition disorders	5	(6.1)	5	4.8	7	(3.6)	8	2.8	12	(4.5)	13	3.4
Hyperglycaemia	2	(2.4)	2	1.9	1	(0.5)	1	0.4	3	(1.1)	3	0.8
Dyslipidaemia	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
Hypercholesterolaemia	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Impaired fasting glucose	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Hyperlipidaemia	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Hyperphosphataemia	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Iodine deficiency	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Iron deficiency	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Blood and lymphatic system disorders	5	(6.1)	5	4.8	7	(3.6)	7	2.5	12	(4.5)	12	3.1
Anaemia	2	(2.4)	2	1.9	3	(1.5)	3	1.1	5	(1.9)	5	1.3
Iron deficiency anaemia	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Lymphadenopathy	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
Eosinophilia	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Monocytosis	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Thrombocytopenia	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of mild adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Immune system disorders	2 (2.4)	4	3.8	8 (4.1)	9	3.2	9 (3.4)	13	3.4
Seasonal allergy	1 (1.2)	2	1.9	5 (2.6)	6	2.1	5 (1.9)	8	2.1
Food allergy	1 (1.2)	1	1.0	2 (1.0)	2	0.7	3 (1.1)	3	0.8
Allergy to metals	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Drug hypersensitivity	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Endocrine disorders	1 (1.2)	1	1.0	7 (3.6)	7	2.5	8 (3.0)	8	2.1
Hypothyroidism	1 (1.2)	1	1.0	4 (2.1)	4	1.4	5 (1.9)	5	1.3
Glucocorticoid deficiency	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Secondary adrenocortical insufficiency	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Secondary hypothyroidism	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Psychiatric disorders	3 (3.7)	3	2.9	4 (2.1)	4	1.4	7 (2.6)	7	1.8
Attention deficit hyperactivity disorder	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Tic	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Anxiety	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Enuresis	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Generalised anxiety disorder	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (2.4)	2	1.9	4 (2.1)	4	1.4	6 (2.3)	6	1.5
Skin papilloma	1 (1.2)	1	1.0	3 (1.5)	3	1.1	4 (1.5)	4	1.0
Lipoma	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Lymphangioma	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Ear and labyrinth disorders	1 (1.2)	1	1.0	3 (1.5)	4	1.4	4 (1.5)	5	1.3
Cerumen impaction	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Ear pain	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Tinnitus	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Vascular disorders	1 (1.2)	1	1.0	2 (1.0)	4	1.4	3 (1.1)	5	1.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of mild adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Haematoma	0				1	(0.5)	3	1.1	1	(0.4)	3	0.8
Hot flush	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Vein disorder	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Reproductive system and breast disorders	0				2	(1.0)	4	1.4	2	(0.8)	4	1.0
Balanoposthitis	0				2	(1.0)	4	1.4	2	(0.8)	4	1.0
Hepatobiliary disorders	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Gallbladder disorder	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

14: Summary of adverse events possibly or probably related to Norditropin or somapacitan by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	15	(18.3)	33	31.6	39	(20.1)	85	30.1	54	(20.4)	118	30.5
General disorders and administration site conditions	4	(4.9)	4	3.8	14	(7.2)	23	8.1	18	(6.8)	27	7.0
Injection site pain	1	(1.2)	1	1.0	3	(1.5)	5	1.8	4	(1.5)	6	1.5
Injection site bruising	1	(1.2)	1	1.0	2	(1.0)	2	0.7	3	(1.1)	3	0.8
Fatigue	0				2	(1.0)	4	1.4	2	(0.8)	4	1.0
Injection site haematoma	0				2	(1.0)	4	1.4	2	(0.8)	4	1.0
Chest discomfort	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Face oedema	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Generalised oedema	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Injection site discomfort	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Injection site hypersensitivity	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Injection site reaction	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Local reaction	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Oedema peripheral	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Pyrexia	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Swelling face	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Nervous system disorders	7	(8.5)	11	10.5	7	(3.6)	9	3.2	14	(5.3)	20	5.2
Headache	7	(8.5)	10	9.6	5	(2.6)	7	2.5	12	(4.5)	17	4.4
Dizziness	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Migraine	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Somnolence	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Musculoskeletal and connective tissue disorders	2	(2.4)	3	2.9	8	(4.1)	16	5.7	10	(3.8)	19	4.9

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events possibly or probably related to Norditropin or somapacitan by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Pain in extremity	2 (2.4)	3	2.9	3 (1.5)	8	2.8	5 (1.9)	11	2.8
Arthralgia	0			2 (1.0)	3	1.1	2 (0.8)	3	0.8
Groin pain	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Growing pains	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Hip deformity	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Muscle hypertrophy	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Soft tissue swelling	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Gastrointestinal disorders	3 (3.7)	4	3.8	5 (2.6)	8	2.8	8 (3.0)	12	3.1
Vomiting	3 (3.7)	3	2.9	3 (1.5)	5	1.8	6 (2.3)	8	2.1
Abdominal pain upper	1 (1.2)	1	1.0	1 (0.5)	2	0.7	2 (0.8)	3	0.8
Nausea	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Investigations	1 (1.2)	1	1.0	7 (3.6)	8	2.8	8 (3.0)	9	2.3
Low density lipoprotein increased	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Blood creatine phosphokinase increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Blood glucose abnormal	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Blood glucose increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Blood phosphorus increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Electrocardiogram abnormal	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Haematocrit increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Haemoglobin increased	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Metabolism and nutrition disorders	3 (3.7)	3	2.9	5 (2.6)	6	2.1	8 (3.0)	9	2.3
Hypercholesterolaemia	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Hyperglycaemia	2 (2.4)	2	1.9	1 (0.5)	1	0.4	3 (1.1)	3	0.8
Impaired fasting glucose	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Hyperphosphataemia	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Skin and subcutaneous tissue disorders	2 (2.4)	2	1.9	3 (1.5)	3	1.1	5 (1.9)	5	1.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events possibly or probably related to Norditropin or somapacitan by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Dermatitis atopic	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Haemorrhage subcutaneous	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Skin atrophy	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Skin fissures	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Urticaria	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Eye disorders	1 (1.2)	2	1.9	2 (1.0)	2	0.7	3 (1.1)	4	1.0
Eye pain	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Periorbital oedema	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Swelling of eyelid	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Vision blurred	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Psychiatric disorders	1 (1.2)	1	1.0	2 (1.0)	2	0.7	3 (1.1)	3	0.8
Anxiety	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Attention deficit hyperactivity disorder	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Nightmare	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Blood and lymphatic system disorders	0			2 (1.0)	2	0.7	2 (0.8)	2	0.5
Iron deficiency anaemia	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Lymphadenopathy	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Injury, poisoning and procedural complications	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Accidental overdose	1 (1.2)	1	1.0	1 (0.5)	1	0.4	2 (0.8)	2	0.5
Vascular disorders	0			1 (0.5)	3	1.1	1 (0.4)	3	0.8
Haematoma	0			1 (0.5)	3	1.1	1 (0.4)	3	0.8
Endocrine disorders	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Hypothyroidism	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events possibly or probably related to Norditropin or somapacitan by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Hepatobiliary disorders	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Nonalcoholic fatty liver disease	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Immune system disorders	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Drug hypersensitivity	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

15: Summary of serious adverse events possibly or probably related to Norditropin or somapacitan by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	0				1	(0.5)	2	0.7	1	(0.4)	2	0.5
Gastrointestinal disorders	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Vomiting	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
General disorders and administration site conditions	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Generalised oedema	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

16: Summary of severe adverse events possibly or probably related to Norditropin or somapacitan by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	1	(1.2)	1	1.0	2	(1.0)	5	1.8	3	(1.1)	6	1.5
Nervous system disorders	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Headache	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
General disorders and administration site conditions	0				1	(0.5)	2	0.7	1	(0.4)	2	0.5
Fatigue	0				1	(0.5)	2	0.7	1	(0.4)	2	0.5
Musculoskeletal and connective tissue disorders	0				1	(0.5)	2	0.7	1	(0.4)	2	0.5
Pain in extremity	0				1	(0.5)	2	0.7	1	(0.4)	2	0.5

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

17: Summary of most frequent adverse events (>=5%) by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	82			194			265		
Total patient years at risk	104.5			282.7			387.3		
Events	55 (67.1)	243	232.4	142 (73.2)	653	230.9	189 (71.3)	896	231.4
Infections and infestations									
Nasopharyngitis	10 (12.2)	25	23.9	23 (11.9)	71	25.1	32 (12.1)	96	24.8
Influenza	5 (6.1)	6	5.7	11 (5.7)	15	5.3	16 (6.0)	21	5.4
Bronchitis	7 (8.5)	8	7.7	7 (3.6)	9	3.2	14 (5.3)	17	4.4
Rhinitis	6 (7.3)	7	6.7	8 (4.1)	10	3.5	14 (5.3)	17	4.4
General disorders and administration site conditions									
Pyrexia	9 (11.0)	17	16.3	24 (12.4)	30	10.6	32 (12.1)	47	12.1
Gastrointestinal disorders									
Vomiting	5 (6.1)	10	9.6	11 (5.7)	15	5.3	16 (6.0)	25	6.5
Nervous system disorders									
Headache	8 (9.8)	13	12.4	18 (9.3)	26	9.2	26 (9.8)	39	10.1
Musculoskeletal and connective tissue disorders									
Pain in extremity	3 (3.7)	5	4.8	14 (7.2)	19	6.7	17 (6.4)	24	6.2

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

18: Summary of most frequent adverse events (>=2%) by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	82			194			265		
Total patient years at risk	104.5			282.7			387.3		
Events	55	(67.1)	243 232.4	142	(73.2)	653 230.9	189	(71.3)	896 231.4
Infections and infestations									
Nasopharyngitis	10	(12.2)	25 23.9	23	(11.9)	71 25.1	32	(12.1)	96 24.8
Influenza	5	(6.1)	6 5.7	11	(5.7)	15 5.3	16	(6.0)	21 5.4
Bronchitis	7	(8.5)	8 7.7	7	(3.6)	9 3.2	14	(5.3)	17 4.4
Rhinitis	6	(7.3)	7 6.7	8	(4.1)	10 3.5	14	(5.3)	17 4.4
Respiratory tract infection	4	(4.9)	5 4.8	7	(3.6)	12 4.2	11	(4.2)	17 4.4
Upper respiratory tract infection	3	(3.7)	4 3.8	7	(3.6)	11 3.9	10	(3.8)	15 3.9
Otitis media	3	(3.7)	3 2.9	7	(3.6)	10 3.5	10	(3.8)	13 3.4
Gastroenteritis	3	(3.7)	3 2.9	6	(3.1)	6 2.1	9	(3.4)	9 2.3
COVID-19	3	(3.7)	3 2.9	3	(1.5)	3 1.1	6	(2.3)	6 1.5
Gastroenteritis viral	0			5	(2.6)	8 2.8	5	(1.9)	8 2.1
Viral infection	1	(1.2)	1 1.0	4	(2.1)	6 2.1	5	(1.9)	7 1.8
Otitis media acute	1	(1.2)	1 1.0	4	(2.1)	5 1.8	5	(1.9)	6 1.5
Molluscum contagiosum	3	(3.7)	3 2.9	2	(1.0)	2 0.7	5	(1.9)	5 1.3
Tonsillitis	1	(1.2)	1 1.0	4	(2.1)	4 1.4	5	(1.9)	5 1.3
Ear infection	2	(2.4)	2 1.9	2	(1.0)	2 0.7	4	(1.5)	4 1.0
Tooth abscess	3	(3.7)	3 2.9	1	(0.5)	1 0.4	4	(1.5)	4 1.0
General disorders and administration site conditions									
Pyrexia	9	(11.0)	17 16.3	24	(12.4)	30 10.6	32	(12.1)	47 12.1
Injection site bruising	2	(2.4)	2 1.9	3	(1.5)	5 1.8	5	(1.9)	7 1.8
Gastrointestinal disorders									
Vomiting	5	(6.1)	10 9.6	11	(5.7)	15 5.3	16	(6.0)	25 6.5
Constipation	1	(1.2)	1 1.0	9	(4.6)	12 4.2	10	(3.8)	13 3.4

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of most frequent adverse events (>=2%) by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Diarrhoea	2	(2.4)	3	2.9	6	(3.1)	10	3.5	8	(3.0)	13	3.4
Nausea	1	(1.2)	1	1.0	5	(2.6)	6	2.1	6	(2.3)	7	1.8
Abdominal pain	1	(1.2)	1	1.0	4	(2.1)	5	1.8	5	(1.9)	6	1.5
Respiratory, thoracic and mediastinal disorders												
Cough	4	(4.9)	4	3.8	9	(4.6)	10	3.5	13	(4.9)	14	3.6
Rhinitis allergic	3	(3.7)	3	2.9	6	(3.1)	8	2.8	9	(3.4)	11	2.8
Oropharyngeal pain	1	(1.2)	2	1.9	4	(2.1)	4	1.4	5	(1.9)	6	1.5
Skin and subcutaneous tissue disorders												
Urticaria	3	(3.7)	3	2.9	2	(1.0)	5	1.8	5	(1.9)	8	2.1
Dermatitis	2	(2.4)	2	1.9	3	(1.5)	3	1.1	5	(1.9)	5	1.3
Nervous system disorders												
Headache	8	(9.8)	13	12.4	18	(9.3)	26	9.2	26	(9.8)	39	10.1
Musculoskeletal and connective tissue disorders												
Pain in extremity	3	(3.7)	5	4.8	14	(7.2)	19	6.7	17	(6.4)	24	6.2
Arthralgia	3	(3.7)	3	2.9	4	(2.1)	6	2.1	7	(2.6)	9	2.3
Growing pains	0				4	(2.1)	5	1.8	4	(1.5)	5	1.3
Injury, poisoning and procedural complications												
Accidental overdose	2	(2.4)	2	1.9	1	(0.5)	1	0.4	3	(1.1)	3	0.8
Metabolism and nutrition disorders												
Hyperglycaemia	2	(2.4)	2	1.9	2	(1.0)	2	0.7	4	(1.5)	4	1.0
Eye disorders												
Strabismus	2	(2.4)	3	2.9	0				2	(0.8)	3	0.8

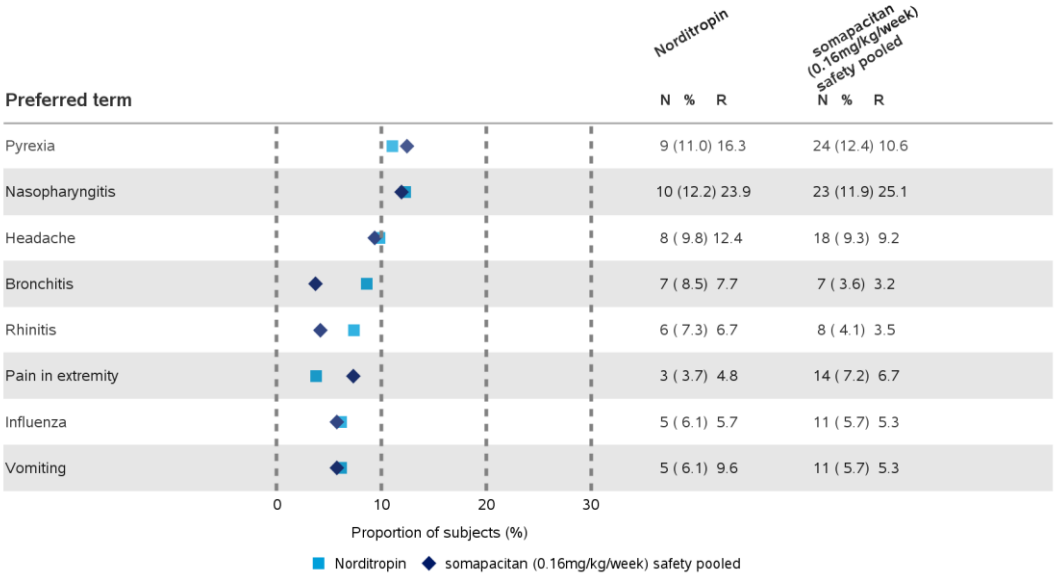
N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of most frequent adverse events (>=2%) by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Blood and lymphatic system disorders												
Anaemia	2	(2.4)	2	1.9	3	(1.5)	3	1.1	5	(1.9)	5	1.3
Immune system disorders												
Seasonal allergy	2	(2.4)	3	2.9	5	(2.6)	6	2.1	6	(2.3)	9	2.3
Endocrine disorders												
Hypothyroidism	1	(1.2)	1	1.0	4	(2.1)	4	1.4	5	(1.9)	5	1.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

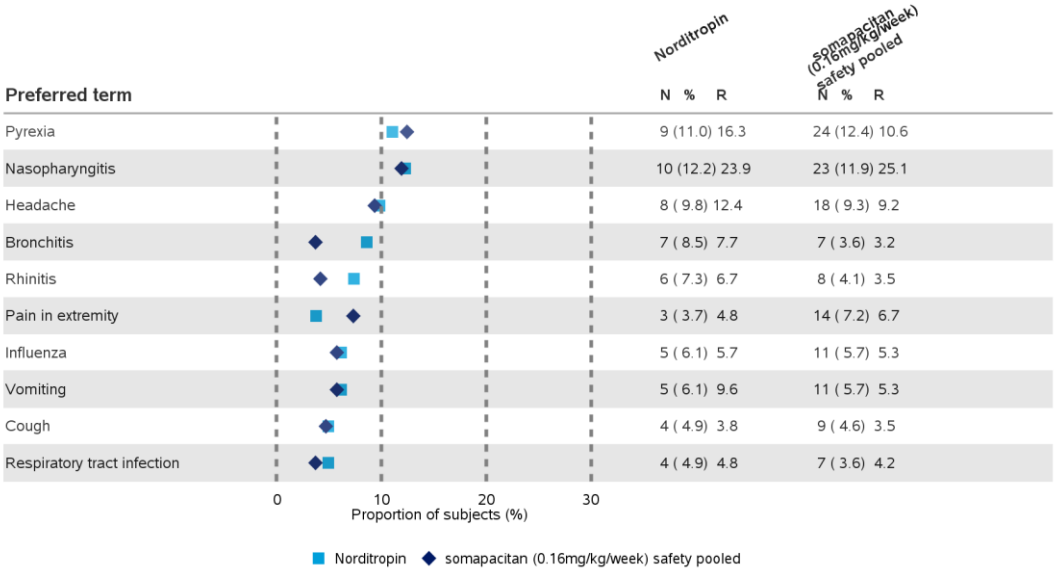
19: Most frequent adverse events by preferred term (>=5%) - on-treatment - plot - safety analysis set



%: Percentage, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

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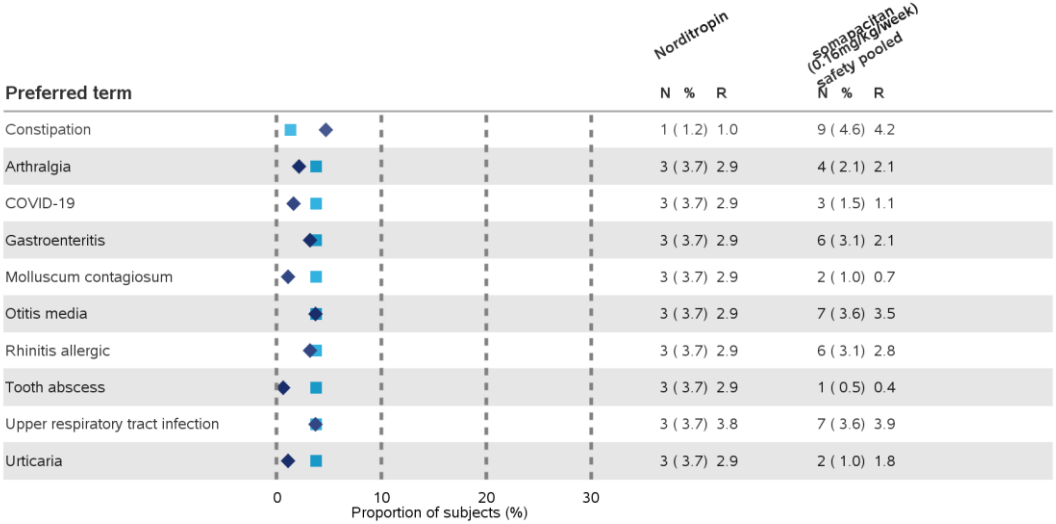
20: Most frequent adverse events by preferred term (>=2%) - on-treatment - plot 1 - safety analysis set



%: Percentage, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
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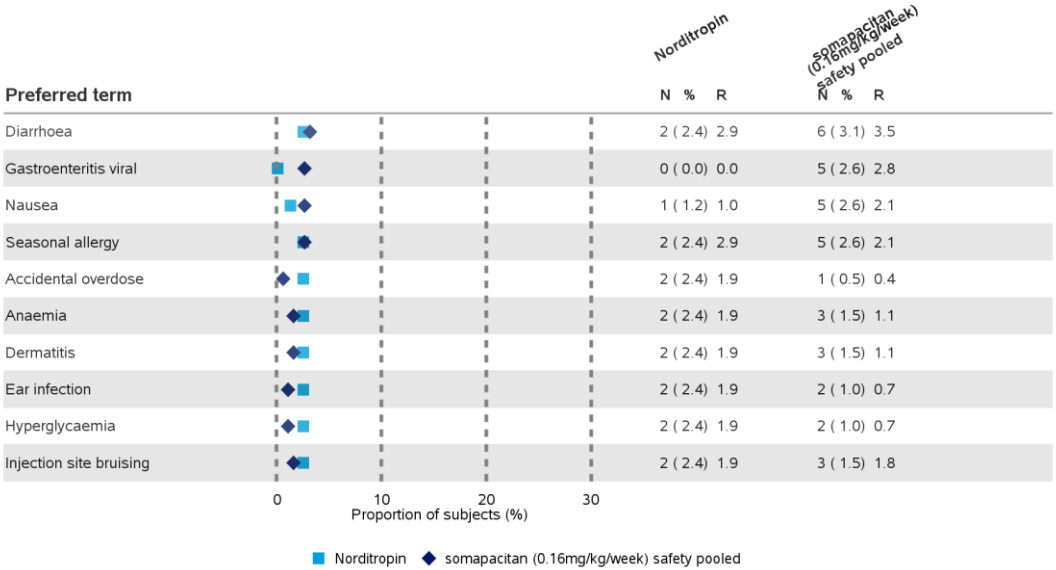
21: Most frequent adverse events by preferred term (>=2%) - on-treatment - plot 2 - safety analysis set



%: Percentage, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

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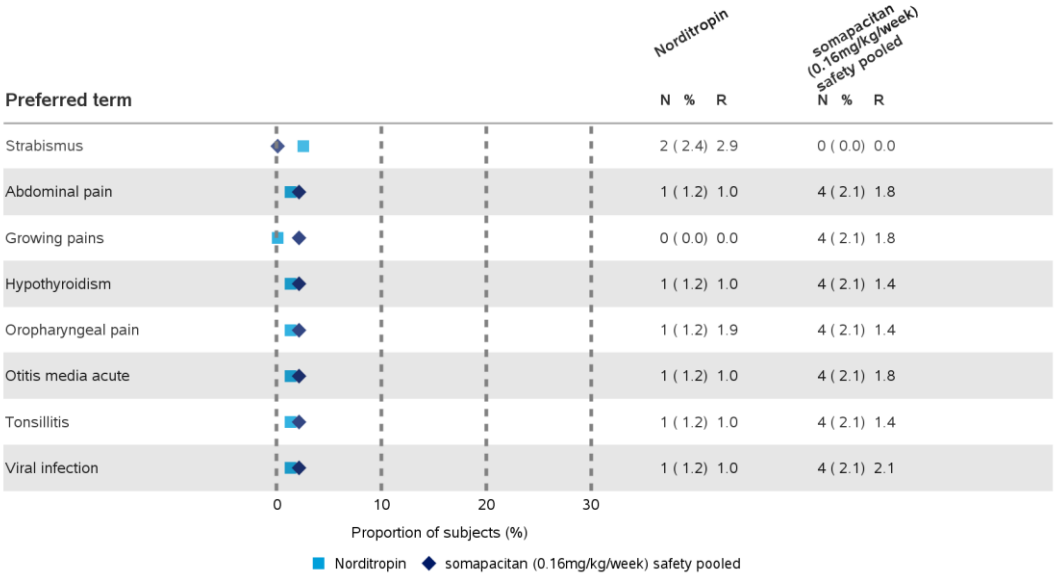
22: Most frequent adverse events by preferred term (>=2%) - on-treatment - plot 3 - safety analysis set



%: Percentage, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

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23: Most frequent adverse events by preferred term (>=2%) - on-treatment - plot 4 - safety analysis set



%: Percentage, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

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24: Summary of adverse events - on-treatment - Male - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	50			99			149		
Total patient years at risk	50.8			99.9			150.7		
All adverse events	26	(52.0)	94 184.9	69	(69.7)	224 224.3	95	(63.8)	318 211.0
Serious adverse events									
Yes	0			5	(5.1)	7 7.0	5	(3.4)	7 4.6
No	26	(52.0)	94 184.9	68	(68.7)	217 217.3	94	(63.1)	311 206.4
Severity									
Mild	24	(48.0)	84 165.3	63	(63.6)	186 186.3	87	(58.4)	270 179.2
Moderate	5	(10.0)	10 19.7	20	(20.2)	35 35.1	25	(16.8)	45 29.9
Severe	0			3	(3.0)	3 3.0	3	(2.0)	3 2.0
Causality									
Probable	3	(6.0)	4 7.9	9	(9.1)	13 13.0	12	(8.1)	17 11.3
Possible	5	(10.0)	12 23.6	11	(11.1)	23 23.0	16	(10.7)	35 23.2
Unlikely	24	(48.0)	78 153.4	67	(67.7)	188 188.3	91	(61.1)	266 176.5
Missing	0			0			0		
Action taken to trial product due to AE									
Drug interrupted	2	(4.0)	2 3.9	2	(2.0)	2 2.0	4	(2.7)	4 2.7
Drug withdrawn	0			0			0		
Dose reduced	1	(2.0)	1 2.0	1	(1.0)	1 1.0	2	(1.3)	2 1.3
Dose increased	0			1	(1.0)	1 1.0	1	(0.7)	1 0.7
Dose not changed	25	(50.0)	89 175.1	65	(65.7)	198 198.3	90	(60.4)	287 190.5
Unknown	0			2	(2.0)	2 2.0	2	(1.3)	2 1.3
Missing	0			0			0		
Related to technical complaint									
Yes	1	(2.0)	1 2.0	0			1	(0.7)	1 0.7
No	26	(52.0)	93 183.0	69	(69.7)	224 224.3	95	(63.8)	317 210.4
Injection site reaction									
Yes	1	(2.0)	1 2.0	2	(2.0)	2 2.0	3	(2.0)	3 2.0

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
AE causality is based on judgement of investigators.

Summary of adverse events - on-treatment - Male - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
No	26 (52.0)	93	183.0	69 (69.7)	222	222.3	95 (63.8)	315	209.0
Outcome									
Recovered/resolved	25 (50.0)	82	161.3	67 (67.7)	172	172.3	92 (61.7)	254	168.6
Recovering/resolving	0			4 (4.0)	8	8.0	4 (2.7)	8	5.3
Recovered/resolved with sequelae	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
Not recovered/not resolved	7 (14.0)	11	21.6	25 (25.3)	44	44.1	32 (21.5)	55	36.5
Fatal	0			0			0		
Unknown	0			0			0		
Missing	0			0			0		
Treatment									
Treatment discontinuations due to adverse events	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
AE causality is based on judgement of investigators.

25: Summary of adverse events by system organ class and preferred term - on-treatment - Male - trial 4263 - safety analysis set

	Norditropin				somapacitan				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	50				99				149			
Total patient years at risk	50.8				99.9				150.7			
Events	26	(52.0)	94	184.9	69	(69.7)	224	224.3	95	(63.8)	318	211.0
Infections and infestations	18	(36.0)	27	53.1	37	(37.4)	65	65.1	55	(36.9)	92	61.1
Nasopharyngitis	4	(8.0)	6	11.8	9	(9.1)	12	12.0	13	(8.7)	18	11.9
Bronchitis	2	(4.0)	2	3.9	4	(4.0)	6	6.0	6	(4.0)	8	5.3
Rhinitis	1	(2.0)	2	3.9	4	(4.0)	5	5.0	5	(3.4)	7	4.6
COVID-19	2	(4.0)	2	3.9	3	(3.0)	3	3.0	5	(3.4)	5	3.3
Respiratory tract infection	1	(2.0)	1	2.0	3	(3.0)	5	5.0	4	(2.7)	6	4.0
Influenza	2	(4.0)	2	3.9	2	(2.0)	2	2.0	4	(2.7)	4	2.7
Molluscum contagiosum	3	(6.0)	3	5.9	1	(1.0)	1	1.0	4	(2.7)	4	2.7
Upper respiratory tract infection	1	(2.0)	1	2.0	2	(2.0)	4	4.0	3	(2.0)	5	3.3
Ear infection	1	(2.0)	1	2.0	2	(2.0)	2	2.0	3	(2.0)	3	2.0
Tooth abscess	2	(4.0)	2	3.9	1	(1.0)	1	1.0	3	(2.0)	3	2.0
Viral infection	0				2	(2.0)	4	4.0	2	(1.3)	4	2.7
Hand-foot-and-mouth disease	0				2	(2.0)	2	2.0	2	(1.3)	2	1.3
Otitis media	0				2	(2.0)	2	2.0	2	(1.3)	2	1.3
Pharyngitis streptococcal	1	(2.0)	2	3.9	0				1	(0.7)	2	1.3
Acute sinusitis	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Enteritis infectious	1	(2.0)	1	2.0	0				1	(0.7)	1	0.7
Gastroenteritis viral	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Gastrointestinal viral infection	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Herpangina	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Herpes dermatitis	1	(2.0)	1	2.0	0				1	(0.7)	1	0.7
Hordeolum	1	(2.0)	1	2.0	0				1	(0.7)	1	0.7
Impetigo	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Infection	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Infection parasitic	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Latent tuberculosis	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Pharyngitis	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Pneumonia	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - on-treatment - Male - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Respiratory tract infection viral	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Sinusitis	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Streptococcal infection	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Tonsillitis	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Tonsillitis streptococcal	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Viral upper respiratory tract infection	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
General disorders and administration site conditions	7 (14.0)	16	31.5	16 (16.2)	23	23.0	23 (15.4)	39	25.9
Pyrexia	5 (10.0)	10	19.7	7 (7.1)	10	10.0	12 (8.1)	20	13.3
Injection site bruising	1 (2.0)	1	2.0	2 (2.0)	2	2.0	3 (2.0)	3	2.0
Injection site haematoma	0			2 (2.0)	4	4.0	2 (1.3)	4	2.7
Injection site pain	0			2 (2.0)	2	2.0	2 (1.3)	2	1.3
Asthenia	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
Chest discomfort	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Face oedema	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Hyperthermia	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Injection site hypersensitivity	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
Injection site swelling	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Oedema peripheral	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
PFAPA syndrome	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
Pain	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
Peripheral swelling	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Nervous system disorders	4 (8.0)	9	17.7	15 (15.2)	20	20.0	19 (12.8)	29	19.2
Headache	3 (6.0)	8	15.7	13 (13.1)	17	17.0	16 (10.7)	25	16.6
Cognitive disorder	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Dizziness	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Fine motor skill dysfunction	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
Presyncope	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Skin and subcutaneous tissue disorders	4 (8.0)	5	9.8	13 (13.1)	18	18.0	17 (11.4)	23	15.3
Urticaria	1 (2.0)	1	2.0	2 (2.0)	5	5.0	3 (2.0)	6	4.0

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - on-treatment - Male - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Rash	1	(2.0)	2	3.9	1	(1.0)	1	1.0	2	(1.3)	3	2.0
Dermatitis	1	(2.0)	1	2.0	1	(1.0)	1	1.0	2	(1.3)	2	1.3
Erythema	0				2	(2.0)	2	2.0	2	(1.3)	2	1.3
Alopecia	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Dermatitis atopic	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Henoch-Schonlein purpura	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Keratosis pilaris	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Miliaria	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Poikiloderma	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Pruritus	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Psoriasis	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Skin fissures	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Skin lesion	1	(2.0)	1	2.0	0				1	(0.7)	1	0.7
Injury, poisoning and procedural complications	3	(6.0)	4	7.9	13	(13.1)	15	15.0	16	(10.7)	19	12.6
Accidental overdose	2	(4.0)	2	3.9	0				2	(1.3)	2	1.3
Hand fracture	0				2	(2.0)	2	2.0	2	(1.3)	2	1.3
Head injury	0				2	(2.0)	2	2.0	2	(1.3)	2	1.3
Accidental underdose	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Concussion	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Contusion	1	(2.0)	1	2.0	0				1	(0.7)	1	0.7
Eye contusion	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Fall	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Foot fracture	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Joint dislocation	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Medication error	1	(2.0)	1	2.0	0				1	(0.7)	1	0.7
Nasal injury	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Procedural pain	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Skin abrasion	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Skin laceration	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Venomous sting	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Musculoskeletal and connective tissue disorders	3	(6.0)	6	11.8	10	(10.1)	15	15.0	13	(8.7)	21	13.9

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - on-treatment - Male - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Pain in extremity	2	(4.0)	4	7.9	7	(7.1)	9	9.0	9	(6.0)	13	8.6
Arthralgia	1	(2.0)	1	2.0	1	(1.0)	2	2.0	2	(1.3)	3	2.0
Myalgia	0				2	(2.0)	2	2.0	2	(1.3)	2	1.3
Arthritis reactive	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Growing pains	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Musculoskeletal stiffness	1	(2.0)	1	2.0	0				1	(0.7)	1	0.7
Respiratory, thoracic and mediastinal disorders	3	(6.0)	3	5.9	10	(10.1)	15	15.0	13	(8.7)	18	11.9
Cough	1	(2.0)	1	2.0	4	(4.0)	4	4.0	5	(3.4)	5	3.3
Asthma	0				2	(2.0)	3	3.0	2	(1.3)	3	2.0
Respiratory disorder	1	(2.0)	1	2.0	1	(1.0)	1	1.0	2	(1.3)	2	1.3
Upper respiratory tract inflammation	0				2	(2.0)	2	2.0	2	(1.3)	2	1.3
Rhinitis allergic	0				1	(1.0)	2	2.0	1	(0.7)	2	1.3
Adenoidal hypertrophy	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Nasal congestion	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Oropharyngeal pain	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Pneumonitis	1	(2.0)	1	2.0	0				1	(0.7)	1	0.7
Gastrointestinal disorders	4	(8.0)	9	17.7	8	(8.1)	18	18.0	12	(8.1)	27	17.9
Vomiting	2	(4.0)	4	7.9	5	(5.1)	9	9.0	7	(4.7)	13	8.6
Diarrhoea	2	(4.0)	3	5.9	2	(2.0)	2	2.0	4	(2.7)	5	3.3
Constipation	1	(2.0)	1	2.0	1	(1.0)	1	1.0	2	(1.3)	2	1.3
Nausea	1	(2.0)	1	2.0	1	(1.0)	1	1.0	2	(1.3)	2	1.3
Abdominal pain upper	0				1	(1.0)	2	2.0	1	(0.7)	2	1.3
Abdominal pain	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Gastrooesophageal reflux disease	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Toothache	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Metabolism and nutrition disorders	4	(8.0)	4	7.9	5	(5.1)	6	6.0	9	(6.0)	10	6.6
Hyperglycaemia	2	(4.0)	2	3.9	1	(1.0)	1	1.0	3	(2.0)	3	2.0
Hypercholesterolaemia	1	(2.0)	1	2.0	1	(1.0)	1	1.0	2	(1.3)	2	1.3
Dehydration	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Hyperlipidaemia	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7

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Summary of adverse events by system organ class and preferred term - on-treatment - Male - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Impaired fasting glucose	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Iodine deficiency	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Iron deficiency	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
Psychiatric disorders	3 (6.0)	3	5.9	4 (4.0)	4	4.0	7 (4.7)	7	4.6
Tic	1 (2.0)	1	2.0	1 (1.0)	1	1.0	2 (1.3)	2	1.3
Anxiety	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Attention deficit hyperactivity disorder	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
Enuresis	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Generalised anxiety disorder	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
Nightmare	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Endocrine disorders	1 (2.0)	1	2.0	5 (5.1)	5	5.0	6 (4.0)	6	4.0
Hypothyroidism	1 (2.0)	1	2.0	2 (2.0)	2	2.0	3 (2.0)	3	2.0
Secondary hypothyroidism	0			2 (2.0)	2	2.0	2 (1.3)	2	1.3
Adrenocorticotropic hormone deficiency	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Investigations	2 (4.0)	3	5.9	3 (3.0)	4	4.0	5 (3.4)	7	4.6
Aspiration joint	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
Blood glucose increased	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Cortisol decreased	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Low density lipoprotein increased	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
SARS-CoV-2 test positive	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Thyroxine decreased	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
Tri-iodothyronine increased	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7
Eye disorders	1 (2.0)	1	2.0	3 (3.0)	5	5.0	4 (2.7)	6	4.0
Eye irritation	0			1 (1.0)	2	2.0	1 (0.7)	2	1.3
Eye pruritus	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Eyelid cyst	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Hypermetropia	0			1 (1.0)	1	1.0	1 (0.7)	1	0.7
Strabismus	1 (2.0)	1	2.0	0			1 (0.7)	1	0.7

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
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Summary of adverse events by system organ class and preferred term - on-treatment - Male - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Blood and lymphatic system disorders	1	(2.0)	1	2.0	3	(3.0)	3	3.0	4	(2.7)	4	2.7
Lymphadenopathy	0				2	(2.0)	2	2.0	2	(1.3)	2	1.3
Anaemia	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Eosinophilia	1	(2.0)	1	2.0	0				1	(0.7)	1	0.7
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	(2.0)	1	2.0	2	(2.0)	2	2.0	3	(2.0)	3	2.0
Lipoma	1	(2.0)	1	2.0	0				1	(0.7)	1	0.7
Lymphangioma	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Skin papilloma	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Immune system disorders	1	(2.0)	1	2.0	1	(1.0)	1	1.0	2	(1.3)	2	1.3
Food allergy	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Seasonal allergy	1	(2.0)	1	2.0	0				1	(0.7)	1	0.7
Reproductive system and breast disorders	0				2	(2.0)	2	2.0	2	(1.3)	2	1.3
Balanoposthitis	0				2	(2.0)	2	2.0	2	(1.3)	2	1.3
Ear and labyrinth disorders	0				1	(1.0)	2	2.0	1	(0.7)	2	1.3
Cerumen impaction	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Tinnitus	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Congenital, familial and genetic disorders	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7
Cryptorchism	0				1	(1.0)	1	1.0	1	(0.7)	1	0.7

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26: Summary of adverse events - on-treatment - Female - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	18			33			51		
Total patient years at risk	18.3			33.6			51.9		
All adverse events	15	(83.3)	53 290.3	25	(75.8)	86 256.0	40	(78.4)	139 268.1
Serious adverse events									
Yes	2	(11.1)	3 16.4	1	(3.0)	1 3.0	3	(5.9)	4 7.7
No	15	(83.3)	50 273.9	25	(75.8)	85 253.0	40	(78.4)	135 260.4
Severity									
Mild	11	(61.1)	35 191.7	24	(72.7)	67 199.4	35	(68.6)	102 196.7
Moderate	7	(38.9)	17 93.1	7	(21.2)	15 44.6	14	(27.5)	32 61.7
Severe	1	(5.6)	1 5.5	1	(3.0)	4 11.9	2	(3.9)	5 9.6
Causality									
Probable	1	(5.6)	1 5.5	3	(9.1)	3 8.9	4	(7.8)	4 7.7
Possible	4	(22.2)	9 49.3	9	(27.3)	22 65.5	13	(25.5)	31 59.8
Unlikely	14	(77.8)	43 235.5	23	(69.7)	61 181.6	37	(72.5)	104 200.6
Missing	0			0			0		
Action taken to trial product due to AE									
Drug interrupted	3	(16.7)	3 16.4	0			3	(5.9)	3 5.8
Drug withdrawn	0			0			0		
Dose reduced	1	(5.6)	5 27.4	0			1	(2.0)	5 9.6
Dose increased	0			0			0		
Dose not changed	13	(72.2)	40 219.1	24	(72.7)	82 244.1	37	(72.5)	122 235.3
Unknown	0			0			0		
Missing	0			0			0		
Related to technical complaint									
Yes	0			0			0		
No	15	(83.3)	53 290.3	25	(75.8)	86 256.0	40	(78.4)	139 268.1
Injection site reaction									
Yes	2	(11.1)	2 11.0	0			2	(3.9)	2 3.9

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
AE causality is based on judgement of investigators.

Summary of adverse events - on-treatment - Female - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
No	15 (83.3)	51	279.4	25 (75.8)	86	256.0	40 (78.4)	137	264.2
Outcome									
Recovered/resolved	15 (83.3)	48	262.9	22 (66.7)	71	211.3	37 (72.5)	119	229.5
Recovering/resolving	1 (5.6)	1	5.5	1 (3.0)	1	3.0	2 (3.9)	2	3.9
Recovered/resolved with sequelae	0			1 (3.0)	1	3.0	1 (2.0)	1	1.9
Not recovered/not resolved	4 (22.2)	4	21.9	9 (27.3)	10	29.8	13 (25.5)	14	27.0
Fatal	0			0			0		
Unknown	0			1 (3.0)	3	8.9	1 (2.0)	3	5.8
Missing	0			0			0		
Treatment									
Treatment discontinuations due to adverse events	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
AE causality is based on judgement of investigators.

27: Summary of adverse events by system organ class and preferred term - on-treatment - Female - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	18			33			51		
Total patient years at risk	18.3			33.6			51.9		
Events	15	(83.3)	53 290.3	25	(75.8)	86 256.0	40	(78.4)	139 268.1
Infections and infestations	9	(50.0)	21 115.0	13	(39.4)	23 68.5	22	(43.1)	44 84.9
Nasopharyngitis	3	(16.7)	7 38.3	6	(18.2)	10 29.8	9	(17.6)	17 32.8
Bronchitis	3	(16.7)	3 16.4	0			3	(5.9)	3 5.8
Rhinitis	2	(11.1)	2 11.0	1	(3.0)	1 3.0	3	(5.9)	3 5.8
Otitis media	2	(11.1)	2 11.0	0			2	(3.9)	2 3.9
Otitis media acute	0			2	(6.1)	2 6.0	2	(3.9)	2 3.9
Respiratory tract infection	1	(5.6)	1 5.5	1	(3.0)	1 3.0	2	(3.9)	2 3.9
COVID-19	1	(5.6)	1 5.5	0			1	(2.0)	1 1.9
Eye infection	1	(5.6)	1 5.5	0			1	(2.0)	1 1.9
Fungal infection	0			1	(3.0)	1 3.0	1	(2.0)	1 1.9
Gastroenteritis	1	(5.6)	1 5.5	0			1	(2.0)	1 1.9
Gastroenteritis viral	0			1	(3.0)	1 3.0	1	(2.0)	1 1.9
Hordeolum	0			1	(3.0)	1 3.0	1	(2.0)	1 1.9
Influenza	0			1	(3.0)	1 3.0	1	(2.0)	1 1.9
Molluscum contagiosum	0			1	(3.0)	1 3.0	1	(2.0)	1 1.9
Paronychia	1	(5.6)	1 5.5	0			1	(2.0)	1 1.9
Pharyngitis streptococcal	0			1	(3.0)	1 3.0	1	(2.0)	1 1.9
Tonsillitis	1	(5.6)	1 5.5	0			1	(2.0)	1 1.9
Tracheitis	0			1	(3.0)	1 3.0	1	(2.0)	1 1.9
Upper respiratory tract infection	0			1	(3.0)	1 3.0	1	(2.0)	1 1.9
Urinary tract infection	0			1	(3.0)	1 3.0	1	(2.0)	1 1.9
Viral infection	1	(5.6)	1 5.5	0			1	(2.0)	1 1.9
General disorders and administration site conditions	4	(22.2)	4 21.9	7	(21.2)	13 38.7	11	(21.6)	17 32.8
Pyrexia	2	(11.1)	2 11.0	3	(9.1)	4 11.9	5	(9.8)	6 11.6
Swelling face	0			3	(9.1)	3 8.9	3	(5.9)	3 5.8
Fatigue	0			2	(6.1)	4 11.9	2	(3.9)	4 7.7

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Summary of adverse events by system organ class and preferred term - on-treatment - Female - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Injection site bruising	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Injection site pain	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Local reaction	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Swelling	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Gastrointestinal disorders	3	(16.7)	5	27.4	6	(18.2)	11	32.7	9	(17.6)	16	30.9
Constipation	0				3	(9.1)	4	11.9	3	(5.9)	4	7.7
Vomiting	2	(11.1)	2	11.0	1	(3.0)	1	3.0	3	(5.9)	3	5.8
Abdominal pain upper	1	(5.6)	1	5.5	1	(3.0)	2	6.0	2	(3.9)	3	5.8
Abdominal pain	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Diarrhoea	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Gastritis	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Haematochezia	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Nausea	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Umbilical hernia	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Nervous system disorders	3	(16.7)	4	21.9	4	(12.1)	6	17.9	7	(13.7)	10	19.3
Headache	3	(16.7)	3	16.4	3	(9.1)	5	14.9	6	(11.8)	8	15.4
Dizziness	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Somnolence	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Musculoskeletal and connective tissue disorders	1	(5.6)	2	11.0	5	(15.2)	9	26.8	6	(11.8)	11	21.2
Pain in extremity	0				5	(15.2)	8	23.8	5	(9.8)	8	15.4
Arthralgia	1	(5.6)	1	5.5	1	(3.0)	1	3.0	2	(3.9)	2	3.9
Neck pain	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Respiratory, thoracic and mediastinal disorders	2	(11.1)	5	27.4	3	(9.1)	5	14.9	5	(9.8)	10	19.3
Cough	1	(5.6)	1	5.5	2	(6.1)	3	8.9	3	(5.9)	4	7.7
Oropharyngeal pain	1	(5.6)	2	11.0	1	(3.0)	1	3.0	2	(3.9)	3	5.8
Asthma	1	(5.6)	2	11.0	0				1	(2.0)	2	3.9
Rhinorrhoea	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Investigations	1	(5.6)	1	5.5	4	(12.1)	4	11.9	5	(9.8)	5	9.6

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - on-treatment - Female - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Blood cholesterol abnormal	0			1 (3.0)	1	3.0	1 (2.0)	1	1.9
Blood creatine phosphokinase increased	0			1 (3.0)	1	3.0	1 (2.0)	1	1.9
Blood thyroid stimulating hormone increased	0			1 (3.0)	1	3.0	1 (2.0)	1	1.9
Glycosylated haemoglobin increased	1 (5.6)	1	5.5	0			1 (2.0)	1	1.9
Low density lipoprotein increased	0			1 (3.0)	1	3.0	1 (2.0)	1	1.9
Skin and subcutaneous tissue disorders	1 (5.6)	1	5.5	4 (12.1)	4	11.9	5 (9.8)	5	9.6
Dermatitis atopic	0			1 (3.0)	1	3.0	1 (2.0)	1	1.9
Dry skin	0			1 (3.0)	1	3.0	1 (2.0)	1	1.9
Lipodystrophy acquired	0			1 (3.0)	1	3.0	1 (2.0)	1	1.9
Pruritus	0			1 (3.0)	1	3.0	1 (2.0)	1	1.9
Urticaria	1 (5.6)	1	5.5	0			1 (2.0)	1	1.9
Endocrine disorders	1 (5.6)	1	5.5	3 (9.1)	3	8.9	4 (7.8)	4	7.7
Hypothyroidism	0			2 (6.1)	2	6.0	2 (3.9)	2	3.9
Adrenocortical insufficiency acute	1 (5.6)	1	5.5	0			1 (2.0)	1	1.9
Secondary adrenocortical insufficiency	0			1 (3.0)	1	3.0	1 (2.0)	1	1.9
Blood and lymphatic system disorders	2 (11.1)	2	11.0	1 (3.0)	1	3.0	3 (5.9)	3	5.8
Iron deficiency anaemia	1 (5.6)	1	5.5	1 (3.0)	1	3.0	2 (3.9)	2	3.9
Hypochromic anaemia	1 (5.6)	1	5.5	0			1 (2.0)	1	1.9
Injury, poisoning and procedural complications	1 (5.6)	1	5.5	2 (6.1)	2	6.0	3 (5.9)	3	5.8
Accidental overdose	0			1 (3.0)	1	3.0	1 (2.0)	1	1.9
Contusion	0			1 (3.0)	1	3.0	1 (2.0)	1	1.9
Lower limb fracture	1 (5.6)	1	5.5	0			1 (2.0)	1	1.9

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - on-treatment - Female - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Metabolism and nutrition disorders	1	(5.6)	1	5.5	2	(6.1)	2	6.0	3	(5.9)	3	5.8
Dyslipidaemia	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Hypercholesterolaemia	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Zinc deficiency	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Eye disorders	1	(5.6)	2	11.0	1	(3.0)	1	3.0	2	(3.9)	3	5.8
Eye pain	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Periorbital oedema	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Vision blurred	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Ear and labyrinth disorders	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Ear pain	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Immune system disorders	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Seasonal allergy	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Skin papilloma	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Psychiatric disorders	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Sleep disorder	0				1	(3.0)	1	3.0	1	(2.0)	1	1.9
Vascular disorders	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9
Hot flush	1	(5.6)	1	5.5	0				1	(2.0)	1	1.9

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

28: Summary of adverse events - on-treatment - age < 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	33			64			97		
Total patient years at risk	33.5			64.1			97.5		
All adverse events	20	(60.6)	80 239.2	46	(71.9)	181 282.4	66	(68.0)	261 267.6
Serious adverse events									
Yes	1	(3.0)	2 6.0	3	(4.7)	4 6.2	4	(4.1)	6 6.2
No	20	(60.6)	78 233.2	46	(71.9)	177 276.2	66	(68.0)	255 261.4
Severity									
Mild	16	(48.5)	63 188.3	44	(68.8)	150 234.1	60	(61.9)	213 218.4
Moderate	7	(21.2)	17 50.8	13	(20.3)	26 40.6	20	(20.6)	43 44.1
Severe	0			2	(3.1)	5 7.8	2	(2.1)	5 5.1
Causality									
Probable	0			6	(9.4)	9 14.0	6	(6.2)	9 9.2
Possible	3	(9.1)	4 12.0	14	(21.9)	32 49.9	17	(17.5)	36 36.9
Unlikely	20	(60.6)	76 227.2	44	(68.8)	140 218.5	64	(66.0)	216 221.5
Missing	0			0			0		
Action taken to trial product due to AE									
Drug interrupted	2	(6.1)	2 6.0	1	(1.6)	1 1.6	3	(3.1)	3 3.1
Drug withdrawn	0			0			0		
Dose reduced	0			1	(1.6)	1 1.6	1	(1.0)	1 1.0
Dose increased	0			0			0		
Dose not changed	19	(57.6)	74 221.2	46	(71.9)	169 263.7	65	(67.0)	243 249.1
Unknown	0			0			0		
Missing	0			0			0		
Related to technical complaint									
Yes	0			0			0		
No	20	(60.6)	80 239.2	46	(71.9)	181 282.4	66	(68.0)	261 267.6
Injection site reaction									
Yes	0			1	(1.6)	1 1.6	1	(1.0)	1 1.0

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
AE causality is based on judgement of investigators.

Summary of adverse events - on-treatment - age < 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
No	20 (60.6)	80	239.2	46 (71.9)	180	280.9	66 (68.0)	260	266.6
Outcome									
Recovered/resolved	20 (60.6)	70	209.3	44 (68.8)	139	216.9	64 (66.0)	209	214.3
Recovering/resolving	0			4 (6.3)	6	9.4	4 (4.1)	6	6.2
Recovered/resolved with sequelae	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Not recovered/not resolved	7 (21.2)	10	29.9	20 (31.3)	32	49.9	27 (27.8)	42	43.1
Fatal	0			0			0		
Unknown	0			1 (1.6)	3	4.7	1 (1.0)	3	3.1
Missing	0			0			0		
Treatment									
Treatment discontinuations due to adverse events	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
AE causality is based on judgement of investigators.

29: Summary of adverse events by system organ class and preferred term - on-treatment - age < 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	33			64			97		
Total patient years at risk	33.5			64.1			97.5		
Events	20	(60.6)	80 239.2	46	(71.9)	181 282.4	66	(68.0)	261 267.6
Infections and infestations	17	(51.5)	34 101.6	28	(43.8)	54 84.3	45	(46.4)	88 90.2
Nasopharyngitis	7	(21.2)	13 38.9	9	(14.1)	13 20.3	16	(16.5)	26 26.7
Bronchitis	5	(15.2)	5 14.9	1	(1.6)	3 4.7	6	(6.2)	8 8.2
Rhinitis	2	(6.1)	3 9.0	4	(6.3)	5 7.8	6	(6.2)	8 8.2
Molluscum contagiosum	2	(6.1)	2 6.0	2	(3.1)	2 3.1	4	(4.1)	4 4.1
Otitis media	2	(6.1)	2 6.0	2	(3.1)	2 3.1	4	(4.1)	4 4.1
Upper respiratory tract infection	0			3	(4.7)	5 7.8	3	(3.1)	5 5.1
Respiratory tract infection	0			3	(4.7)	3 4.7	3	(3.1)	3 3.1
Pharyngitis streptococcal	1	(3.0)	2 6.0	1	(1.6)	1 1.6	2	(2.1)	3 3.1
Ear infection	0			2	(3.1)	2 3.1	2	(2.1)	2 2.1
Hand-foot-and-mouth disease	0			2	(3.1)	2 3.1	2	(2.1)	2 2.1
Influenza	1	(3.0)	1 3.0	1	(1.6)	1 1.6	2	(2.1)	2 2.1
Tonsillitis	1	(3.0)	1 3.0	1	(1.6)	1 1.6	2	(2.1)	2 2.1
Viral infection	1	(3.0)	1 3.0	1	(1.6)	1 1.6	2	(2.1)	2 2.1
Acute sinusitis	0			1	(1.6)	1 1.6	1	(1.0)	1 1.0
Eye infection	1	(3.0)	1 3.0	0			1	(1.0)	1 1.0
Gastroenteritis	1	(3.0)	1 3.0	0			1	(1.0)	1 1.0
Herpangina	0			1	(1.6)	1 1.6	1	(1.0)	1 1.0
Hordeolum	1	(3.0)	1 3.0	0			1	(1.0)	1 1.0
Infection parasitic	0			1	(1.6)	1 1.6	1	(1.0)	1 1.0
Latent tuberculosis	0			1	(1.6)	1 1.6	1	(1.0)	1 1.0
Otitis media acute	0			1	(1.6)	1 1.6	1	(1.0)	1 1.0
Paronychia	1	(3.0)	1 3.0	0			1	(1.0)	1 1.0
Pharyngitis	0			1	(1.6)	1 1.6	1	(1.0)	1 1.0
Pneumonia	0			1	(1.6)	1 1.6	1	(1.0)	1 1.0
Respiratory tract infection viral	0			1	(1.6)	1 1.6	1	(1.0)	1 1.0
Sinusitis	0			1	(1.6)	1 1.6	1	(1.0)	1 1.0
Tonsillitis streptococcal	0			1	(1.6)	1 1.6	1	(1.0)	1 1.0

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
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Summary of adverse events by system organ class and preferred term - on-treatment - age < 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Tracheitis	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Urinary tract infection	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Viral upper respiratory tract infection	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
General disorders and administration site conditions	4	(12.1)	12	35.9	15	(23.4)	28	43.7	19	(19.6)	40	41.0
Pyrexia	4	(12.1)	9	26.9	9	(14.1)	13	20.3	13	(13.4)	22	22.6
Swelling face	0				3	(4.7)	3	4.7	3	(3.1)	3	3.1
Fatigue	0				2	(3.1)	4	6.2	2	(2.1)	4	4.1
Injection site haematoma	0				1	(1.6)	3	4.7	1	(1.0)	3	3.1
Asthenia	1	(3.0)	1	3.0	0				1	(1.0)	1	1.0
Face oedema	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Hyperthermia	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Injection site pain	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Injection site swelling	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
PFAPA syndrome	1	(3.0)	1	3.0	0				1	(1.0)	1	1.0
Pain	1	(3.0)	1	3.0	0				1	(1.0)	1	1.0
Peripheral swelling	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Skin and subcutaneous tissue disorders	4	(12.1)	5	14.9	11	(17.2)	13	20.3	15	(15.5)	18	18.5
Urticaria	2	(6.1)	2	6.0	1	(1.6)	1	1.6	3	(3.1)	3	3.1
Rash	1	(3.0)	2	6.0	1	(1.6)	1	1.6	2	(2.1)	3	3.1
Dermatitis	1	(3.0)	1	3.0	1	(1.6)	1	1.6	2	(2.1)	2	2.1
Erythema	0				2	(3.1)	2	3.1	2	(2.1)	2	2.1
Dermatitis atopic	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Dry skin	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Henoch-Schonlein purpura	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Lipodystrophy acquired	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Poikiloderma	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Pruritus	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Psoriasis	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0
Skin fissures	0				1	(1.6)	1	1.6	1	(1.0)	1	1.0

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
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Summary of adverse events by system organ class and preferred term - on-treatment - age < 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Musculoskeletal and connective tissue disorders	2 (6.1)	4	12.0	9 (14.1)	18	28.1	11 (11.3)	22	22.6
Pain in extremity	1 (3.0)	2	6.0	8 (12.5)	13	20.3	9 (9.3)	15	15.4
Arthralgia	1 (3.0)	1	3.0	2 (3.1)	3	4.7	3 (3.1)	4	4.1
Arthritis reactive	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Myalgia	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Neck pain	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
Respiratory, thoracic and mediastinal disorders	2 (6.1)	5	14.9	9 (14.1)	15	23.4	11 (11.3)	20	20.5
Cough	1 (3.0)	1	3.0	4 (6.3)	5	7.8	5 (5.2)	6	6.2
Asthma	1 (3.0)	2	6.0	2 (3.1)	3	4.7	3 (3.1)	5	5.1
Oropharyngeal pain	1 (3.0)	2	6.0	1 (1.6)	1	1.6	2 (2.1)	3	3.1
Upper respiratory tract inflammation	0			2 (3.1)	2	3.1	2 (2.1)	2	2.1
Adenoidal hypertrophy	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Nasal congestion	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Respiratory disorder	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Rhinorrhoea	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Nervous system disorders	2 (6.1)	2	6.0	7 (10.9)	9	14.0	9 (9.3)	11	11.3
Headache	1 (3.0)	1	3.0	6 (9.4)	8	12.5	7 (7.2)	9	9.2
Fine motor skill dysfunction	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
Somnolence	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Gastrointestinal disorders	3 (9.1)	5	14.9	5 (7.8)	9	14.0	8 (8.2)	14	14.4
Constipation	1 (3.0)	1	3.0	2 (3.1)	2	3.1	3 (3.1)	3	3.1
Diarrhoea	1 (3.0)	2	6.0	1 (1.6)	1	1.6	2 (2.1)	3	3.1
Vomiting	1 (3.0)	1	3.0	1 (1.6)	1	1.6	2 (2.1)	2	2.1
Abdominal pain upper	0			1 (1.6)	2	3.1	1 (1.0)	2	2.1
Abdominal pain	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Haematochezia	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
Nausea	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Umbilical hernia	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - on-treatment - age < 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Metabolism and nutrition disorders	3 (9.1)	3	9.0	5 (7.8)	6	9.4	8 (8.2)	9	9.2
Hypercholesterolaemia	1 (3.0)	1	3.0	2 (3.1)	2	3.1	3 (3.1)	3	3.1
Hyperglycaemia	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Hyperlipidaemia	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Impaired fasting glucose	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Iodine deficiency	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Iron deficiency	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
Zinc deficiency	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
Injury, poisoning and procedural complications	1 (3.0)	1	3.0	7 (10.9)	7	10.9	8 (8.2)	8	8.2
Accidental overdose	1 (3.0)	1	3.0	1 (1.6)	1	1.6	2 (2.1)	2	2.1
Contusion	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Eye contusion	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Fall	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Joint dislocation	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Nasal injury	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Skin laceration	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Blood and lymphatic system disorders	2 (6.1)	2	6.0	4 (6.3)	4	6.2	6 (6.2)	6	6.2
Iron deficiency anaemia	1 (3.0)	1	3.0	1 (1.6)	1	1.6	2 (2.1)	2	2.1
Lymphadenopathy	0			2 (3.1)	2	3.1	2 (2.1)	2	2.1
Anaemia	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Hypochromic anaemia	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
Investigations	2 (6.1)	2	6.0	4 (6.3)	4	6.2	6 (6.2)	6	6.2
Low density lipoprotein increased	0			2 (3.1)	2	3.1	2 (2.1)	2	2.1
Aspiration joint	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
Blood thyroid stimulating hormone increased	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Glycosylated haemoglobin increased	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
SARS-CoV-2 test positive	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
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Summary of adverse events by system organ class and preferred term - on-treatment - age < 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Eye disorders	1 (3.0)	1	3.0	4 (6.3)	6	9.4	5 (5.2)	7	7.2
Eye irritation	0			1 (1.6)	2	3.1	1 (1.0)	2	2.1
Eye pruritus	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Eyelid cyst	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Hypermetropia	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Periorbital oedema	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Strabismus	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
Endocrine disorders	1 (3.0)	1	3.0	3 (4.7)	3	4.7	4 (4.1)	4	4.1
Adrenocortical insufficiency acute	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
Hypothyroidism	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Secondary adrenocortical insufficiency	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Secondary hypothyroidism	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Immune system disorders	1 (3.0)	1	3.0	2 (3.1)	2	3.1	3 (3.1)	3	3.1
Seasonal allergy	1 (3.0)	1	3.0	1 (1.6)	1	1.6	2 (2.1)	2	2.1
Food allergy	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Psychiatric disorders	1 (3.0)	1	3.0	1 (1.6)	1	1.6	2 (2.1)	2	2.1
Sleep disorder	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Tic	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
Ear and labyrinth disorders	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
Ear pain	1 (3.0)	1	3.0	0			1 (1.0)	1	1.0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Skin papilloma	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Reproductive system and breast disorders	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0
Balanoposthitis	0			1 (1.6)	1	1.6	1 (1.0)	1	1.0

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30: Summary of adverse events - on-treatment - age >= 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	35			68			103		
Total patient years at risk	35.6			69.4			105.0		
All adverse events	21	(60.0)	67 188.0	48	(70.6)	129 186.0	69	(67.0)	196 186.7
Serious adverse events									
Yes	1	(2.9)	1 2.8	3	(4.4)	4 5.8	4	(3.9)	5 4.8
No	21	(60.0)	66 185.2	47	(69.1)	125 180.2	68	(66.0)	191 181.9
Severity									
Mild	19	(54.3)	56 157.1	43	(63.2)	103 148.5	62	(60.2)	159 151.4
Moderate	5	(14.3)	10 28.1	14	(20.6)	24 34.6	19	(18.4)	34 32.4
Severe	1	(2.9)	1 2.8	2	(2.9)	2 2.9	3	(2.9)	3 2.9
Causality									
Probable	4	(11.4)	5 14.0	6	(8.8)	7 10.1	10	(9.7)	12 11.4
Possible	6	(17.1)	17 47.7	6	(8.8)	13 18.7	12	(11.7)	30 28.6
Unlikely	18	(51.4)	45 126.3	46	(67.6)	109 157.1	64	(62.1)	154 146.7
Missing	0			0			0		
Action taken to trial product due to AE									
Drug interrupted	3	(8.6)	3 8.4	1	(1.5)	1 1.4	4	(3.9)	4 3.8
Drug withdrawn	0			0			0		
Dose reduced	2	(5.7)	6 16.8	0			2	(1.9)	6 5.7
Dose increased	0			1	(1.5)	1 1.4	1	(1.0)	1 1.0
Dose not changed	19	(54.3)	55 154.3	43	(63.2)	111 160.0	62	(60.2)	166 158.1
Unknown	0			2	(2.9)	2 2.9	2	(1.9)	2 1.9
Missing	0			0			0		
Related to technical complaint									
Yes	1	(2.9)	1 2.8	0			1	(1.0)	1 1.0
No	21	(60.0)	66 185.2	48	(70.6)	129 186.0	69	(67.0)	195 185.7
Injection site reaction									
Yes	3	(8.6)	3 8.4	1	(1.5)	1 1.4	4	(3.9)	4 3.8

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
AE causality is based on judgement of investigators.

Summary of adverse events - on-treatment - age >= 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
No	21 (60.0)	64	179.6	48 (70.6)	128	184.5	69 (67.0)	192	182.9
Outcome									
Recovered/resolved	20 (57.1)	60	168.4	45 (66.2)	104	149.9	65 (63.1)	164	156.2
Recovering/resolving	1 (2.9)	1	2.8	1 (1.5)	3	4.3	2 (1.9)	4	3.8
Recovered/resolved with sequelae	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Not recovered/not resolved	4 (11.4)	5	14.0	14 (20.6)	22	31.7	18 (17.5)	27	25.7
Fatal	0			0			0		
Unknown	0			0			0		
Missing	0			0			0		
Treatment									
Treatment discontinuations due to adverse events	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
AE causality is based on judgement of investigators.

31: Summary of adverse events by system organ class and preferred term - on-treatment - age >= 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	35			68			103		
Total patient years at risk	35.6			69.4			105.0		
Events	21	(60.0)	67 188.0	48	(70.6)	129 186.0	69	(67.0)	196 186.7
Infections and infestations	10	(28.6)	14 39.3	22	(32.4)	34 49.0	32	(31.1)	48 45.7
Nasopharyngitis	0			6	(8.8)	9 13.0	6	(5.8)	9 8.6
COVID-19	3	(8.6)	3 8.4	3	(4.4)	3 4.3	6	(5.8)	6 5.7
Respiratory tract infection	2	(5.7)	2 5.6	1	(1.5)	3 4.3	3	(2.9)	5 4.8
Bronchitis	0			3	(4.4)	3 4.3	3	(2.9)	3 2.9
Influenza	1	(2.9)	1 2.8	2	(2.9)	2 2.9	3	(2.9)	3 2.9
Tooth abscess	2	(5.7)	2 5.6	1	(1.5)	1 1.4	3	(2.9)	3 2.9
Gastroenteritis viral	0			2	(2.9)	2 2.9	2	(1.9)	2 1.9
Rhinitis	1	(2.9)	1 2.8	1	(1.5)	1 1.4	2	(1.9)	2 1.9
Viral infection	0			1	(1.5)	3 4.3	1	(1.0)	3 2.9
Ear infection	1	(2.9)	1 2.8	0			1	(1.0)	1 1.0
Enteritis infectious	1	(2.9)	1 2.8	0			1	(1.0)	1 1.0
Fungal infection	0			1	(1.5)	1 1.4	1	(1.0)	1 1.0
Gastrointestinal viral infection	0			1	(1.5)	1 1.4	1	(1.0)	1 1.0
Herpes dermatitis	1	(2.9)	1 2.8	0			1	(1.0)	1 1.0
Hordeolum	0			1	(1.5)	1 1.4	1	(1.0)	1 1.0
Impetigo	0			1	(1.5)	1 1.4	1	(1.0)	1 1.0
Infection	0			1	(1.5)	1 1.4	1	(1.0)	1 1.0
Molluscum contagiosum	1	(2.9)	1 2.8	0			1	(1.0)	1 1.0
Otitis media acute	0			1	(1.5)	1 1.4	1	(1.0)	1 1.0
Streptococcal infection	0			1	(1.5)	1 1.4	1	(1.0)	1 1.0
Upper respiratory tract infection	1	(2.9)	1 2.8	0			1	(1.0)	1 1.0
Nervous system disorders	5	(14.3)	11 30.9	12	(17.6)	17 24.5	17	(16.5)	28 26.7
Headache	5	(14.3)	10 28.1	10	(14.7)	14 20.2	15	(14.6)	24 22.9
Dizziness	1	(2.9)	1 2.8	1	(1.5)	1 1.4	2	(1.9)	2 1.9
Cognitive disorder	0			1	(1.5)	1 1.4	1	(1.0)	1 1.0
Presyncope	0			1	(1.5)	1 1.4	1	(1.0)	1 1.0

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Summary of adverse events by system organ class and preferred term - on-treatment - age >= 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
General disorders and administration site conditions	7	(20.0)	8	22.4	8	(11.8)	8	11.5	15	(14.6)	16	15.2
Injection site bruising	2	(5.7)	2	5.6	2	(2.9)	2	2.9	4	(3.9)	4	3.8
Pyrexia	3	(8.6)	3	8.4	1	(1.5)	1	1.4	4	(3.9)	4	3.8
Injection site pain	1	(2.9)	1	2.8	1	(1.5)	1	1.4	2	(1.9)	2	1.9
Chest discomfort	0				1	(1.5)	1	1.4	1	(1.0)	1	1.0
Injection site haematoma	0				1	(1.5)	1	1.4	1	(1.0)	1	1.0
Injection site hypersensitivity	1	(2.9)	1	2.8	0				1	(1.0)	1	1.0
Local reaction	0				1	(1.5)	1	1.4	1	(1.0)	1	1.0
Oedema peripheral	1	(2.9)	1	2.8	0				1	(1.0)	1	1.0
Swelling	0				1	(1.5)	1	1.4	1	(1.0)	1	1.0
Gastrointestinal disorders	4	(11.4)	9	25.3	9	(13.2)	20	28.8	13	(12.6)	29	27.6
Vomiting	3	(8.6)	5	14.0	5	(7.4)	9	13.0	8	(7.8)	14	13.3
Diarrhoea	1	(2.9)	1	2.8	2	(2.9)	2	2.9	3	(2.9)	3	2.9
Abdominal pain upper	1	(2.9)	1	2.8	1	(1.5)	2	2.9	2	(1.9)	3	2.9
Constipation	0				2	(2.9)	3	4.3	2	(1.9)	3	2.9
Nausea	1	(2.9)	1	2.8	1	(1.5)	1	1.4	2	(1.9)	2	1.9
Abdominal pain	0				1	(1.5)	1	1.4	1	(1.0)	1	1.0
Gastritis	1	(2.9)	1	2.8	0				1	(1.0)	1	1.0
Gastrooesophageal reflux disease	0				1	(1.5)	1	1.4	1	(1.0)	1	1.0
Toothache	0				1	(1.5)	1	1.4	1	(1.0)	1	1.0
Injury, poisoning and procedural complications	3	(8.6)	4	11.2	8	(11.8)	10	14.4	11	(10.7)	14	13.3
Hand fracture	0				2	(2.9)	2	2.9	2	(1.9)	2	1.9
Head injury	0				2	(2.9)	2	2.9	2	(1.9)	2	1.9
Accidental overdose	1	(2.9)	1	2.8	0				1	(1.0)	1	1.0
Accidental underdose	0				1	(1.5)	1	1.4	1	(1.0)	1	1.0
Concussion	0				1	(1.5)	1	1.4	1	(1.0)	1	1.0
Contusion	1	(2.9)	1	2.8	0				1	(1.0)	1	1.0
Foot fracture	0				1	(1.5)	1	1.4	1	(1.0)	1	1.0
Lower limb fracture	1	(2.9)	1	2.8	0				1	(1.0)	1	1.0
Medication error	1	(2.9)	1	2.8	0				1	(1.0)	1	1.0

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	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Procedural pain	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Skin abrasion	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Venomous sting	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Musculoskeletal and connective tissue disorders	2 (5.7)	4	11.2	6 (8.8)	6	8.7	8 (7.8)	10	9.5
Pain in extremity	1 (2.9)	2	5.6	4 (5.9)	4	5.8	5 (4.9)	6	5.7
Arthralgia	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Growing pains	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Musculoskeletal stiffness	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Myalgia	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Skin and subcutaneous tissue disorders	1 (2.9)	1	2.8	6 (8.8)	9	13.0	7 (6.8)	10	9.5
Urticaria	0			1 (1.5)	4	5.8	1 (1.0)	4	3.8
Alopecia	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Dermatitis atopic	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Keratosis pilaris	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Miliaria	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Pruritus	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Skin lesion	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Respiratory, thoracic and mediastinal disorders	3 (8.6)	3	8.4	4 (5.9)	5	7.2	7 (6.8)	8	7.6
Cough	1 (2.9)	1	2.8	2 (2.9)	2	2.9	3 (2.9)	3	2.9
Rhinitis allergic	0			1 (1.5)	2	2.9	1 (1.0)	2	1.9
Oropharyngeal pain	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Pneumonitis	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Respiratory disorder	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Endocrine disorders	1 (2.9)	1	2.8	5 (7.4)	5	7.2	6 (5.8)	6	5.7
Hypothyroidism	1 (2.9)	1	2.8	3 (4.4)	3	4.3	4 (3.9)	4	3.8
Adrenocorticotropic hormone deficiency	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Secondary hypothyroidism	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0

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Summary of adverse events by system organ class and preferred term - on-treatment - age >= 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Psychiatric disorders	2 (5.7)	2	5.6	4 (5.9)	4	5.8	6 (5.8)	6	5.7
Anxiety	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Attention deficit hyperactivity disorder	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Enuresis	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Generalised anxiety disorder	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Nightmare	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Tic	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Investigations	1 (2.9)	2	5.6	3 (4.4)	4	5.8	4 (3.9)	6	5.7
Blood cholesterol abnormal	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Blood creatine phosphokinase increased	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Blood glucose increased	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Cortisol decreased	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Thyroxine decreased	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Tri-iodothyronine increased	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Metabolism and nutrition disorders	2 (5.7)	2	5.6	2 (2.9)	2	2.9	4 (3.9)	4	3.8
Hyperglycaemia	2 (5.7)	2	5.6	0			2 (1.9)	2	1.9
Dehydration	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Dyslipidaemia	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (5.7)	2	5.6	1 (1.5)	1	1.4	3 (2.9)	3	2.9
Lipoma	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Lymphangioma	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Skin papilloma	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Ear and labyrinth disorders	0			1 (1.5)	2	2.9	1 (1.0)	2	1.9
Cerumen impaction	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Tinnitus	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Eye disorders	1 (2.9)	2	5.6	0			1 (1.0)	2	1.9

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - on-treatment - age >= 6 - trial 4263 - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Eye pain	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Vision blurred	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Blood and lymphatic system disorders	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Eosinophilia	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Congenital, familial and genetic disorders	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Cryptorchism	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Reproductive system and breast disorders	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Balanoposthitis	0			1 (1.5)	1	1.4	1 (1.0)	1	1.0
Vascular disorders	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0
Hot flush	1 (2.9)	1	2.8	0			1 (1.0)	1	1.0

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

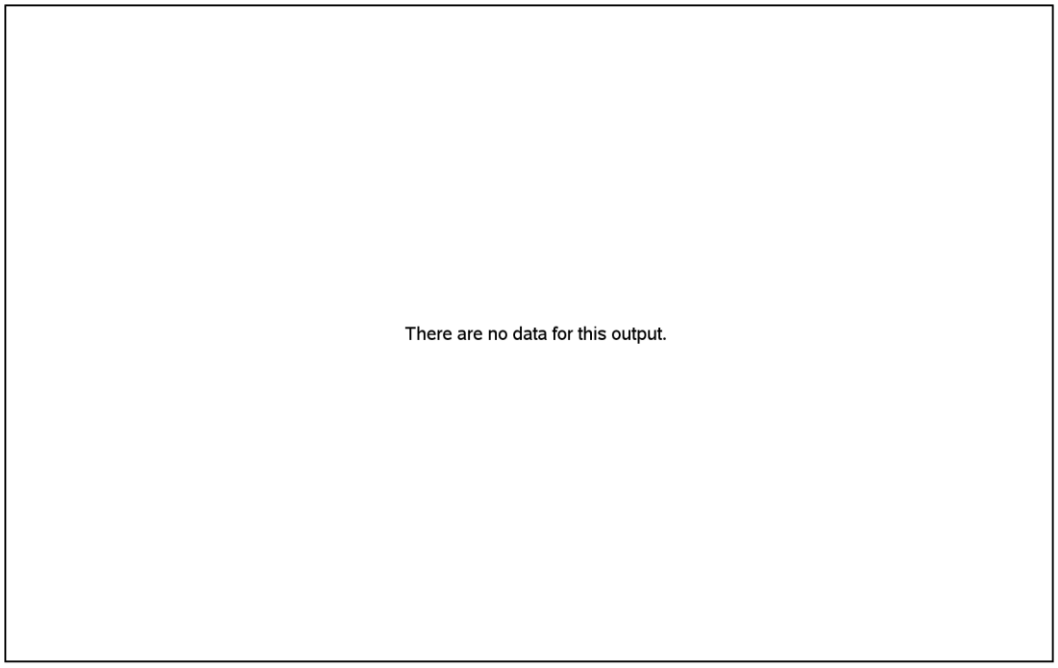
32: Listing of laboratory test results - subjects with one measurement of fasting glucose >=7.0 mmol/L or HbA1c >=6.5 % - glucose metabolism - safety analysis set

Treatment group/ Subject ID	Sex (M/F)/ Age (yrs)/ BMI (kg/m^2)	Visit	On treatment (Y/N)	Fasting (Y/N)	Fasting plasma glucose (mmol/L)	@	Fasting insulin (pmol/L)	@	HbA1c (%)	@
somapacitan (0.08mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]003	M/[redacted].2/16.5	Visit 1 (Week -3)	N	Y	3.28	L	8		5.5	
		Visit 5 (Week 26)	Y	Y	4.44		32		5.7	
		Visit 7 (Week 52)	Y	Y	4.27		17		5.6	
		Visit 9 (Week 78)	Y	Y	4.50		23		ND	
		Visit 11 (Week 104)	Y	Y	4.66		36		5.8	
		Visit 13 (Week 130)	Y	Y	7.55	H	24		5.6	
		Visit 15 (Week 156)	Y	Y	5.05		71		5.6	
		Visit 18 (Week 182)	Y	Y	4.94		19		5.5	
		Visit 20 (Week 208)	Y	Y	4.88		81		5.7	
somapacitan (0.16mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]001	F/[redacted].0/14.0	Visit 1 (Week -3)	N	Y	5.22		49		5.0	
		Visit 5 (Week 26)	Y	Y	5.38		38		5.3	
		Visit 7 (Week 52)	Y	Y	ND		47		5.3	
		Visit 9 (Week 78)	Y	Y	7.88	H	ND		5.2	
		Visit 9 (Week 78)	Y	Y	4.66*		15			
		Visit 11 (Week 104)	Y	Y	4.50		27		5.2	
		Visit 13 (Week 130)	Y	Y	4.50		29		5.2	
		Visit 15 (Week 156)	Y	Y	4.94		36		5.3	
		Visit 18 (Week 182)	Y	Y	5.16		23		5.2	
		Visit 20 (Week 208)	Y	Y	5.50		89		5.2	
somapacitan (0.16mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]005	F/[redacted].9/15.0	Visit 1 (Week -3)	N	Y	4.33		6		5.1	
		Visit 5 (Week 26)	Y	Y	6.27	H	94		5.3	
		Visit 7 (Week 52)	Y	Y	4.88		53		5.9	

Listing of laboratory test results - subjects with one measurement of fasting glucose >=7.0 mmol/L or HbA1c >=6.5 % - glucose metabolism - safety analysis set

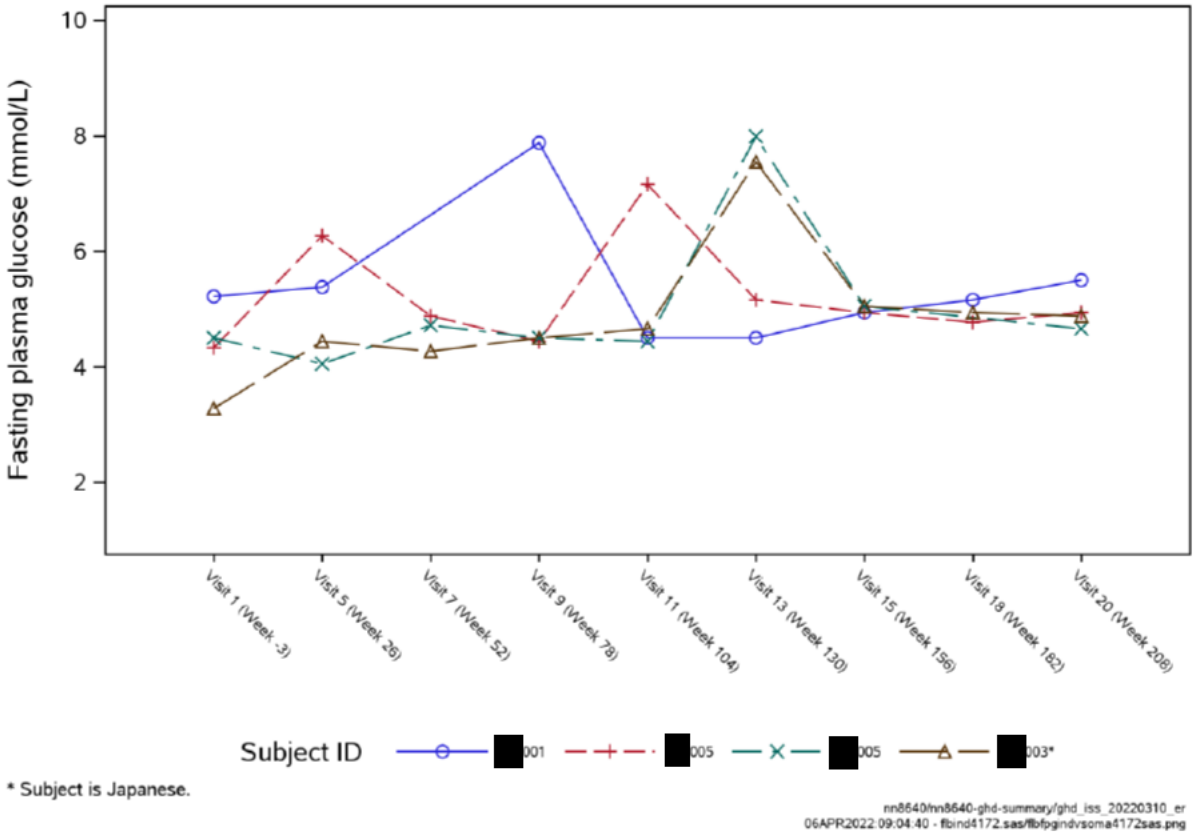
Treatment group/ Subject ID	Sex (M/F)/ Age (yrs)/ BMI (kg/m^2)	Visit	On treatment (Y/N)	Fasting (Y/N)	Fasting plasma glucose (mmol/L)	@	Fasting insulin (pmol/L)	@	HbA1c (%)	@
somapacitan (0.16mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]005	F/[redacted].9/15.0	Visit 9 (Week 78)	Y	Y	4.44		22		5.7	
		Visit 11 (Week 104)	Y	Y	7.16	H	251		5.8	
		Visit 13 (Week 130)	Y	Y	5.16		46		6.0	
		Visit 15 (Week 156)	Y	Y	4.94		65		ND	
		Visit 18 (Week 182)	Y	Y	4.77		23		5.5	
		Visit 20 (Week 208)	Y	Y	4.94		44		5.7	
somapacitan (0.16mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]005	F/[redacted].7/14.5	Visit 1 (Week -3)	N	Y	4.50		15		ND	
		Visit 1 (Week -3)	N	Y					5.9	
		Visit 5 (Week 26)	Y	Y	4.05		11		5.7	
		Visit 7 (Week 52)	Y	Y	4.72		30		5.6	
		Visit 9 (Week 78)	Y	Y	4.50		25		5.9	
		Visit 11 (Week 104)	Y	Y	4.44		106		6.0	
		Visit 13 (Week 130)	Y	Y	7.99	H	2E3		6.0	
		Visit 15 (Week 156)	Y	Y	5.05		95		5.8	
		Visit 20 (Week 208)	Y	Y	4.66		75		ND	

33: Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - trial 4172 - Norditropin/somapacitan - safety analysis set



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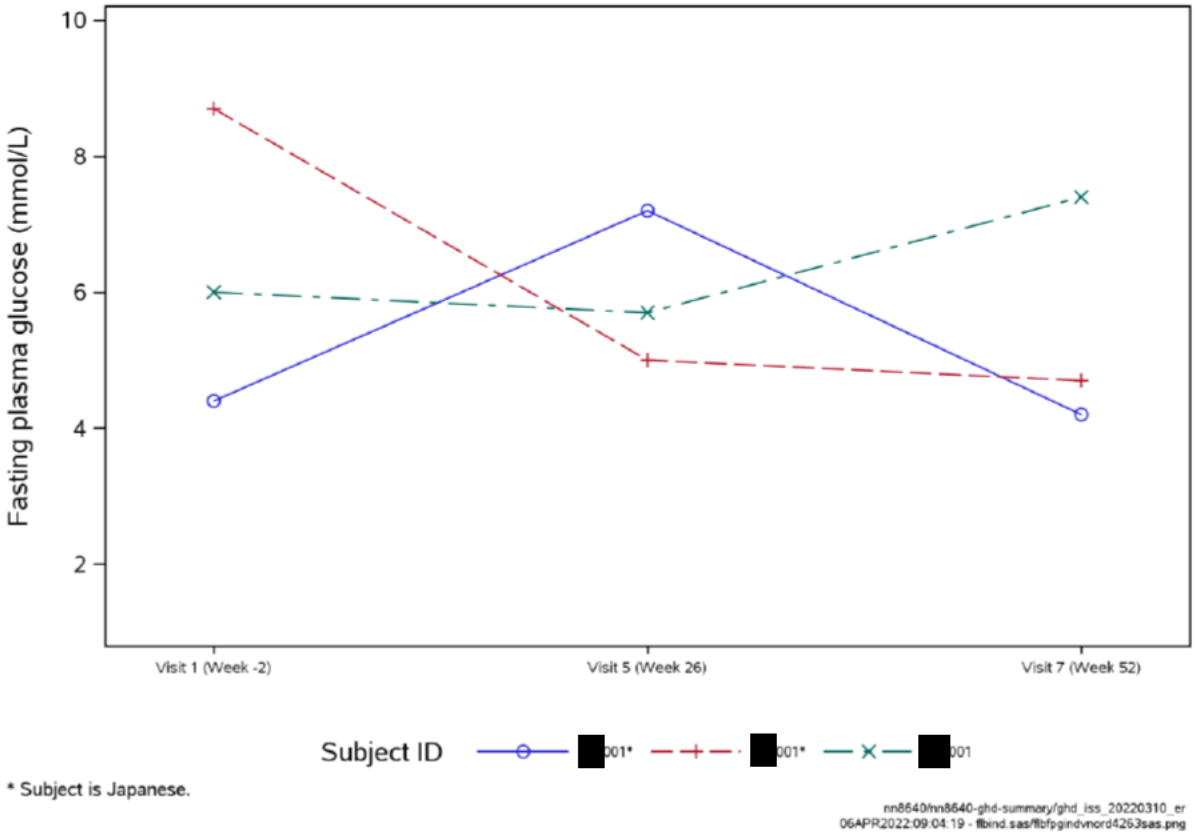
34: Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - trial 4172 - somapacitan - safety analysis set



* Subject is Japanese.

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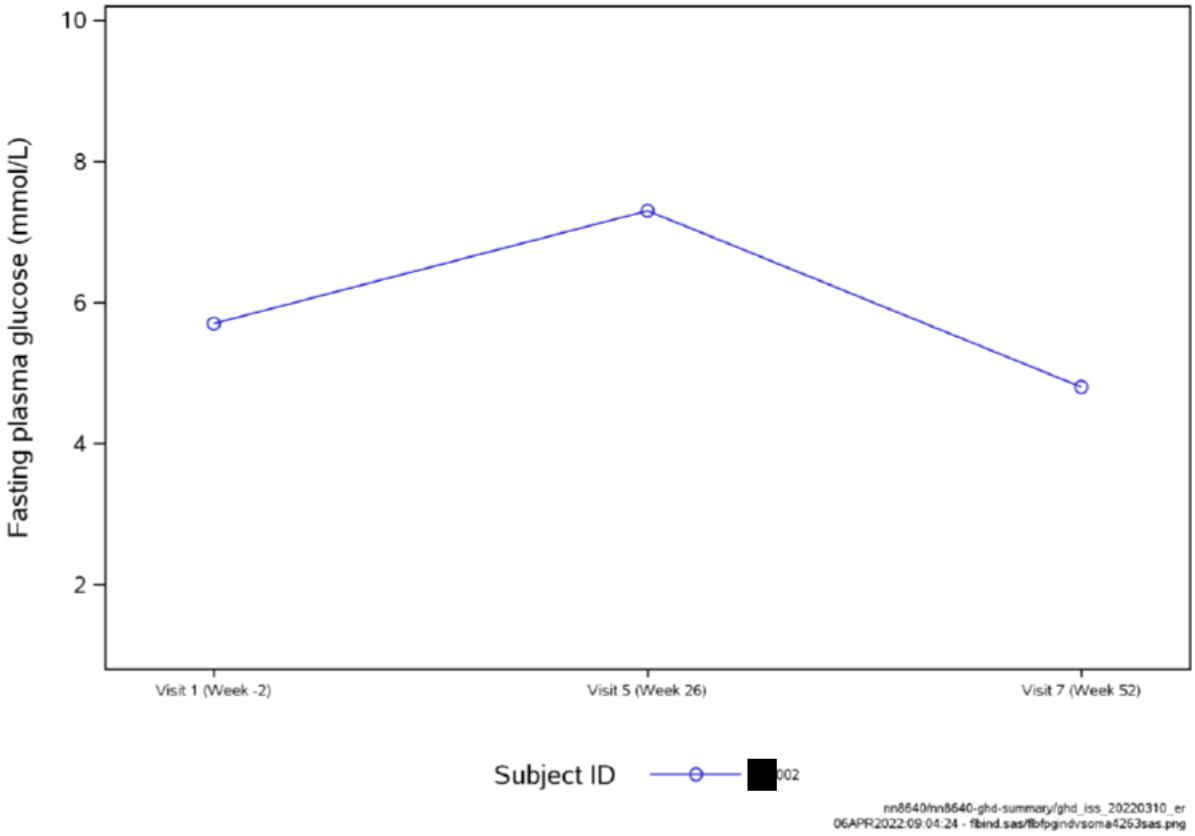
35: Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - trial 4263 - Norditropin - safety analysis set



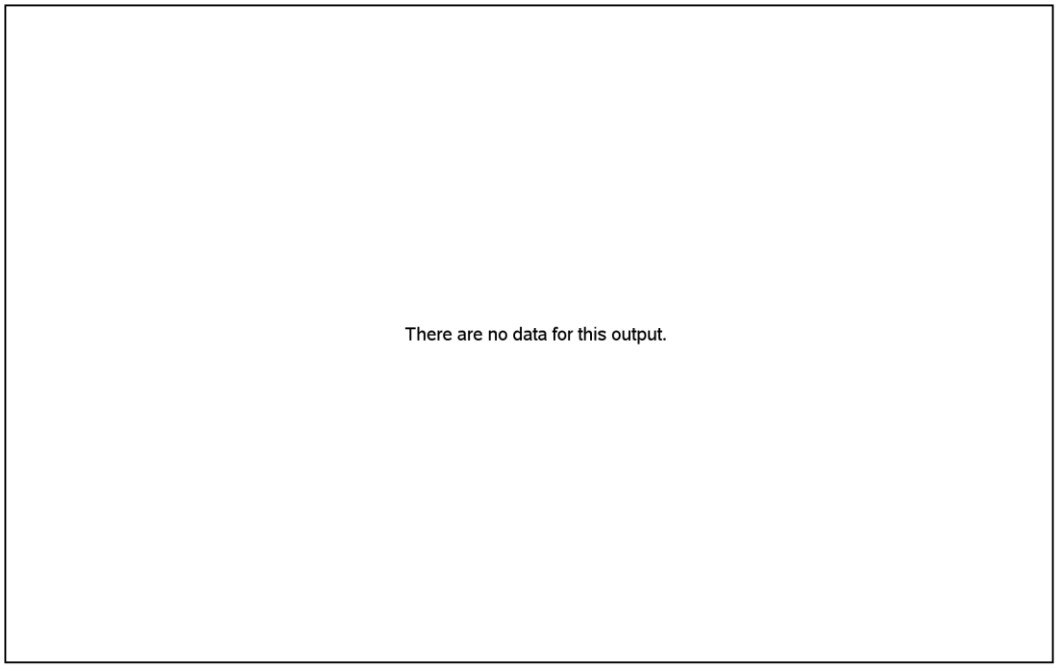
* Subject is Japanese.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:04:19 - fbind.sas/fbfpgindvnord4263sas.png

36: Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - trial 4263 - somapacitan - safety analysis set

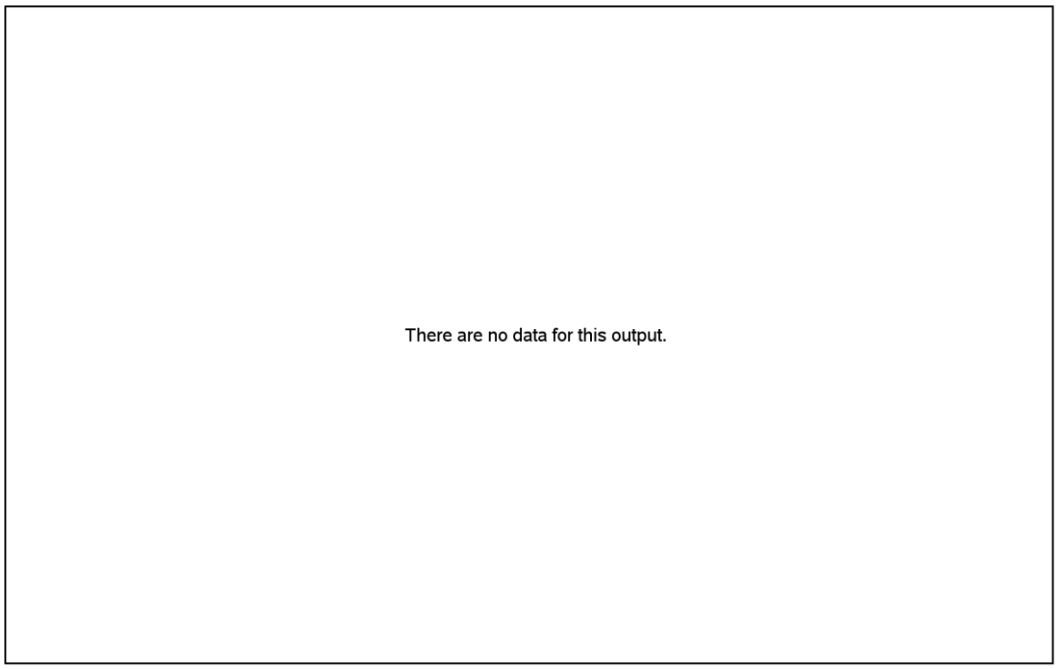


37: HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - trial 4172 - Norditropin/somapacitan - safety analysis set



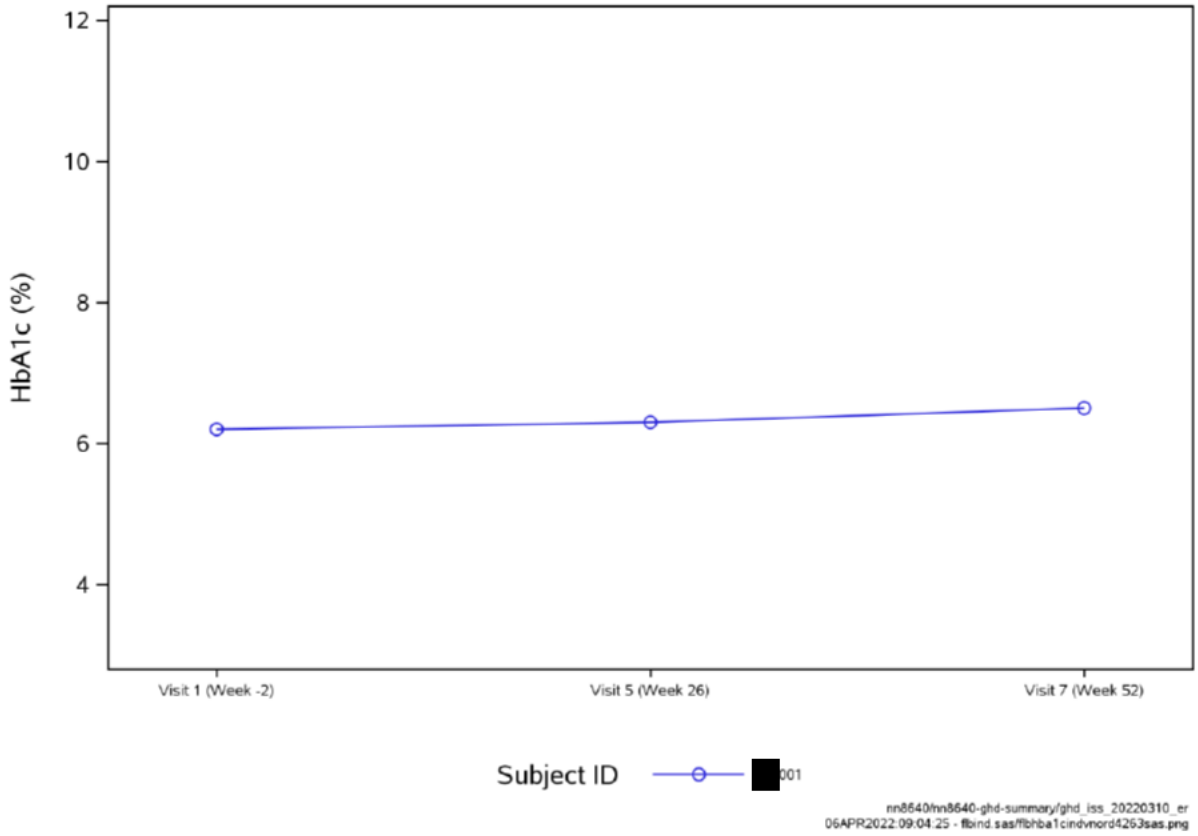
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06APR2022:09:04:42 - flbind4172.sas/flbhba1cindvnord4172sas.png

38: HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - trial 4172 - somapacitan - safety analysis set

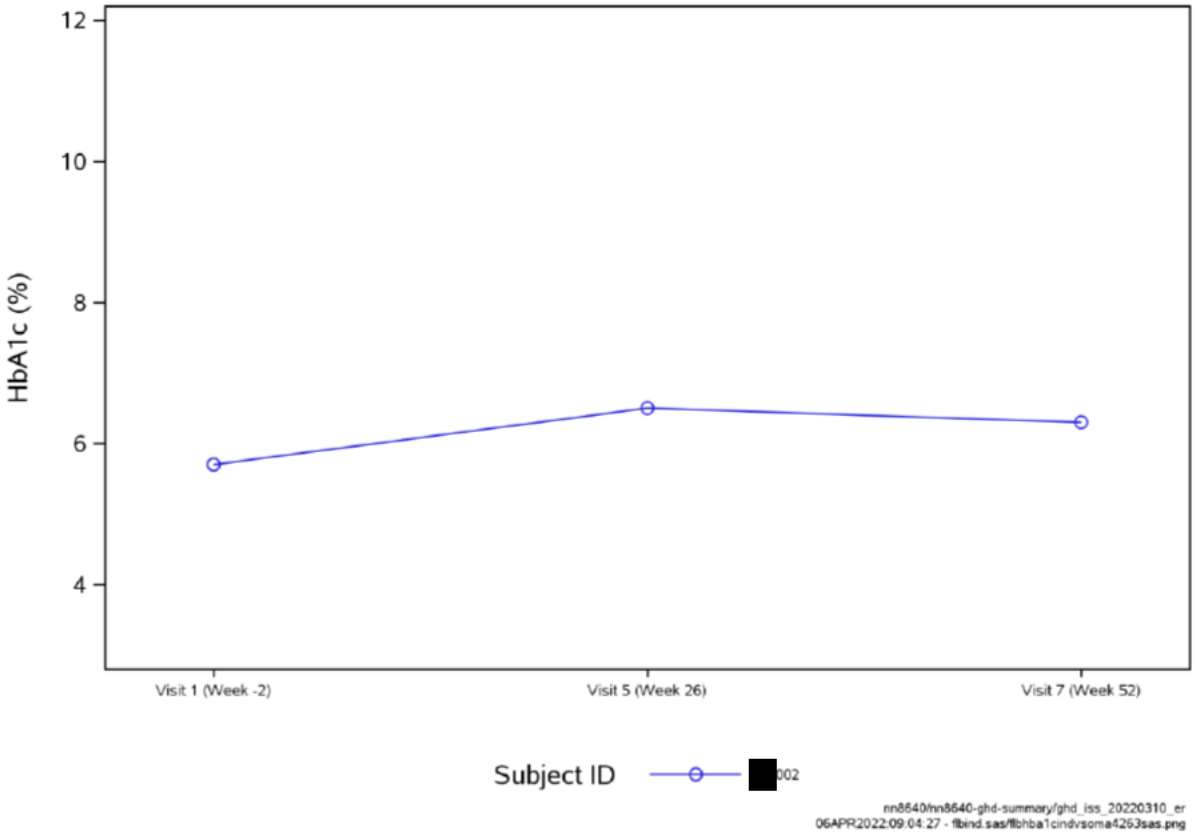


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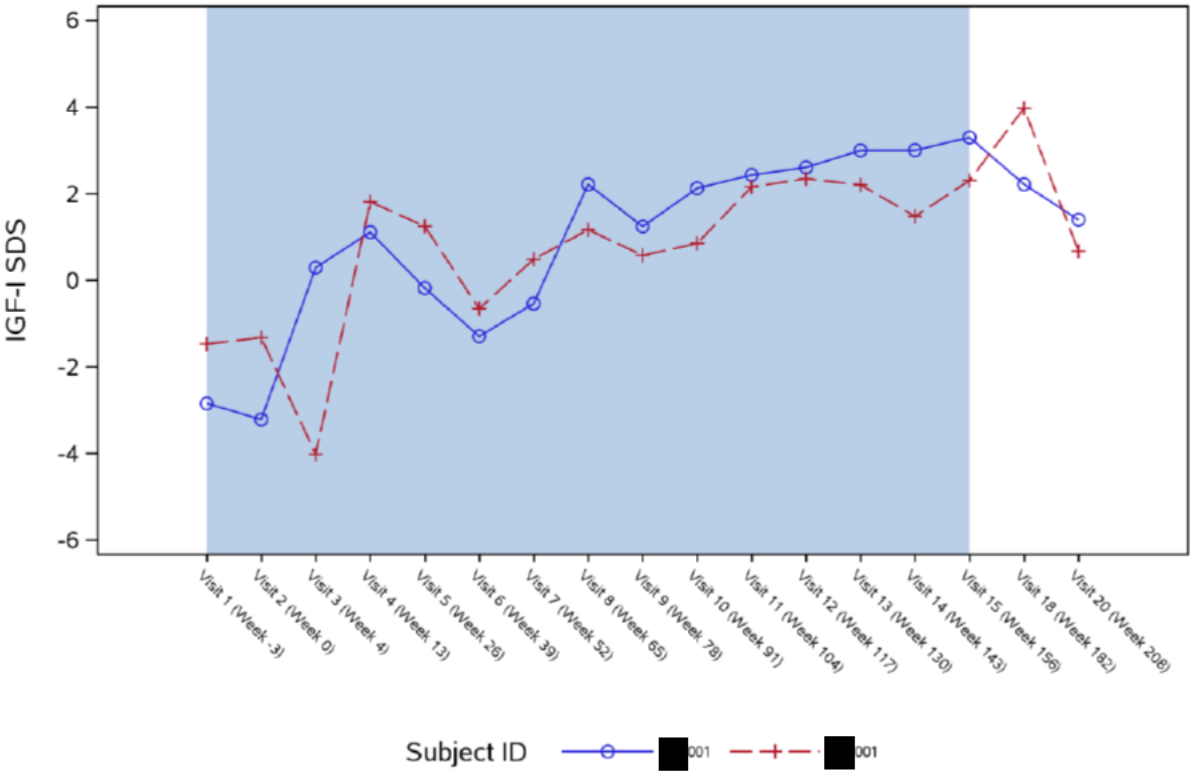
39: HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - trial 4263 - Norditropin - safety analysis set



40: HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - trial 4263 - somapacitan - safety analysis set



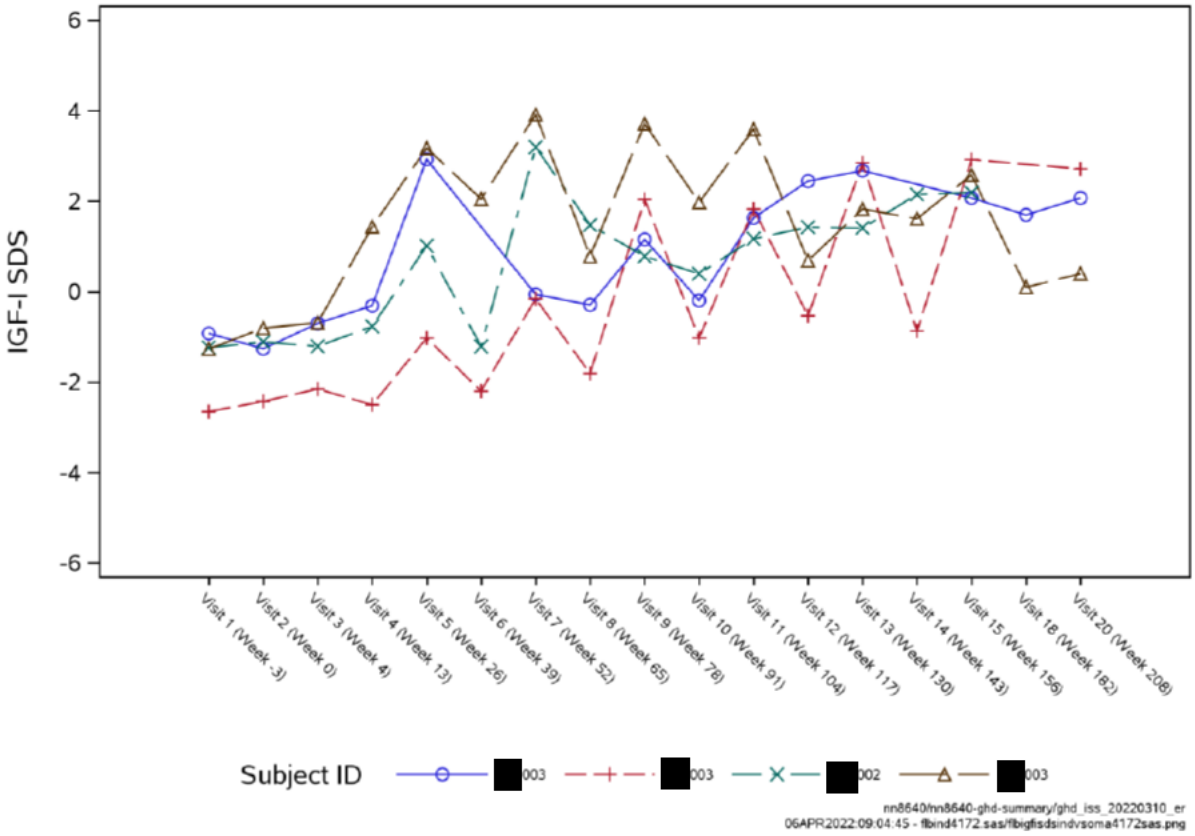
41: IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 for two or more consecutive visits - trial 4172 - Norditropin/somapacitan - safety analysis set



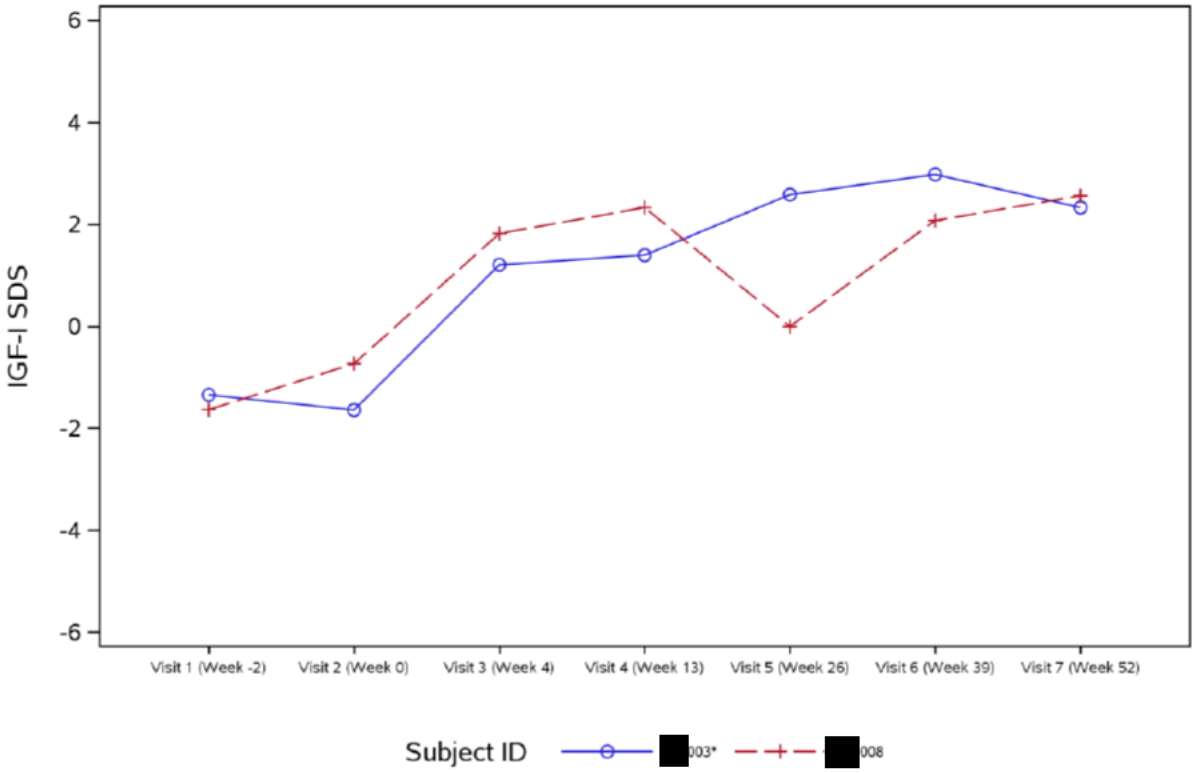
From visit 2 to visit 15 subjects are receiving Norditropin. From visit 15 and onwards they are receiving somapacitan.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:04:44 - fbind4172.sas/fbigfisdsindvnord4172sas.png

42: IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 for two or more consecutive visits - trial 4172 - somapacitan - safety analysis set



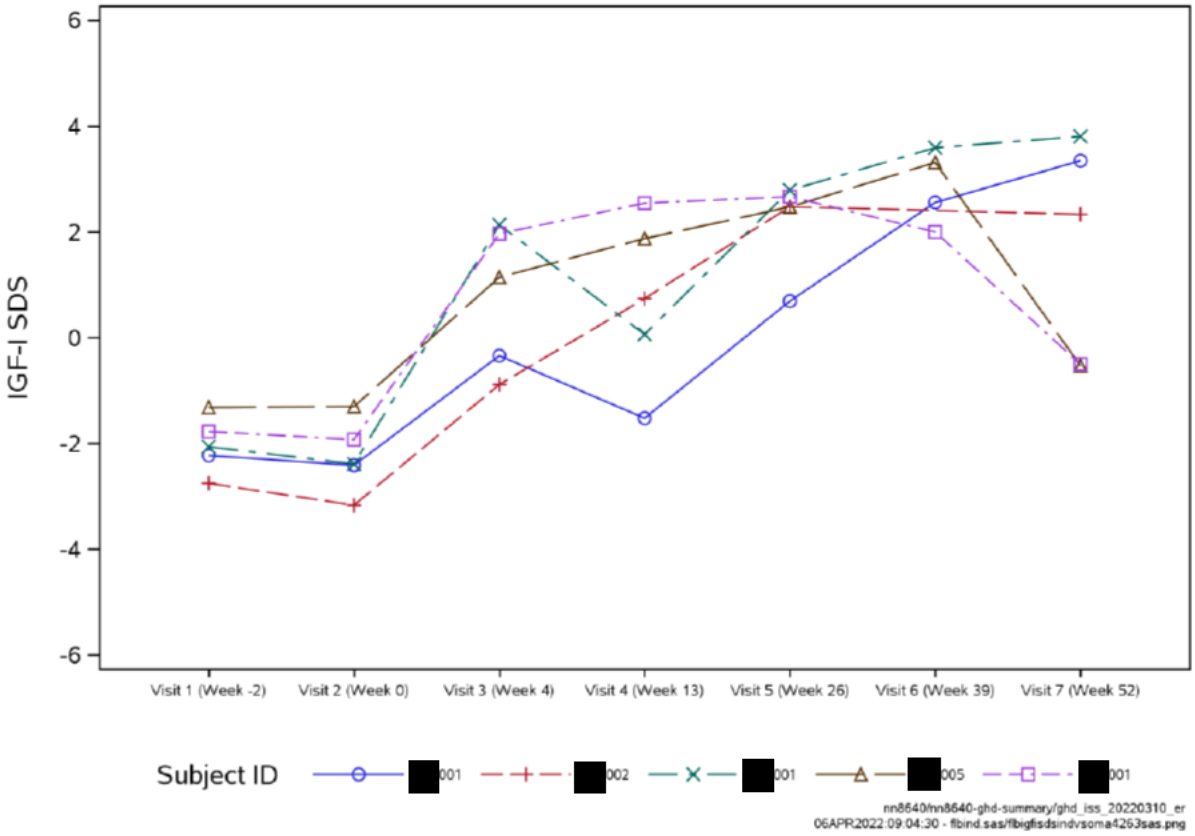
43: IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 for two or more consecutive visits - trial 4263 - Norditropin - safety analysis set



* Subject is Japanese.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:04:29 - fbind.sas/fbigfisdsindvnord4263sas.png

44: IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 for two or more consecutive visits - trial 4263 - somapacitan - safety analysis set



45: Hypothyroidism - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	1	(1.2)	1	1.0	6	(3.1)	6	2.1	7	(2.6)	7	1.8
Endocrine disorders	1	(1.2)	1	1.0	6	(3.1)	6	2.1	7	(2.6)	7	1.8
Hypothyroidism	1	(1.2)	1	1.0	4	(2.1)	4	1.4	5	(1.9)	5	1.3
Secondary hypothyroidism	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

46: Adrenocortical insufficiency - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	1	(1.2)	1	1.0	4	(2.1)	4	1.4	5	(1.9)	5	1.3
Endocrine disorders	1	(1.2)	1	1.0	4	(2.1)	4	1.4	5	(1.9)	5	1.3
Adrenal insufficiency	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Adrenocortical insufficiency acute	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Adrenocorticotropic hormone deficiency	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Glucocorticoid deficiency	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Secondary adrenocortical insufficiency	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

47: Pancreatitis - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

There are no data for this output.

48: Vomiting - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	5	(6.1)	10	9.6	11	(5.7)	15	5.3	16	(6.0)	25	6.5
Gastrointestinal disorders	5	(6.1)	10	9.6	11	(5.7)	15	5.3	16	(6.0)	25	6.5
Vomiting	5	(6.1)	10	9.6	11	(5.7)	15	5.3	16	(6.0)	25	6.5

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

49: Peripheral oedema- summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
General disorders and administration site conditions	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Oedema peripheral	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

50: Fatigue- summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	0				2	(1.0)	4	1.4	2	(0.8)	4	1.0
General disorders and administration site conditions	0				2	(1.0)	4	1.4	2	(0.8)	4	1.0
Fatigue	0				2	(1.0)	4	1.4	2	(0.8)	4	1.0

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

51: Asthenia - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
General disorders and administration site conditions	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Asthenia	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

52: Allergic reactions - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	82			194			265		
Total patient years at risk	104.5			282.7			387.3		
Events	10 (12.2)	13	12.4	22 (11.3)	41	14.5	31 (11.7)	54	13.9
Skin and subcutaneous tissue disorders	7 (8.5)	8	7.7	14 (7.2)	21	7.4	20 (7.5)	29	7.5
Urticaria	3 (3.7)	3	2.9	2 (1.0)	5	1.8	5 (1.9)	8	2.1
Dermatitis	2 (2.4)	2	1.9	3 (1.5)	3	1.1	5 (1.9)	5	1.3
Rash	1 (1.2)	2	1.9	3 (1.5)	4	1.4	4 (1.5)	6	1.5
Eczema	1 (1.2)	1	1.0	3 (1.5)	4	1.4	4 (1.5)	5	1.3
Dermatitis atopic	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Dermatitis allergic	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Henoch-Schonlein purpura	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Respiratory, thoracic and mediastinal disorders	3 (3.7)	3	2.9	6 (3.1)	8	2.8	9 (3.4)	11	2.8
Rhinitis allergic	3 (3.7)	3	2.9	6 (3.1)	8	2.8	9 (3.4)	11	2.8
Eye disorders	0			5 (2.6)	5	1.8	5 (1.9)	5	1.3
Conjunctivitis allergic	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Periorbital oedema	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Swelling of eyelid	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
General disorders and administration site conditions	1 (1.2)	1	1.0	4 (2.1)	4	1.4	5 (1.9)	5	1.3
Swelling face	0			3 (1.5)	3	1.1	3 (1.1)	3	0.8
Face oedema	0			1 (0.5)	1	0.4	1 (0.4)	1	0.3
Injection site hypersensitivity	1 (1.2)	1	1.0	0			1 (0.4)	1	0.3
Immune system disorders	1 (1.2)	1	1.0	2 (1.0)	2	0.7	3 (1.1)	3	0.8

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

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

	Norditropin			somapacitan (0.16mg/kg/week) safety pooled			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Anaphylactic reaction	0			1	(0.5)	1 0.4	1	(0.4)	1 0.3
Anaphylactic shock	0			1	(0.5)	1 0.4	1	(0.4)	1 0.3
Drug hypersensitivity	1	(1.2)	1 1.0	0			1	(0.4)	1 0.3
Infections and infestations	0			1	(0.5)	1 0.4	1	(0.4)	1 0.3
Dermatitis infected	0			1	(0.5)	1 0.4	1	(0.4)	1 0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

53: Hypersensitivity (anaphylactic reactions) - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
Immune system disorders	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
Anaphylactic reaction	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Anaphylactic shock	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

54: Injections site reactions - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	4	(4.9)	4	3.8	10	(5.2)	17	6.0	14	(5.3)	21	5.4
General disorders and administration site conditions	4	(4.9)	4	3.8	10	(5.2)	17	6.0	14	(5.3)	21	5.4
Injection site bruising	2	(2.4)	2	1.9	3	(1.5)	5	1.8	5	(1.9)	7	1.8
Injection site pain	1	(1.2)	1	1.0	3	(1.5)	5	1.8	4	(1.5)	6	1.5
Injection site haematoma	0				2	(1.0)	4	1.4	2	(0.8)	4	1.0
Injection site discomfort	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Injection site hypersensitivity	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Injection site reaction	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Injection site swelling	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

55: Lipohypertrophy/lipodystrophy/lipoatrophy - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Skin and subcutaneous tissue disorders	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Lipodystrophy acquired	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

56: Covid-19 - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	3	(3.7)	3	2.9	3	(1.5)	3	1.1	6	(2.3)	6	1.5
Infections and infestations	3	(3.7)	3	2.9	3	(1.5)	3	1.1	6	(2.3)	6	1.5
COVID-19	3	(3.7)	3	2.9	3	(1.5)	3	1.1	6	(2.3)	6	1.5

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

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57: Blood alkaline phosphate increased (bone) - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

There are no data for this output.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:05:28 - taesocptsumpool.sas/taealkasocptsumontrsas.txt

58: Drug specific antibodies present - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

There are no data for this output.

59: ECG related AEs - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

There are no data for this output.

60: Type 2 diabetes incl. hyperglycaemia - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	4	(4.9)	4	3.8	5	(2.6)	5	1.8	9	(3.4)	9	2.3
Metabolism and nutrition disorders	3	(3.7)	3	2.9	3	(1.5)	3	1.1	6	(2.3)	6	1.5
Hyperglycaemia	2	(2.4)	2	1.9	2	(1.0)	2	0.7	4	(1.5)	4	1.0
Impaired fasting glucose	1	(1.2)	1	1.0	1	(0.5)	1	0.4	2	(0.8)	2	0.5
Investigations	1	(1.2)	1	1.0	2	(1.0)	2	0.7	3	(1.1)	3	0.8
Blood glucose increased	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
Glycosylated haemoglobin increased	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

61: Arthralgia - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	3	(3.7)	3	2.9	4	(2.1)	6	2.1	7	(2.6)	9	2.3
Musculoskeletal and connective tissue disorders	3	(3.7)	3	2.9	4	(2.1)	6	2.1	7	(2.6)	9	2.3
Arthralgia	3	(3.7)	3	2.9	4	(2.1)	6	2.1	7	(2.6)	9	2.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

62: Myalgia - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	0				3	(1.5)	3	1.1	3	(1.1)	3	0.8
Musculoskeletal and connective tissue disorders	0				3	(1.5)	3	1.1	3	(1.1)	3	0.8
Myalgia	0				3	(1.5)	3	1.1	3	(1.1)	3	0.8

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

63: Joint stiffness - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

There are no data for this output.

64: Muscle stiffness - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Musculoskeletal and connective tissue disorders	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Musculoskeletal stiffness	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

65: Scoliosis - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

There are no data for this output.

66: Neoplasms - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	2	(2.4)	2	1.9	4	(2.1)	4	1.4	6	(2.3)	6	1.5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2	(2.4)	2	1.9	4	(2.1)	4	1.4	6	(2.3)	6	1.5
Skin papilloma	1	(1.2)	1	1.0	3	(1.5)	3	1.1	4	(1.5)	4	1.0
Lipoma	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Lymphangioma	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

67: Headache - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	8	(9.8)	13	12.4	18	(9.3)	26	9.2	26	(9.8)	39	10.1
Nervous system disorders	8	(9.8)	13	12.4	18	(9.3)	26	9.2	26	(9.8)	39	10.1
Headache	8	(9.8)	13	12.4	18	(9.3)	26	9.2	26	(9.8)	39	10.1

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

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68: Paraesthesia - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

There are no data for this output.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:05:34 - taesocptsumpool.sas/taeparaessocptsumontrsas.txt

69: Stroke - summary of adverse events by system organ class and preferred term- on-treatment - safety analysis set

There are no data for this output.

70: Carpal tunnel syndome - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

There are no data for this output.

71: Benign intracranial hypertension - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

There are no data for this output.

72: Rare events - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	2	(2.4)	2	1.9	11	(5.7)	12	4.2	13	(4.9)	14	3.6
General disorders and administration site conditions	0				4	(2.1)	4	1.4	4	(1.5)	4	1.0
Swelling face	0				3	(1.5)	3	1.1	3	(1.1)	3	0.8
Face oedema	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Eye disorders	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
Periorbital oedema	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Swelling of eyelid	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Immune system disorders	0				2	(1.0)	2	0.7	2	(0.8)	2	0.5
Anaphylactic reaction	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Anaphylactic shock	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Blood and lymphatic system disorders	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Thrombocytopenia	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Congenital, familial and genetic disorders	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Cryptorchism	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Hepatobiliary disorders	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Nonalcoholic fatty liver disease	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Investigations	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Electrocardiogram QT prolonged	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

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

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Renal and urinary disorders	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Nephrotic syndrome	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Respiratory, thoracic and mediastinal disorders	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3
Pneumonitis	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

73: Medication errors - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	3	(3.7)	3	2.9	2	(1.0)	2	0.7	5	(1.9)	5	1.3
Injury, poisoning and procedural complications	3	(3.7)	3	2.9	2	(1.0)	2	0.7	5	(1.9)	5	1.3
Accidental overdose	2	(2.4)	2	1.9	1	(0.5)	1	0.4	3	(1.1)	3	0.8
Accidental underdose	0				1	(0.5)	1	0.4	1	(0.4)	1	0.3
Medication error	1	(1.2)	1	1.0	0				1	(0.4)	1	0.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

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74: Abuse or misuse - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

There are no data for this output.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:05:37 - taesocptsumpool.sas/taeabusesocptsumontrsas.txt

75: Overdose - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

	Norditropin				somapacitan (0.16mg/kg/week) safety pooled				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	82				194				265			
Total patient years at risk	104.5				282.7				387.3			
Events	2	(2.4)	2	1.9	1	(0.5)	1	0.4	3	(1.1)	3	0.8
Injury, poisoning and procedural complications	2	(2.4)	2	1.9	1	(0.5)	1	0.4	3	(1.1)	3	0.8
Accidental overdose	2	(2.4)	2	1.9	1	(0.5)	1	0.4	3	(1.1)	3	0.8

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

76: Suspected transmission of an infectious agent via trial product - summary of adverse events by system organ class and preferred term - on-treatment - safety analysis set

There are no data for this output.

77: summary of exposed subjects and patient years of exposure - trial 4172 - safety analysis set

Treatment group Main + Extension / Safety extension	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)		somapacitan (0.04mg/kg/week)/ somapacitan (0.16mg/kg/week)		somapacitan (0.08mg/kg/week)/ somapacitan (0.16mg/kg/week)		somapacitan (0.16mg/kg/week)/ somapacitan (0.16mg/kg/week)		somapacitan (0.04/0.08/0.16mg/kg/week) pooled	
	N	PYE	N	PYE	N	PYE	N	PYE	N	PYE
Main (Weeks 0-26)	14	6.7	16	7.3	15	7.6	14	7.2	45	22.0
Extension (Weeks 0-52)	13	13.0	14	14.1	15	15.1	14	14.3	43	43.4
Safety extension (Weeks 52-156)	11	22.2	13	25.7	14	28.1	13	25.7	40	79.5
Long-term safety extension (Weeks 156-208)	11	10.8	12	11.7	14	14.0	13	13.1	39	38.8

N: Number of subjects, PYE: Patient years of exposure

78: Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Number of subjects	14	45
Alanine aminotransferase (ALT) (U/L)		
Visit 1 (Week -3)		
N	14	44
Mean (SD)	12.9 (3.7)	15.3 (3.5)
Median	12.5	15.0
Min ; Max	6 ; 20	7 ; 23
Visit 4 (Week 13)		
N	12	43
Mean (SD)	15.7 (3.6)	15.7 (4.4)
Median	16.0	15.0
Min ; Max	10 ; 20	9 ; 29
Visit 5 (Week 26)		
N	13	42
Mean (SD)	13.2 (3.6)	14.7 (4.0)
Median	12.0	15.0
Min ; Max	7 ; 19	8 ; 25
Visit 6 (Week 39)		
N	13	42
Mean (SD)	14.3 (4.0)	13.7 (3.2)
Median	13.0	13.0
Min ; Max	10 ; 23	6 ; 22
Visit 7 (Week 52)		
N	13	42
Mean (SD)	14.5 (7.5)	13.5 (3.4)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	13.0	14.0
Min ; Max	7 ; 38	7 ; 22
Visit 9 (Week 78)		
N	11	39
Mean (SD)	16.0 (6.3)	13.7 (3.1)
Median	15.0	13.0
Min ; Max	10 ; 31	9 ; 21
Visit 11 (Week 104)		
N	11	38
Mean (SD)	13.5 (3.9)	13.7 (3.4)
Median	12.0	13.0
Min ; Max	9 ; 22	6 ; 25
Visit 13 (Week 130)		
N	11	40
Mean (SD)	13.2 (5.2)	13.8 (7.7)
Median	11.0	12.0
Min ; Max	9 ; 27	7 ; 55
Visit 15 (Week 156)		
N	11	38
Mean (SD)	15.2 (9.1)	12.0 (3.3)
Median	13.0	12.0
Min ; Max	10 ; 42	6 ; 24
Visit 18 (Week 182)		
N	10	31
Mean (SD)	12.7 (3.4)	12.3 (3.7)
Median	12.0	12.0
Min ; Max	9 ; 19	5 ; 25

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 20 (Week 208)		
N	11	36
Mean (SD)	15.6 (14.3)	12.6 (4.1)
Median	11.0	12.0
Min ; Max	9 ; 58	7 ; 21
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	15.6 (14.3)	12.6 (4.1)
Median	11.0	12.0
Min ; Max	9 ; 58	7 ; 21
Overall minimum value for each subject*		
N	13	43
Mean (SD)	9.9 (2.0)	10.2 (2.4)
Median	10.0	10.0
Min ; Max	7 ; 14	5 ; 16
Overall maximum value for each subject*		
N	13	43
Mean (SD)	20.6 (11.9)	19.4 (7.0)
Median	19.0	18.0
Min ; Max	11 ; 58	10 ; 55
Aspartate aminotransferase (AST) (U/L)		
Visit 1 (Week -3)		
N	11	31

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	33.3 (7.0)	35.2 (8.1)
Median	33.0	34.0
Min ; Max	23 ; 43	18 ; 51
Visit 4 (Week 13)		
N	11	38
Mean (SD)	33.9 (5.5)	33.3 (6.6)
Median	34.0	32.0
Min ; Max	26 ; 42	20 ; 48
Visit 5 (Week 26)		
N	13	42
Mean (SD)	30.4 (7.5)	31.2 (7.3)
Median	28.0	29.0
Min ; Max	18 ; 43	19 ; 47
Visit 6 (Week 39)		
N	13	42
Mean (SD)	32.3 (11.3)	30.0 (6.8)
Median	28.0	29.0
Min ; Max	21 ; 65	18 ; 50
Visit 7 (Week 52)		
N	13	42
Mean (SD)	29.5 (8.4)	29.3 (6.3)
Median	29.0	29.0
Min ; Max	21 ; 54	17 ; 44
Visit 9 (Week 78)		
N	11	39
Mean (SD)	32.2 (8.8)	28.4 (6.3)
Median	31.0	29.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	22 ; 49	18 ; 44
Visit 11 (Week 104)		
N	11	38
Mean (SD)	27.6 (5.5)	27.5 (5.5)
Median	27.0	27.0
Min ; Max	22 ; 39	14 ; 43
Visit 13 (Week 130)		
N	11	40
Mean (SD)	28.5 (6.8)	27.4 (6.9)
Median	27.0	27.5
Min ; Max	21 ; 47	16 ; 47
Visit 15 (Week 156)		
N	11	38
Mean (SD)	27.9 (8.8)	25.4 (7.5)
Median	26.0	25.5
Min ; Max	18 ; 50	16 ; 62
Visit 18 (Week 182)		
N	10	31
Mean (SD)	26.5 (6.4)	25.6 (5.7)
Median	27.0	25.0
Min ; Max	18 ; 34	15 ; 41
Visit 20 (Week 208)		
N	11	36
Mean (SD)	24.8 (5.6)	24.7 (6.2)
Median	22.0	24.5
Min ; Max	18 ; 37	14 ; 45

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	24.8 (5.6)	24.7 (6.2)
Median	22.0	24.5
Min ; Max	18 ; 37	14 ; 45
Overall minimum value for each subject*		
N	13	43
Mean (SD)	22.9 (4.8)	22.7 (4.2)
Median	22.0	23.0
Min ; Max	18 ; 34	14 ; 30
Overall maximum value for each subject*		
N	13	43
Mean (SD)	37.4 (11.2)	35.6 (8.1)
Median	34.0	34.0
Min ; Max	26 ; 65	20 ; 62
Bilirubin (total) (umol/L)		
Visit 1 (Week -3)		
N	14	44
Mean (SD)	5.36 (2.63)	5.58 (3.49)
Median	4.70	5.30
Min ; Max	1.3 ; 10.3	1.3 ; 18.0
Visit 4 (Week 13)		
N	12	43
Mean (SD)	4.20 (1.67)	5.92 (5.61)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	4.35	4.30
Min ; Max	1.3 ; 7.5	1.3 ; 33.3
Visit 5 (Week 26)		
N	13	42
Mean (SD)	5.28 (2.72)	5.07 (3.94)
Median	5.10	4.00
Min ; Max	1.3 ; 10.8	1.3 ; 17.6
Visit 6 (Week 39)		
N	13	42
Mean (SD)	4.13 (2.16)	5.33 (3.14)
Median	3.90	4.50
Min ; Max	1.3 ; 7.4	1.3 ; 16.2
Visit 7 (Week 52)		
N	13	43
Mean (SD)	5.22 (2.68)	5.69 (4.54)
Median	5.10	4.40
Min ; Max	1.3 ; 9.6	1.3 ; 22.1
Visit 9 (Week 78)		
N	11	39
Mean (SD)	5.40 (1.85)	5.64 (3.22)
Median	4.80	4.80
Min ; Max	2.9 ; 7.9	1.3 ; 15.2
Visit 11 (Week 104)		
N	11	38
Mean (SD)	6.16 (3.04)	5.80 (3.31)
Median	5.50	5.30
Min ; Max	2.7 ; 11.6	1.3 ; 18.5

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 13 (Week 130)		
N	11	40
Mean (SD)	6.36 (4.19)	5.65 (4.11)
Median	4.40	4.70
Min ; Max	3.2 ; 17.4	1.3 ; 21.9
Visit 15 (Week 156)		
N	11	38
Mean (SD)	7.15 (6.16)	6.72 (5.03)
Median	6.00	5.30
Min ; Max	2.6 ; 25.0	1.3 ; 26.8
Visit 18 (Week 182)		
N	10	31
Mean (SD)	4.88 (2.06)	6.72 (3.39)
Median	4.35	6.20
Min ; Max	1.3 ; 7.5	1.3 ; 14.7
Visit 20 (Week 208)		
N	11	36
Mean (SD)	6.30 (3.41)	6.06 (4.24)
Median	5.10	4.70
Min ; Max	2.7 ; 13.5	1.3 ; 19.3
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	6.30 (3.41)	6.06 (4.24)
Median	5.10	4.70
Min ; Max	2.7 ; 13.5	1.3 ; 19.3

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Overall minimum value for each subject*		
N	13	43
Mean (SD)	2.72 (1.59)	3.02 (2.50)
Median	2.70	2.60
Min ; Max	1.3 ; 5.3	1.3 ; 11.1
Overall maximum value for each subject*		
N	13	43
Mean (SD)	8.13 (5.64)	9.15 (5.50)
Median	7.50	7.50
Min ; Max	2.7 ; 25.0	3.8 ; 33.3
Calcium (total) (mmol/L)		
Visit 1 (Week -3)		
N	14	43
Mean (SD)	2.451 (0.059)	2.413 (0.088)
Median	2.435	2.400
Min ; Max	2.35 ; 2.55	2.22 ; 2.60
Visit 4 (Week 13)		
N	12	43
Mean (SD)	2.459 (0.068)	2.422 (0.083)
Median	2.435	2.420
Min ; Max	2.40 ; 2.62	2.20 ; 2.68
Visit 5 (Week 26)		
N	13	41
Mean (SD)	2.463 (0.088)	2.444 (0.084)
Median	2.480	2.450

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	2.32 ; 2.62	2.25 ; 2.60
Visit 6 (Week 39)		
N	13	42
Mean (SD)	2.432 (0.089)	2.414 (0.083)
Median	2.450	2.410
Min ; Max	2.22 ; 2.55	2.18 ; 2.55
Visit 7 (Week 52)		
N	13	43
Mean (SD)	2.411 (0.142)	2.444 (0.097)
Median	2.420	2.450
Min ; Max	2.02 ; 2.60	2.22 ; 2.68
Visit 9 (Week 78)		
N	11	40
Mean (SD)	2.465 (0.100)	2.446 (0.073)
Median	2.420	2.450
Min ; Max	2.35 ; 2.65	2.25 ; 2.62
Visit 11 (Week 104)		
N	11	39
Mean (SD)	2.416 (0.111)	2.441 (0.161)
Median	2.480	2.450
Min ; Max	2.18 ; 2.52	1.58 ; 2.62
Visit 13 (Week 130)		
N	11	40
Mean (SD)	2.459 (0.068)	2.421 (0.103)
Median	2.450	2.410
Min ; Max	2.35 ; 2.60	2.00 ; 2.58

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 15 (Week 156)		
N	11	38
Mean (SD)	2.445 (0.143)	2.449 (0.087)
Median	2.450	2.450
Min ; Max	2.08 ; 2.68	2.28 ; 2.62
Visit 18 (Week 182)		
N	10	32
Mean (SD)	2.422 (0.091)	2.409 (0.106)
Median	2.425	2.420
Min ; Max	2.32 ; 2.60	1.92 ; 2.52
Visit 20 (Week 208)		
N	11	36
Mean (SD)	2.426 (0.102)	2.474 (0.085)
Median	2.450	2.480
Min ; Max	2.25 ; 2.60	2.32 ; 2.72
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	2.426 (0.102)	2.474 (0.085)
Median	2.450	2.480
Min ; Max	2.25 ; 2.60	2.32 ; 2.72
Overall minimum value for each subject*		
N	13	43
Mean (SD)	2.275 (0.124)	2.304 (0.152)
Median	2.320	2.320
Min ; Max	2.02 ; 2.45	1.58 ; 2.50

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Overall maximum value for each subject*		
N	13	43
Mean (SD)	2.553 (0.063)	2.543 (0.068)
Median	2.520	2.550
Min ; Max	2.45 ; 2.68	2.40 ; 2.72
Creatinine (umol/L)		
Visit 1 (Week -3)		
N	14	44
Mean (SD)	22.3 (8.8)	21.1 (9.3)
Median	18.0	18.0
Min ; Max	9 ; 35	9 ; 44
Visit 4 (Week 13)		
N	12	43
Mean (SD)	19.4 (8.3)	21.8 (9.8)
Median	18.0	18.0
Min ; Max	9 ; 35	9 ; 44
Visit 5 (Week 26)		
N	13	42
Mean (SD)	24.7 (8.8)	21.7 (8.0)
Median	27.0	18.0
Min ; Max	9 ; 35	9 ; 35
Visit 6 (Week 39)		
N	13	42
Mean (SD)	22.7 (9.2)	22.8 (8.7)
Median	27.0	27.0
Min ; Max	9 ; 35	9 ; 44

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 7 (Week 52)		
N	13	43
Mean (SD)	26.1 (6.5)	23.0 (9.0)
Median	27.0	27.0
Min ; Max	18 ; 35	9 ; 44
Visit 9 (Week 78)		
N	11	40
Mean (SD)	26.6 (10.2)	21.7 (8.5)
Median	27.0	27.0
Min ; Max	9 ; 44	9 ; 35
Visit 11 (Week 104)		
N	11	39
Mean (SD)	25.9 (8.2)	22.6 (9.8)
Median	27.0	27.0
Min ; Max	9 ; 35	9 ; 35
Visit 13 (Week 130)		
N	11	40
Mean (SD)	25.9 (8.2)	25.2 (8.1)
Median	27.0	27.0
Min ; Max	9 ; 35	9 ; 44
Visit 15 (Week 156)		
N	11	38
Mean (SD)	26.0 (9.1)	25.3 (9.3)
Median	27.0	27.0
Min ; Max	9 ; 44	9 ; 44
Visit 18 (Week 182)		
N	10	32

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	30.9 (8.3)	28.0 (7.5)
Median	35.0	27.0
Min ; Max	18 ; 44	9 ; 35
Visit 20 (Week 208)		
N	11	36
Mean (SD)	29.7 (9.7)	30.0 (9.3)
Median	35.0	31.0
Min ; Max	9 ; 44	9 ; 44
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	29.7 (9.7)	30.0 (9.3)
Median	35.0	31.0
Min ; Max	9 ; 44	9 ; 44
Overall minimum value for each subject*		
N	13	43
Mean (SD)	18.6 (8.4)	17.8 (8.2)
Median	18.0	18.0
Min ; Max	9 ; 35	9 ; 35
Overall maximum value for each subject*		
N	13	43
Mean (SD)	31.3 (6.5)	32.2 (7.9)
Median	35.0	35.0
Min ; Max	18 ; 44	18 ; 44
Phosphate (mmol/L)		

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 1 (Week -3)		
N	14	44
Mean (SD)	1.583 (0.226)	1.539 (0.146)
Median	1.535	1.520
Min ; Max	1.29 ; 2.00	1.26 ; 1.91
Visit 4 (Week 13)		
N	12	43
Mean (SD)	1.723 (0.143)	1.683 (0.183)
Median	1.725	1.680
Min ; Max	1.49 ; 1.94	1.26 ; 2.07
Visit 5 (Week 26)		
N	13	42
Mean (SD)	1.811 (0.153)	1.752 (0.171)
Median	1.810	1.725
Min ; Max	1.58 ; 2.07	1.32 ; 2.20
Visit 6 (Week 39)		
N	13	42
Mean (SD)	1.725 (0.150)	1.722 (0.210)
Median	1.780	1.740
Min ; Max	1.39 ; 1.91	1.20 ; 2.10
Visit 7 (Week 52)		
N	13	43
Mean (SD)	1.788 (0.200)	1.759 (0.158)
Median	1.740	1.740
Min ; Max	1.42 ; 2.10	1.45 ; 2.07
Visit 9 (Week 78)		
N	11	38

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	1.748 (0.155)	1.835 (0.165)
Median	1.710	1.840
Min ; Max	1.55 ; 2.03	1.45 ; 2.33
Visit 11 (Week 104)		
N	10	35
Mean (SD)	1.735 (0.081)	1.839 (0.156)
Median	1.710	1.840
Min ; Max	1.62 ; 1.87	1.52 ; 2.16
Visit 13 (Week 130)		
N	10	39
Mean (SD)	1.669 (0.188)	1.780 (0.164)
Median	1.725	1.810
Min ; Max	1.36 ; 1.94	1.36 ; 2.16
Visit 15 (Week 156)		
N	11	35
Mean (SD)	1.735 (0.127)	1.774 (0.149)
Median	1.710	1.780
Min ; Max	1.55 ; 2.03	1.45 ; 2.10
Visit 18 (Week 182)		
N	9	27
Mean (SD)	1.646 (0.260)	1.770 (0.189)
Median	1.650	1.740
Min ; Max	1.36 ; 2.10	1.45 ; 2.23
Visit 20 (Week 208)		
N	11	36
Mean (SD)	1.704 (0.151)	1.755 (0.184)
Median	1.680	1.710

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	1.36 ; 1.87	1.36 ; 2.33
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	1.704 (0.151)	1.755 (0.184)
Median	1.680	1.710
Min ; Max	1.36 ; 1.87	1.36 ; 2.33
Overall minimum value for each subject*		
N	13	43
Mean (SD)	1.578 (0.148)	1.533 (0.141)
Median	1.620	1.520
Min ; Max	1.36 ; 1.78	1.20 ; 1.87
Overall maximum value for each subject*		
N	13	43
Mean (SD)	1.894 (0.129)	1.930 (0.180)
Median	1.910	1.940
Min ; Max	1.71 ; 2.10	1.49 ; 2.33
Potassium (mmol/L)		
Visit 1 (Week -3)		
N	14	44
Mean (SD)	4.50 (0.28)	4.35 (0.36)
Median	4.40	4.40
Min ; Max	4.2 ; 5.2	2.8 ; 5.0
Visit 4 (Week 13)		

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
N	12	41
Mean (SD)	4.36 (0.30)	4.39 (0.37)
Median	4.30	4.40
Min ; Max	4.0 ; 5.1	3.1 ; 5.3
Visit 5 (Week 26)		
N	12	41
Mean (SD)	4.40 (0.30)	4.44 (0.30)
Median	4.35	4.40
Min ; Max	4.0 ; 4.9	3.7 ; 5.2
Visit 6 (Week 39)		
N	13	42
Mean (SD)	4.35 (0.17)	4.40 (0.30)
Median	4.40	4.50
Min ; Max	4.1 ; 4.6	3.6 ; 5.1
Visit 7 (Week 52)		
N	12	43
Mean (SD)	4.41 (0.30)	4.44 (0.37)
Median	4.35	4.40
Min ; Max	4.0 ; 5.1	3.4 ; 5.2
Visit 9 (Week 78)		
N	11	40
Mean (SD)	4.58 (0.34)	4.40 (0.29)
Median	4.50	4.40
Min ; Max	4.2 ; 5.3	3.4 ; 5.1
Visit 11 (Week 104)		
N	11	39
Mean (SD)	4.35 (0.34)	4.45 (0.32)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	4.30	4.40
Min ; Max	4.0 ; 5.1	3.9 ; 5.4
Visit 13 (Week 130)		
N	11	40
Mean (SD)	4.46 (0.34)	4.36 (0.37)
Median	4.50	4.30
Min ; Max	4.1 ; 5.1	3.5 ; 5.3
Visit 15 (Week 156)		
N	11	38
Mean (SD)	4.47 (0.33)	4.31 (0.28)
Median	4.40	4.25
Min ; Max	4.0 ; 5.0	3.8 ; 5.0
Visit 18 (Week 182)		
N	11	34
Mean (SD)	4.47 (0.38)	4.44 (0.38)
Median	4.30	4.35
Min ; Max	4.0 ; 5.0	3.3 ; 5.2
Visit 20 (Week 208)		
N	10	36
Mean (SD)	4.35 (0.27)	4.41 (0.37)
Median	4.35	4.40
Min ; Max	3.8 ; 4.7	3.6 ; 5.2
Visit 20 (Week 208) Treatment completers		
N	10	36
Mean (SD)	4.35 (0.27)	4.41 (0.37)
Median	4.35	4.40

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	3.8 ; 4.7	3.6 ; 5.2
Overall minimum value for each subject*		
N	13	43
Mean (SD)	4.11 (0.17)	4.03 (0.23)
Median	4.10	4.00
Min ; Max	3.8 ; 4.4	3.1 ; 4.4
Overall maximum value for each subject*		
N	13	43
Mean (SD)	4.84 (0.29)	4.82 (0.33)
Median	4.90	4.80
Min ; Max	4.4 ; 5.3	4.0 ; 5.5
Sodium (mmol/L)		
Visit 1 (Week -3)		
N	14	44
Mean (SD)	138.1 (1.7)	138.4 (1.7)
Median	138.0	138.0
Min ; Max	135 ; 141	135 ; 142
Visit 4 (Week 13)		
N	12	43
Mean (SD)	139.1 (1.7)	138.7 (1.7)
Median	139.0	138.0
Min ; Max	136 ; 142	135 ; 143
Visit 5 (Week 26)		
N	13	42

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	139.2 (2.0)	139.6 (1.9)
Median	139.0	140.0
Min ; Max	137 ; 144	136 ; 143
Visit 6 (Week 39)		
N	13	42
Mean (SD)	139.3 (2.1)	139.4 (1.9)
Median	140.0	140.0
Min ; Max	136 ; 143	136 ; 143
Visit 7 (Week 52)		
N	13	43
Mean (SD)	138.2 (3.1)	139.4 (1.7)
Median	139.0	140.0
Min ; Max	129 ; 141	136 ; 144
Visit 9 (Week 78)		
N	11	40
Mean (SD)	139.2 (1.3)	139.7 (1.5)
Median	139.0	140.0
Min ; Max	137 ; 141	137 ; 143
Visit 11 (Week 104)		
N	11	39
Mean (SD)	140.3 (2.0)	139.9 (1.9)
Median	140.0	140.0
Min ; Max	138 ; 145	136 ; 147
Visit 13 (Week 130)		
N	11	40
Mean (SD)	139.4 (1.4)	140.3 (1.6)
Median	139.0	140.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	138 ; 143	137 ; 145
Visit 15 (Week 156)		
N	11	38
Mean (SD)	139.1 (1.5)	139.8 (1.5)
Median	139.0	140.0
Min ; Max	136 ; 141	136 ; 143
Visit 18 (Week 182)		
N	11	34
Mean (SD)	139.1 (1.8)	139.8 (1.8)
Median	139.0	140.0
Min ; Max	137 ; 143	136 ; 144
Visit 20 (Week 208)		
N	11	36
Mean (SD)	138.9 (2.3)	139.2 (1.8)
Median	140.0	139.0
Min ; Max	135 ; 143	136 ; 143
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	138.9 (2.3)	139.2 (1.8)
Median	140.0	139.0
Min ; Max	135 ; 143	136 ; 143
Overall minimum value for each subject*		
N	13	43
Mean (SD)	136.5 (2.6)	137.3 (1.1)
Median	137.0	137.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	129 ; 140	135 ; 140
Overall maximum value for each subject*		
N	13	43
Mean (SD)	141.5 (2.1)	142.0 (1.5)
Median	142.0	142.0
Min ; Max	137 ; 145	139 ; 147
Chloride (mmol/L)		
Visit 1 (Week -3)		
N	14	44
Mean (SD)	99.3 (1.9)	100.5 (2.2)
Median	100.0	101.0
Min ; Max	95 ; 102	94 ; 105
Visit 4 (Week 13)		
N	12	43
Mean (SD)	101.8 (2.1)	100.9 (2.2)
Median	101.5	101.0
Min ; Max	99 ; 106	94 ; 106
Visit 5 (Week 26)		
N	13	42
Mean (SD)	100.6 (2.1)	100.6 (2.5)
Median	100.0	101.0
Min ; Max	98 ; 105	94 ; 107
Visit 6 (Week 39)		
N	13	42
Mean (SD)	101.1 (1.4)	101.4 (2.1)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	101.0	101.0
Min ; Max	99 ; 104	97 ; 106
Visit 7 (Week 52)		
N	13	43
Mean (SD)	99.8 (3.6)	100.4 (1.9)
Median	100.0	101.0
Min ; Max	90 ; 104	93 ; 104
Visit 9 (Week 78)		
N	11	40
Mean (SD)	101.1 (1.8)	102.0 (1.6)
Median	101.0	102.0
Min ; Max	99 ; 104	98 ; 106
Visit 11 (Week 104)		
N	11	39
Mean (SD)	102.9 (2.9)	102.7 (2.2)
Median	104.0	103.0
Min ; Max	98 ; 108	99 ; 109
Visit 13 (Week 130)		
N	11	40
Mean (SD)	102.7 (2.3)	103.8 (2.4)
Median	103.0	103.5
Min ; Max	99 ; 106	99 ; 108
Visit 15 (Week 156)		
N	11	38
Mean (SD)	101.8 (2.6)	102.9 (2.2)
Median	102.0	103.0
Min ; Max	97 ; 105	97 ; 107

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 18 (Week 182)		
N	10	32
Mean (SD)	102.5 (2.3)	102.7 (2.0)
Median	101.5	103.0
Min ; Max	100 ; 106	97 ; 106
Visit 20 (Week 208)		
N	11	36
Mean (SD)	102.0 (2.6)	103.4 (2.4)
Median	102.0	103.0
Min ; Max	97 ; 106	98 ; 108
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	102.0 (2.6)	103.4 (2.4)
Median	102.0	103.0
Min ; Max	97 ; 106	98 ; 108
Overall minimum value for each subject*		
N	13	43
Mean (SD)	98.3 (2.9)	98.9 (2.1)
Median	99.0	99.0
Min ; Max	90 ; 102	93 ; 103
Overall maximum value for each subject*		
N	13	43
Mean (SD)	104.5 (1.9)	105.1 (1.9)
Median	105.0	105.0
Min ; Max	100 ; 108	101 ; 109

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Uric acid (umol/L)		
Visit 1 (Week -3)		
N	14	44
Mean (SD)	226.5 (54.3)	227.7 (50.4)
Median	232.0	226.0
Min ; Max	143 ; 369	149 ; 363
Visit 4 (Week 13)		
N	12	43
Mean (SD)	231.9 (35.3)	246.5 (40.7)
Median	235.0	250.0
Min ; Max	178 ; 297	149 ; 351
Visit 5 (Week 26)		
N	13	42
Mean (SD)	241.1 (52.7)	230.2 (46.4)
Median	226.0	220.0
Min ; Max	161 ; 339	155 ; 375
Visit 6 (Week 39)		
N	13	42
Mean (SD)	218.6 (45.0)	243.6 (48.2)
Median	208.0	244.0
Min ; Max	167 ; 303	131 ; 345
Visit 7 (Week 52)		
N	13	43
Mean (SD)	253.0 (72.6)	223.0 (51.4)
Median	274.0	214.0
Min ; Max	167 ; 363	113 ; 345

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 9 (Week 78)		
N	11	39
Mean (SD)	222.5 (50.8)	239.0 (49.5)
Median	226.0	238.0
Min ; Max	161 ; 286	155 ; 345
Visit 11 (Week 104)		
N	11	38
Mean (SD)	232.0 (30.1)	228.9 (51.0)
Median	232.0	220.0
Min ; Max	196 ; 286	143 ; 327
Visit 13 (Week 130)		
N	11	40
Mean (SD)	228.7 (37.9)	233.2 (50.1)
Median	232.0	235.0
Min ; Max	161 ; 291	113 ; 363
Visit 15 (Week 156)		
N	11	38
Mean (SD)	227.5 (42.0)	227.6 (46.9)
Median	202.0	223.0
Min ; Max	178 ; 297	113 ; 351
Visit 18 (Week 182)		
N	10	31
Mean (SD)	237.2 (63.6)	246.8 (47.7)
Median	229.0	256.0
Min ; Max	143 ; 327	131 ; 357
Visit 20 (Week 208)		
N	11	36

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	232.9 (56.5)	235.9 (51.4)
Median	238.0	238.0
Min ; Max	178 ; 327	107 ; 357
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	232.9 (56.5)	235.9 (51.4)
Median	238.0	238.0
Min ; Max	178 ; 327	107 ; 357
Overall minimum value for each subject*		
N	13	43
Mean (SD)	187.2 (28.5)	189.0 (33.5)
Median	184.0	190.0
Min ; Max	143 ; 232	101 ; 274
Overall maximum value for each subject*		
N	13	43
Mean (SD)	280.1 (53.8)	287.7 (45.1)
Median	274.0	291.0
Min ; Max	208 ; 363	178 ; 375
Total protein (g/L)		
Visit 1 (Week -3)		
N	14	44
Mean (SD)	72.7 (3.4)	69.3 (4.3)
Median	72.5	69.0
Min ; Max	68 ; 77	61 ; 79

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 4 (Week 13)		
N	12	43
Mean (SD)	70.3 (4.0)	68.8 (4.3)
Median	69.5	68.0
Min ; Max	65 ; 79	60 ; 78
Visit 5 (Week 26)		
N	13	42
Mean (SD)	71.4 (4.2)	68.5 (5.0)
Median	71.0	68.0
Min ; Max	65 ; 79	57 ; 79
Visit 6 (Week 39)		
N	13	42
Mean (SD)	70.8 (5.0)	68.9 (4.3)
Median	71.0	68.5
Min ; Max	63 ; 78	62 ; 79
Visit 7 (Week 52)		
N	13	43
Mean (SD)	68.3 (9.2)	69.5 (4.4)
Median	69.0	70.0
Min ; Max	40 ; 77	61 ; 78
Visit 9 (Week 78)		
N	11	39
Mean (SD)	73.5 (6.6)	70.0 (4.3)
Median	73.0	68.0
Min ; Max	65 ; 86	63 ; 79
Visit 11 (Week 104)		
N	11	38

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	72.0 (4.4)	70.2 (4.3)
Median	72.0	69.5
Min ; Max	65 ; 77	64 ; 84
Visit 13 (Week 130)		
N	11	40
Mean (SD)	72.3 (4.2)	70.1 (4.3)
Median	71.0	70.0
Min ; Max	67 ; 79	62 ; 82
Visit 15 (Week 156)		
N	11	38
Mean (SD)	73.4 (2.5)	69.9 (5.2)
Median	74.0	69.5
Min ; Max	69 ; 78	62 ; 86
Visit 18 (Week 182)		
N	10	31
Mean (SD)	71.4 (4.3)	69.4 (3.1)
Median	73.5	70.0
Min ; Max	63 ; 76	63 ; 75
Visit 20 (Week 208)		
N	11	36
Mean (SD)	72.2 (5.1)	70.8 (5.5)
Median	73.0	70.0
Min ; Max	62 ; 80	63 ; 93
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	72.2 (5.1)	70.8 (5.5)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	73.0	70.0
Min ; Max	62 ; 80	63 ; 93
Overall minimum value for each subject*		
N	13	43
Mean (SD)	65.7 (8.4)	65.6 (3.4)
Median	68.0	65.0
Min ; Max	40 ; 73	57 ; 73
Overall maximum value for each subject*		
N	13	43
Mean (SD)	76.2 (4.6)	73.9 (5.3)
Median	77.0	73.0
Min ; Max	70 ; 86	66 ; 93
Albumin (g/L)		
Visit 1 (Week -3)		
N	14	44
Mean (SD)	47.1 (2.1)	45.9 (2.7)
Median	47.0	46.0
Min ; Max	44 ; 50	41 ; 51
Visit 4 (Week 13)		
N	12	43
Mean (SD)	44.9 (2.1)	45.5 (2.2)
Median	45.0	45.0
Min ; Max	42 ; 49	40 ; 52
Visit 5 (Week 26)		

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
N	13	42
Mean (SD)	45.0 (2.1)	44.5 (2.3)
Median	45.0	45.0
Min ; Max	41 ; 49	40 ; 49
Visit 6 (Week 39)		
N	13	42
Mean (SD)	44.5 (3.0)	44.8 (3.0)
Median	45.0	45.0
Min ; Max	40 ; 50	37 ; 50
Visit 7 (Week 52)		
N	13	43
Mean (SD)	41.8 (8.5)	44.4 (2.6)
Median	44.0	45.0
Min ; Max	14 ; 46	39 ; 50
Visit 9 (Week 78)		
N	11	40
Mean (SD)	46.0 (2.7)	44.8 (2.2)
Median	46.0	45.0
Min ; Max	42 ; 50	41 ; 51
Visit 11 (Week 104)		
N	11	39
Mean (SD)	45.8 (2.0)	44.9 (2.3)
Median	46.0	45.0
Min ; Max	42 ; 49	39 ; 51
Visit 13 (Week 130)		
N	11	40
Mean (SD)	46.0 (2.4)	44.7 (2.7)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	46.0	45.0
Min ; Max	43 ; 49	37 ; 50
Visit 15 (Week 156)		
N	11	38
Mean (SD)	46.6 (2.3)	45.9 (3.3)
Median	46.0	45.5
Min ; Max	42 ; 50	40 ; 54
Visit 18 (Week 182)		
N	11	34
Mean (SD)	46.2 (2.2)	46.0 (2.0)
Median	46.0	46.0
Min ; Max	43 ; 50	42 ; 51
Visit 20 (Week 208)		
N	11	36
Mean (SD)	45.5 (1.9)	46.5 (2.8)
Median	46.0	46.5
Min ; Max	42 ; 49	42 ; 57
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	45.5 (1.9)	46.5 (2.8)
Median	46.0	46.5
Min ; Max	42 ; 49	42 ; 57
Overall minimum value for each subject*		
N	13	43
Mean (SD)	40.5 (8.1)	42.4 (2.1)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	42.0	43.0
Min ; Max	14 ; 45	37 ; 46
Overall maximum value for each subject*		
N	13	43
Mean (SD)	47.7 (1.9)	48.3 (2.8)
Median	48.0	48.0
Min ; Max	44 ; 50	43 ; 57
Creatine kinase (U/L)		
Visit 1 (Week -3)		
N	14	44
Mean (SD)	80.7 (23.9)	110.7 (50.3)
Median	84.0	103.5
Min ; Max	34 ; 113	20 ; 268
Visit 4 (Week 13)		
N	12	43
Mean (SD)	128.6 (38.1)	145.2 (103.0)
Median	121.5	132.0
Min ; Max	88 ; 204	30 ; 716
Visit 5 (Week 26)		
N	13	42
Mean (SD)	120.8 (34.3)	124.3 (63.2)
Median	125.0	117.0
Min ; Max	47 ; 165	28 ; 393
Visit 6 (Week 39)		
N	13	42

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	149.9 (129.3)	114.9 (44.4)
Median	104.0	111.0
Min ; Max	80 ; 564	12 ; 235
Visit 7 (Week 52)		
N	13	42
Mean (SD)	106.3 (33.4)	118.7 (47.5)
Median	112.0	110.0
Min ; Max	53 ; 158	18 ; 222
Visit 9 (Week 78)		
N	11	39
Mean (SD)	115.5 (24.8)	130.2 (91.8)
Median	117.0	112.0
Min ; Max	69 ; 144	18 ; 622
Visit 11 (Week 104)		
N	11	38
Mean (SD)	121.4 (39.1)	136.8 (78.4)
Median	109.0	133.0
Min ; Max	72 ; 187	19 ; 516
Visit 13 (Week 130)		
N	11	40
Mean (SD)	108.4 (27.2)	130.8 (77.4)
Median	121.0	109.0
Min ; Max	78 ; 154	29 ; 458
Visit 15 (Week 156)		
N	11	37
Mean (SD)	103.0 (28.5)	116.0 (48.8)
Median	99.0	123.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	61 ; 167	17 ; 297
Visit 18 (Week 182)		
N	10	31
Mean (SD)	112.2 (62.7)	133.5 (103.1)
Median	97.0	111.0
Min ; Max	68 ; 285	10 ; 613
Visit 20 (Week 208)		
N	11	36
Mean (SD)	98.3 (33.8)	148.4 (122.8)
Median	90.0	121.5
Min ; Max	63 ; 177	19 ; 718
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	98.3 (33.8)	148.4 (122.8)
Median	90.0	121.5
Min ; Max	63 ; 177	19 ; 718
Overall minimum value for each subject*		
N	13	43
Mean (SD)	77.7 (18.3)	86.0 (31.1)
Median	83.0	84.0
Min ; Max	47 ; 112	10 ; 169
Overall maximum value for each subject*		
N	13	43
Mean (SD)	197.9 (118.3)	524.4 (2261.5)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	167.0	180.0
Min ; Max	113 ; 564	30 ; 15000
Alkaline phosphatase (AP) (U/L)		
Visit 1 (Week -3)		
N	14	44
Mean (SD)	209.4 (41.0)	183.8 (43.0)
Median	217.5	185.0
Min ; Max	152 ; 279	76 ; 302
Visit 4 (Week 13)		
N	12	43
Mean (SD)	285.8 (61.4)	249.7 (59.0)
Median	284.5	242.0
Min ; Max	200 ; 392	177 ; 455
Visit 5 (Week 26)		
N	13	41
Mean (SD)	278.8 (51.8)	243.4 (59.4)
Median	284.0	239.0
Min ; Max	194 ; 358	142 ; 389
Visit 6 (Week 39)		
N	13	42
Mean (SD)	258.7 (52.8)	248.6 (60.0)
Median	244.0	244.5
Min ; Max	166 ; 369	151 ; 456
Visit 7 (Week 52)		
N	13	43
Mean (SD)	256.7 (56.7)	235.1 (45.1)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	277.0	228.0
Min ; Max	174 ; 331	157 ; 330
Visit 9 (Week 78)		
N	11	40
Mean (SD)	264.6 (59.3)	262.6 (58.2)
Median	254.0	265.0
Min ; Max	146 ; 358	148 ; 379
Visit 11 (Week 104)		
N	11	39
Mean (SD)	261.4 (38.2)	247.4 (51.3)
Median	277.0	245.0
Min ; Max	200 ; 310	139 ; 375
Visit 13 (Week 130)		
N	11	40
Mean (SD)	254.1 (35.6)	242.1 (51.5)
Median	259.0	239.0
Min ; Max	178 ; 291	145 ; 359
Visit 15 (Week 156)		
N	11	38
Mean (SD)	255.2 (43.4)	242.2 (61.2)
Median	247.0	228.0
Min ; Max	188 ; 310	137 ; 416
Visit 18 (Week 182)		
N	10	32
Mean (SD)	248.0 (69.5)	241.9 (53.0)
Median	247.5	232.5
Min ; Max	156 ; 404	152 ; 375

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 20 (Week 208)		
N	11	36
Mean (SD)	268.9 (77.8)	266.2 (70.2)
Median	254.0	242.5
Min ; Max	168 ; 411	150 ; 423
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	268.9 (77.8)	266.2 (70.2)
Median	254.0	242.5
Min ; Max	168 ; 411	150 ; 423
Overall minimum value for each subject*		
N	13	43
Mean (SD)	217.8 (40.3)	199.1 (37.9)
Median	215.0	199.0
Min ; Max	146 ; 279	137 ; 293
Overall maximum value for each subject*		
N	13	43
Mean (SD)	315.9 (62.7)	299.7 (63.6)
Median	322.0	291.0
Min ; Max	200 ; 411	201 ; 456
eGFR (Schwartz) (mL/min/1.73m^2)		
Visit 1 (Week -3)		
N	13	33

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	159.3 (36.7)	153.2 (37.1)
Median	158.6	153.8
Min ; Max	108.3 ; 231.2	85.8 ; 213.4
Visit 4 (Week 13)		
N	9	32
Mean (SD)	173.5 (41.3)	152.0 (35.3)
Median	181.0	144.2
Min ; Max	110.2 ; 233.8	96.4 ; 242.2
Visit 5 (Week 26)		
N	11	35
Mean (SD)	145.1 (32.2)	162.3 (35.0)
Median	144.1	154.7
Min ; Max	103.8 ; 208.2	110.5 ; 238.3
Visit 6 (Week 39)		
N	10	35
Mean (SD)	152.0 (20.0)	159.1 (32.7)
Median	150.4	152.6
Min ; Max	122.7 ; 187.8	99.7 ; 231.9
Visit 7 (Week 52)		
N	13	36
Mean (SD)	156.3 (30.1)	162.9 (37.6)
Median	155.3	158.0
Min ; Max	107.3 ; 197.0	99.6 ; 238.2
Visit 9 (Week 78)		
N	10	31
Mean (SD)	155.5 (36.9)	169.4 (33.8)
Median	144.3	163.6

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	110.9 ; 207.6	113.9 ; 248.5
Visit 11 (Week 104)		
N	10	29
Mean (SD)	161.3 (31.5)	167.0 (38.9)
Median	151.9	154.7
Min ; Max	128.5 ; 212.4	115.7 ; 258.9
Visit 13 (Week 130)		
N	10	37
Mean (SD)	167.4 (35.2)	176.2 (40.8)
Median	155.4	163.9
Min ; Max	132.6 ; 229.5	103.7 ; 270.0
Visit 15 (Week 156)		
N	10	34
Mean (SD)	173.4 (36.5)	181.4 (48.5)
Median	172.4	167.7
Min ; Max	118.6 ; 229.3	107.3 ; 271.7
Visit 18 (Week 182)		
N	10	31
Mean (SD)	162.2 (45.5)	175.0 (38.8)
Median	149.0	162.6
Min ; Max	110.0 ; 253.7	132.9 ; 258.9
Visit 20 (Week 208)		
N	10	34
Mean (SD)	158.1 (36.1)	162.5 (41.6)
Median	152.6	156.3
Min ; Max	111.2 ; 243.0	108.0 ; 272.3

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 20 (Week 208) Treatment completers		
N	10	34
Mean (SD)	158.1 (36.1)	162.5 (41.6)
Median	152.6	156.3
Min ; Max	111.2 ; 243.0	108.0 ; 272.3
Overall minimum value for each subject*		
N	13	43
Mean (SD)	133.8 (21.7)	138.9 (29.7)
Median	134.1	135.2
Min ; Max	103.8 ; 181.0	96.4 ; 218.1
Overall maximum value for each subject*		
N	13	43
Mean (SD)	203.0 (33.5)	209.9 (37.8)
Median	208.2	218.1
Min ; Max	147.1 ; 253.7	123.0 ; 272.3

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

79: Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Number of subjects	1	2	7
Alanine aminotransferase (ALT) (U/L)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	12.0 (.)	23.5 (16.3)	15.7 (6.9)
Median	12.0	23.5	14.0
Min ; Max	12 ; 12	12 ; 35	11 ; 31
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	15.0 (.)	16.5 (12.0)	13.0 (1.7)
Median	15.0	16.5	12.0
Min ; Max	15 ; 15	8 ; 25	12 ; 15
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	12.0 (.)	19.0 (.)	
Median	12.0	19.0	
Min ; Max	12 ; 12	19 ; 19	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	12.0 (.)	13.5 (7.8)	13.0 (1.7)
Median	12.0	13.5	12.0
Min ; Max	12 ; 12	8 ; 19	12 ; 15
Overall maximum value for each subject*			

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
N	1	2	3
Mean (SD)	15.0 (.)	16.5 (12.0)	13.0 (1.7)
Median	15.0	16.5	12.0
Min ; Max	15 ; 15	8 ; 25	12 ; 15
Aspartate aminotransferase (AST) (U/L)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	35.0 (.)	24.5 (0.7)	29.3 (8.2)
Median	35.0	24.5	29.0
Min ; Max	35 ; 35	24 ; 25	20 ; 42
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	33.0 (.)	19.0 (5.7)	24.3 (0.6)
Median	33.0	19.0	24.0
Min ; Max	33 ; 33	15 ; 23	24 ; 25
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	29.0 (.)	14.0 (.)	
Median	29.0	14.0	
Min ; Max	29 ; 29	14 ; 14	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	29.0 (.)	18.5 (6.4)	24.3 (0.6)
Median	29.0	18.5	24.0
Min ; Max	29 ; 29	14 ; 23	24 ; 25

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	33.0 (.)	19.0 (5.7)	24.3 (0.6)
Median	33.0	19.0	24.0
Min ; Max	33 ; 33	15 ; 23	24 ; 25
Bilirubin (total) (umol/L)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	1.25 (.)	3.40 (0.00)	10.17 (3.43)
Median	1.25	3.40	10.30
Min ; Max	1.3 ; 1.3	3.4 ; 3.4	6.5 ; 16.9
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	1.25 (.)	4.60 (2.40)	7.00 (3.38)
Median	1.25	4.60	6.50
Min ; Max	1.3 ; 1.3	2.9 ; 6.3	3.9 ; 10.6
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	1.25 (.)	1.25 (.)	
Median	1.25	1.25	
Min ; Max	1.3 ; 1.3	1.3 ; 1.3	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	1.25 (.)	3.78 (3.57)	7.00 (3.38)
Median	1.25	3.78	6.50

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Min ; Max	1.3 ; 1.3	1.3 ; 6.3	3.9 ; 10.6
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	1.25 (.)	4.60 (2.40)	7.00 (3.38)
Median	1.25	4.60	6.50
Min ; Max	1.3 ; 1.3	2.9 ; 6.3	3.9 ; 10.6
Calcium (total) (mmol/L)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	2.480 (.)	2.530 (0.071)	2.359 (0.327)
Median	2.480	2.530	2.400
Min ; Max	2.48 ; 2.48	2.48 ; 2.58	1.65 ; 2.60
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	2.400 (.)	2.490 (0.156)	2.360 (0.017)
Median	2.400	2.490	2.350
Min ; Max	2.40 ; 2.40	2.38 ; 2.60	2.35 ; 2.38
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	2.400 (.)	2.520 (.)	
Median	2.400	2.520	
Min ; Max	2.40 ; 2.40	2.52 ; 2.52	
Overall minimum value for each subject*			
N	1	2	3

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Mean (SD)	2.400 (.)	2.450 (0.099)	2.360 (0.017)
Median	2.400	2.450	2.350
Min ; Max	2.40 ; 2.40	2.38 ; 2.52	2.35 ; 2.38
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	2.400 (.)	2.490 (0.156)	2.360 (0.017)
Median	2.400	2.490	2.350
Min ; Max	2.40 ; 2.40	2.38 ; 2.60	2.35 ; 2.38
Creatinine (umol/L)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	18.0 (.)	53.0 (25.5)	36.6 (9.3)
Median	18.0	53.0	35.0
Min ; Max	18 ; 18	35 ; 71	27 ; 53
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	18.0 (.)	44.5 (24.7)	38.3 (13.3)
Median	18.0	44.5	35.0
Min ; Max	18 ; 18	27 ; 62	27 ; 53
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	18.0 (.)	62.0 (.)	
Median	18.0	62.0	
Min ; Max	18 ; 18	62 ; 62	

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	18.0 (.)	44.5 (24.7)	38.3 (13.3)
Median	18.0	44.5	35.0
Min ; Max	18 ; 18	27 ; 62	27 ; 53
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	18.0 (.)	44.5 (24.7)	38.3 (13.3)
Median	18.0	44.5	35.0
Min ; Max	18 ; 18	27 ; 62	27 ; 53
Phosphate (mmol/L)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	1.740 (.)	1.780 (0.226)	1.670 (0.134)
Median	1.740	1.780	1.710
Min ; Max	1.74 ; 1.74	1.62 ; 1.94	1.42 ; 1.84
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	2.070 (.)	2.050 (0.113)	1.570 (0.217)
Median	2.070	2.050	1.680
Min ; Max	2.07 ; 2.07	1.97 ; 2.13	1.32 ; 1.71
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	1.710 (.)	2.130 (.)	
Median	1.710	2.130	

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Min ; Max	1.71 ; 1.71	2.13 ; 2.13	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	1.710 (.)	2.050 (0.113)	1.570 (0.217)
Median	1.710	2.050	1.680
Min ; Max	1.71 ; 1.71	1.97 ; 2.13	1.32 ; 1.71
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	2.070 (.)	2.050 (0.113)	1.570 (0.217)
Median	2.070	2.050	1.680
Min ; Max	2.07 ; 2.07	1.97 ; 2.13	1.32 ; 1.71
Potassium (mmol/L)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	4.70 (.)	4.15 (0.07)	4.29 (0.29)
Median	4.70	4.15	4.30
Min ; Max	4.7 ; 4.7	4.1 ; 4.2	3.9 ; 4.7
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	4.70 (.)	4.45 (0.07)	4.50 (0.17)
Median	4.70	4.45	4.60
Min ; Max	4.7 ; 4.7	4.4 ; 4.5	4.3 ; 4.6
Visit 20 (Week 52)			
N	1	1	

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Mean (SD)	4.30 (.)	4.60 (.)	
Median	4.30	4.60	
Min ; Max	4.3 ; 4.3	4.6 ; 4.6	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	4.30 (.)	4.45 (0.07)	4.50 (0.17)
Median	4.30	4.45	4.60
Min ; Max	4.3 ; 4.3	4.4 ; 4.5	4.3 ; 4.6
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	4.70 (.)	4.50 (0.14)	4.50 (0.17)
Median	4.70	4.50	4.60
Min ; Max	4.7 ; 4.7	4.4 ; 4.6	4.3 ; 4.6
Sodium (mmol/L)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	139.0 (.)	138.5 (0.7)	140.1 (3.6)
Median	139.0	138.5	139.0
Min ; Max	139 ; 139	138 ; 139	137 ; 146
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	138.0 (.)	141.5 (3.5)	139.3 (0.6)
Median	138.0	141.5	139.0
Min ; Max	138 ; 138	139 ; 144	139 ; 140

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	138.0 (.)	143.0 (.)	
Median	138.0	143.0	
Min ; Max	138 ; 138	143 ; 143	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	138.0 (.)	141.0 (2.8)	139.3 (0.6)
Median	138.0	141.0	139.0
Min ; Max	138 ; 138	139 ; 143	139 ; 140
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	138.0 (.)	141.5 (3.5)	139.3 (0.6)
Median	138.0	141.5	139.0
Min ; Max	138 ; 138	139 ; 144	139 ; 140
Chloride (mmol/L)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	107.0 (.)	97.5 (0.7)	101.6 (1.3)
Median	107.0	97.5	101.0
Min ; Max	107 ; 107	97 ; 98	100 ; 104
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	102.0 (.)	99.5 (2.1)	104.3 (2.5)
Median	102.0	99.5	104.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Min ; Max	102 ; 102	98 ; 101	102 ; 107
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	107.0 (.)	98.0 (.)	
Median	107.0	98.0	
Min ; Max	107 ; 107	98 ; 98	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	102.0 (.)	99.5 (2.1)	104.3 (2.5)
Median	102.0	99.5	104.0
Min ; Max	102 ; 102	98 ; 101	102 ; 107
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	107.0 (.)	99.5 (2.1)	104.3 (2.5)
Median	107.0	99.5	104.0
Min ; Max	107 ; 107	98 ; 101	102 ; 107
Uric acid (umol/L)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	321.0 (.)	327.0 (168.3)	275.3 (41.0)
Median	321.0	327.0	280.0
Min ; Max	321 ; 321	208 ; 446	208 ; 315
Visit 18 (Week 26)			
N	1	2	3

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Mean (SD)	333.0 (.)	300.5 (62.9)	251.7 (60.1)
Median	333.0	300.5	220.0
Min ; Max	333 ; 333	256 ; 345	214 ; 321
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	345.0 (.)	452.0 (.)	
Median	345.0	452.0	
Min ; Max	345 ; 345	452 ; 452	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	333.0 (.)	300.5 (62.9)	251.7 (60.1)
Median	333.0	300.5	220.0
Min ; Max	333 ; 333	256 ; 345	214 ; 321
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	345.0 (.)	354.0 (138.6)	251.7 (60.1)
Median	345.0	354.0	220.0
Min ; Max	345 ; 345	256 ; 452	214 ; 321
Total protein (g/L)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	76.0 (.)	75.0 (2.8)	72.1 (4.9)
Median	76.0	75.0	71.0
Min ; Max	76 ; 76	73 ; 77	65 ; 80

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	78.0 (.)	70.5 (2.1)	67.7 (3.2)
Median	78.0	70.5	69.0
Min ; Max	78 ; 78	69 ; 72	64 ; 70
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	72.0 (.)	67.0 (.)	
Median	72.0	67.0	
Min ; Max	72 ; 72	67 ; 67	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	72.0 (.)	68.0 (1.4)	67.7 (3.2)
Median	72.0	68.0	69.0
Min ; Max	72 ; 72	67 ; 69	64 ; 70
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	78.0 (.)	70.5 (2.1)	67.7 (3.2)
Median	78.0	70.5	69.0
Min ; Max	78 ; 78	69 ; 72	64 ; 70
Albumin (g/L)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	48.0 (.)	50.5 (0.7)	48.7 (2.5)
Median	48.0	50.5	49.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Min ; Max	48 ; 48	50 ; 51	45 ; 51
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	47.0 (.)	46.0 (0.0)	45.0 (2.0)
Median	47.0	46.0	45.0
Min ; Max	47 ; 47	46 ; 46	43 ; 47
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	42.0 (.)	43.0 (.)	
Median	42.0	43.0	
Min ; Max	42 ; 42	43 ; 43	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	42.0 (.)	44.5 (2.1)	45.0 (2.0)
Median	42.0	44.5	45.0
Min ; Max	42 ; 42	43 ; 46	43 ; 47
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	47.0 (.)	46.0 (0.0)	45.0 (2.0)
Median	47.0	46.0	45.0
Min ; Max	47 ; 47	46 ; 46	43 ; 47
Creatine kinase (U/L)			
Visit 1 (Week -3)			
N	1	2	7

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Mean (SD)	133.0 (.)	143.0 (66.5)	217.9 (142.6)
Median	133.0	143.0	154.0
Min ; Max	133 ; 133	96 ; 190	113 ; 468
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	97.0 (.)	91.0 (0.0)	120.3 (22.7)
Median	97.0	91.0	112.0
Min ; Max	97 ; 97	91 ; 91	103 ; 146
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	104.0 (.)	117.0 (.)	
Median	104.0	117.0	
Min ; Max	104 ; 104	117 ; 117	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	97.0 (.)	91.0 (0.0)	120.3 (22.7)
Median	97.0	91.0	112.0
Min ; Max	97 ; 97	91 ; 91	103 ; 146
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	104.0 (.)	104.0 (18.4)	120.3 (22.7)
Median	104.0	104.0	112.0
Min ; Max	104 ; 104	91 ; 117	103 ; 146
Alkaline phosphatase (AP) (U/L)			

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	274.0 (.)	224.0 (36.8)	298.7 (121.4)
Median	274.0	224.0	257.0
Min ; Max	274 ; 274	198 ; 250	175 ; 481
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	272.0 (.)	243.0 (15.6)	305.7 (76.7)
Median	272.0	243.0	329.0
Min ; Max	272 ; 272	232 ; 254	220 ; 368
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	285.0 (.)	299.0 (.)	
Median	285.0	299.0	
Min ; Max	285 ; 285	299 ; 299	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	272.0 (.)	243.0 (15.6)	305.7 (76.7)
Median	272.0	243.0	329.0
Min ; Max	272 ; 272	232 ; 254	220 ; 368
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	285.0 (.)	265.5 (47.4)	305.7 (76.7)
Median	285.0	265.5	329.0
Min ; Max	285 ; 285	232 ; 299	220 ; 368

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
eGFR (Schwartz) (mL/min/1.73m^2)			
Visit 1 (Week -3)			
N	1	2	7
Mean (SD)	181.9 (.)	110.7 (47.2)	152.5 (20.6)
Median	181.9	110.7	159.7
Min ; Max	181.9 ; 181.9	77.3 ; 144.1	120.5 ; 170.1
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	192.9 (.)	142.1 (71.9)	154.6 (23.9)
Median	192.9	142.1	161.4
Min ; Max	192.9 ; 192.9	91.2 ; 193.0	128.0 ; 174.3
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	203.0 (.)	93.4 (.)	
Median	203.0	93.4	
Min ; Max	203.0 ; 203.0	93.4 ; 93.4	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	192.9 (.)	142.1 (71.9)	154.6 (23.9)
Median	192.9	142.1	161.4
Min ; Max	192.9 ; 192.9	91.2 ; 193.0	128.0 ; 174.3
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	203.0 (.)	143.2 (70.4)	154.6 (23.9)
Median	203.0	143.2	161.4

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Min ; Max	203.0 ; 203.0	93.4 ; 193.0	128.0 ; 174.3

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

80: Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Number of subjects	14	45
Change in Alanine aminotransferase (ALT) (U/L)		
Visit 4 (Week 13)		
N	12	43
Mean (SD)	2.0 (3.7)	0.5 (4.0)
Median	1.0	0.0
Min ; Max	-3 ; 8	-7 ; 15
Visit 5 (Week 26)		
N	13	42
Mean (SD)	-0.3 (3.3)	-0.4 (4.3)
Median	-1.0	-1.0
Min ; Max	-5 ; 5	-8 ; 15
Visit 6 (Week 39)		
N	13	42
Mean (SD)	0.8 (3.4)	-1.5 (3.0)
Median	1.0	-1.0
Min ; Max	-5 ; 7	-9 ; 4
Visit 7 (Week 52)		
N	13	42
Mean (SD)	1.1 (5.6)	-1.5 (3.2)
Median	1.0	-1.5
Min ; Max	-5 ; 18	-10 ; 6
Visit 9 (Week 78)		
N	11	39
Mean (SD)	2.3 (3.8)	-1.3 (3.7)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	3.0	-2.0
Min ; Max	-3 ; 11	-8 ; 6
Visit 11 (Week 104)		
N	11	38
Mean (SD)	-0.2 (3.2)	-1.1 (3.7)
Median	0.0	-1.0
Min ; Max	-5 ; 6	-8 ; 10
Visit 13 (Week 130)		
N	11	40
Mean (SD)	-0.5 (4.1)	-1.1 (8.0)
Median	-1.0	-2.0
Min ; Max	-7 ; 7	-12 ; 41
Visit 15 (Week 156)		
N	11	38
Mean (SD)	1.5 (7.3)	-3.0 (3.8)
Median	0.0	-3.0
Min ; Max	-5 ; 22	-10 ; 9
Visit 18 (Week 182)		
N	10	31
Mean (SD)	-0.8 (2.8)	-2.5 (4.2)
Median	-1.0	-3.0
Min ; Max	-7 ; 3	-15 ; 5
Visit 20 (Week 208)		
N	11	36
Mean (SD)	1.9 (12.3)	-2.0 (4.2)
Median	-1.0	-1.5
Min ; Max	-6 ; 38	-11 ; 6

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	1.9 (12.3)	-2.0 (4.2)
Median	-1.0	-1.5
Min ; Max	-6 ; 38	-11 ; 6
Overall minimum value for each subject*		
N	13	43
Mean (SD)	-3.5 (2.7)	-4.9 (3.2)
Median	-4.0	-4.0
Min ; Max	-7 ; 2	-15 ; 0
Overall maximum value for each subject*		
N	13	43
Mean (SD)	7.2 (9.7)	4.2 (7.1)
Median	5.0	3.0
Min ; Max	-1 ; 38	-5 ; 41
Change in Aspartate aminotransferase (AST) (U/L)		
Visit 4 (Week 13)		
N	10	31
Mean (SD)	0.0 (4.1)	-1.6 (4.5)
Median	-1.5	-2.0
Min ; Max	-4 ; 10	-10 ; 11
Visit 5 (Week 26)		
N	10	30

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	-2.6 (5.0)	-4.5 (4.5)
Median	-5.0	-4.5
Min ; Max	-8 ; 8	-14 ; 3
Visit 6 (Week 39)		
N	10	30
Mean (SD)	-0.6 (10.1)	-4.8 (4.8)
Median	-2.0	-4.0
Min ; Max	-9 ; 26	-21 ; 2
Visit 7 (Week 52)		
N	10	30
Mean (SD)	-3.4 (7.2)	-5.4 (5.6)
Median	-4.5	-5.0
Min ; Max	-12 ; 13	-22 ; 5
Visit 9 (Week 78)		
N	9	29
Mean (SD)	-0.9 (7.0)	-6.3 (5.7)
Median	-2.0	-7.0
Min ; Max	-11 ; 8	-19 ; 7
Visit 11 (Week 104)		
N	9	29
Mean (SD)	-7.1 (5.8)	-7.3 (6.5)
Median	-5.0	-7.0
Min ; Max	-16 ; 0	-22 ; 7
Visit 13 (Week 130)		
N	9	29
Mean (SD)	-5.8 (6.8)	-7.6 (7.3)
Median	-4.0	-6.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	-16 ; 6	-27 ; 6
Visit 15 (Week 156)		
N	9	27
Mean (SD)	-6.6 (7.3)	-10.3 (9.2)
Median	-6.0	-10.0
Min ; Max	-17 ; 9	-22 ; 26
Visit 18 (Week 182)		
N	8	20
Mean (SD)	-6.1 (3.1)	-9.0 (6.5)
Median	-6.5	-7.0
Min ; Max	-11 ; -1	-26 ; 5
Visit 20 (Week 208)		
N	9	27
Mean (SD)	-9.3 (6.7)	-9.7 (7.6)
Median	-6.0	-9.0
Min ; Max	-22 ; -4	-27 ; 9
Visit 20 (Week 208) Treatment completers		
N	9	27
Mean (SD)	-9.3 (6.7)	-9.7 (7.6)
Median	-6.0	-9.0
Min ; Max	-22 ; -4	-27 ; 9
Overall minimum value for each subject*		
N	10	31
Mean (SD)	-10.9 (5.3)	-12.5 (6.0)
Median	-8.5	-12.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	-22 ; -6	-27 ; -4
Overall maximum value for each subject*		
N	10	31
Mean (SD)	5.2 (9.3)	1.1 (5.4)
Median	2.5	0.0
Min ; Max	-4 ; 26	-6 ; 26
Change in Bilirubin (total) (umol/L)		
Visit 4 (Week 13)		
N	12	43
Mean (SD)	-1.39 (2.49)	0.24 (4.36)
Median	-1.40	-0.10
Min ; Max	-5.2 ; 3.4	-6.6 ; 20.6
Visit 5 (Week 26)		
N	13	42
Mean (SD)	-0.11 (2.51)	-0.53 (3.20)
Median	-0.20	-0.50
Min ; Max	-4.4 ; 4.8	-8.7 ; 7.5
Visit 6 (Week 39)		
N	13	42
Mean (SD)	-1.26 (2.22)	-0.45 (3.14)
Median	-2.00	-0.45
Min ; Max	-6.0 ; 1.9	-11.0 ; 6.3
Visit 7 (Week 52)		
N	13	43

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	-0.17 (2.05)	0.01 (4.02)
Median	-0.40	-0.30
Min ; Max	-4.8 ; 3.2	-9.8 ; 12.7
Visit 9 (Week 78)		
N	11	39
Mean (SD)	-0.27 (2.19)	0.16 (2.85)
Median	-0.40	0.20
Min ; Max	-4.3 ; 3.1	-7.4 ; 7.0
Visit 11 (Week 104)		
N	11	38
Mean (SD)	0.50 (2.70)	0.29 (3.09)
Median	1.30	0.30
Min ; Max	-4.1 ; 5.6	-8.9 ; 10.3
Visit 13 (Week 130)		
N	11	40
Mean (SD)	0.70 (3.60)	0.16 (3.84)
Median	0.90	0.00
Min ; Max	-4.7 ; 7.1	-10.1 ; 9.2
Visit 15 (Week 156)		
N	11	38
Mean (SD)	1.49 (4.82)	1.14 (3.65)
Median	0.00	0.75
Min ; Max	-3.0 ; 14.7	-4.1 ; 14.1
Visit 18 (Week 182)		
N	10	31
Mean (SD)	-0.76 (3.03)	0.70 (3.52)
Median	-0.10	0.70

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	-5.7 ; 3.1	-9.3 ; 7.3
Visit 20 (Week 208)		
N	11	36
Mean (SD)	0.63 (3.07)	0.68 (3.91)
Median	1.20	0.00
Min ; Max	-4.5 ; 5.8	-8.3 ; 11.9
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	0.63 (3.07)	0.68 (3.91)
Median	1.20	0.00
Min ; Max	-4.5 ; 5.8	-8.3 ; 11.9
Overall minimum value for each subject*		
N	13	43
Mean (SD)	-2.67 (2.47)	-2.66 (2.86)
Median	-2.55	-2.70
Min ; Max	-6.0 ; 1.2	-11.0 ; 3.7
Overall maximum value for each subject*		
N	13	43
Mean (SD)	2.74 (4.21)	3.48 (4.29)
Median	2.50	2.80
Min ; Max	-1.2 ; 14.7	-2.5 ; 20.6
Change in Calcium (total) (mmol/L)		

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 4 (Week 13)		
N	12	42
Mean (SD)	-0.002 (0.088)	0.014 (0.070)
Median	-0.025	0.000
Min ; Max	-0.12 ; 0.17	-0.15 ; 0.16
Visit 5 (Week 26)		
N	13	40
Mean (SD)	0.010 (0.093)	0.037 (0.102)
Median	0.000	0.020
Min ; Max	-0.16 ; 0.17	-0.22 ; 0.28
Visit 6 (Week 39)		
N	13	41
Mean (SD)	-0.022 (0.099)	0.004 (0.102)
Median	-0.030	0.000
Min ; Max	-0.23 ; 0.10	-0.25 ; 0.18
Visit 7 (Week 52)		
N	13	42
Mean (SD)	-0.042 (0.151)	0.033 (0.095)
Median	-0.020	0.040
Min ; Max	-0.46 ; 0.15	-0.17 ; 0.28
Visit 9 (Week 78)		
N	11	39
Mean (SD)	0.017 (0.103)	0.042 (0.083)
Median	0.030	0.040
Min ; Max	-0.12 ; 0.23	-0.15 ; 0.30
Visit 11 (Week 104)		
N	11	38

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	-0.032 (0.101)	0.030 (0.167)
Median	-0.030	0.050
Min ; Max	-0.24 ; 0.12	-0.72 ; 0.38
Visit 13 (Week 130)		
N	11	39
Mean (SD)	0.011 (0.092)	0.014 (0.116)
Median	0.020	0.000
Min ; Max	-0.14 ; 0.18	-0.23 ; 0.36
Visit 15 (Week 156)		
N	11	37
Mean (SD)	-0.003 (0.164)	0.046 (0.114)
Median	0.040	0.050
Min ; Max	-0.42 ; 0.26	-0.32 ; 0.25
Visit 18 (Week 182)		
N	10	31
Mean (SD)	-0.031 (0.079)	0.002 (0.104)
Median	-0.030	0.000
Min ; Max	-0.17 ; 0.08	-0.30 ; 0.30
Visit 20 (Week 208)		
N	11	36
Mean (SD)	-0.022 (0.107)	0.082 (0.098)
Median	0.030	0.070
Min ; Max	-0.27 ; 0.10	-0.10 ; 0.34
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	-0.022 (0.107)	0.082 (0.098)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	0.030	0.070
Min ; Max	-0.27 ; 0.10	-0.10 ; 0.34
Overall minimum value for each subject*		
N	13	42
Mean (SD)	-0.178 (0.144)	-0.107 (0.127)
Median	-0.160	-0.090
Min ; Max	-0.46 ; 0.02	-0.72 ; 0.07
Overall maximum value for each subject*		
N	13	42
Mean (SD)	0.100 (0.071)	0.132 (0.096)
Median	0.100	0.120
Min ; Max	-0.03 ; 0.26	-0.05 ; 0.38
Change in Creatinine (umol/L)		
Visit 4 (Week 13)		
N	12	43
Mean (SD)	-2.8 (8.7)	0.6 (6.7)
Median	-8.0	0.0
Min ; Max	-9 ; 18	-9 ; 26
Visit 5 (Week 26)		
N	13	42
Mean (SD)	2.1 (7.3)	0.7 (7.2)
Median	0.0	0.0
Min ; Max	-9 ; 18	-18 ; 9
Visit 6 (Week 39)		

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
N	13	42
Mean (SD)	0.1 (6.3)	1.7 (6.2)
Median	0.0	0.0
Min ; Max	-9 ; 9	-9 ; 18
Visit 7 (Week 52)		
N	13	43
Mean (SD)	3.5 (6.7)	1.8 (6.2)
Median	0.0	0.0
Min ; Max	-8 ; 18	-9 ; 17
Visit 9 (Week 78)		
N	11	40
Mean (SD)	4.0 (6.1)	1.2 (7.2)
Median	0.0	0.0
Min ; Max	0 ; 18	-9 ; 18
Visit 11 (Week 104)		
N	11	39
Mean (SD)	3.3 (6.1)	2.0 (5.1)
Median	0.0	0.0
Min ; Max	0 ; 18	-9 ; 9
Visit 13 (Week 130)		
N	11	40
Mean (SD)	3.3 (6.1)	4.6 (6.4)
Median	0.0	4.0
Min ; Max	0 ; 18	-9 ; 18
Visit 15 (Week 156)		
N	11	38
Mean (SD)	3.4 (7.1)	5.1 (5.9)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	0.0	8.0
Min ; Max	-8 ; 18	-8 ; 18
Visit 18 (Week 182)		
N	10	32
Mean (SD)	7.8 (7.6)	7.3 (6.6)
Median	8.5	8.5
Min ; Max	0 ; 26	-8 ; 18
Visit 20 (Week 208)		
N	11	36
Mean (SD)	7.1 (7.6)	9.9 (6.3)
Median	8.0	9.0
Min ; Max	0 ; 26	0 ; 18
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	7.1 (7.6)	9.9 (6.3)
Median	8.0	9.0
Min ; Max	0 ; 26	0 ; 18
Overall minimum value for each subject*		
N	13	43
Mean (SD)	-4.0 (5.8)	-3.4 (5.1)
Median	-8.0	0.0
Min ; Max	-9 ; 9	-18 ; 9
Overall maximum value for each subject*		
N	13	43

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	8.7 (6.1)	11.0 (5.5)
Median	9.0	9.0
Min ; Max	0 ; 26	0 ; 26
Change in Phosphate (mmol/L)		
Visit 4 (Week 13)		
N	12	43
Mean (SD)	0.116 (0.149)	0.142 (0.222)
Median	0.110	0.200
Min ; Max	-0.09 ; 0.35	-0.33 ; 0.58
Visit 5 (Week 26)		
N	13	42
Mean (SD)	0.218 (0.150)	0.208 (0.194)
Median	0.260	0.195
Min ; Max	-0.13 ; 0.42	-0.17 ; 0.71
Visit 6 (Week 39)		
N	13	42
Mean (SD)	0.132 (0.202)	0.178 (0.269)
Median	0.170	0.165
Min ; Max	-0.22 ; 0.39	-0.55 ; 0.71
Visit 7 (Week 52)		
N	13	43
Mean (SD)	0.195 (0.162)	0.219 (0.170)
Median	0.190	0.190
Min ; Max	-0.26 ; 0.38	-0.10 ; 0.61
Visit 9 (Week 78)		
N	11	38

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	0.168 (0.277)	0.272 (0.226)
Median	0.160	0.275
Min ; Max	-0.38 ; 0.62	-0.20 ; 0.81
Visit 11 (Week 104)		
N	10	35
Mean (SD)	0.139 (0.189)	0.288 (0.219)
Median	0.180	0.250
Min ; Max	-0.29 ; 0.33	-0.16 ; 0.71
Visit 13 (Week 130)		
N	10	39
Mean (SD)	0.131 (0.161)	0.226 (0.222)
Median	0.160	0.190
Min ; Max	-0.20 ; 0.32	-0.16 ; 0.71
Visit 15 (Week 156)		
N	11	35
Mean (SD)	0.155 (0.197)	0.213 (0.181)
Median	0.230	0.200
Min ; Max	-0.19 ; 0.42	-0.17 ; 0.58
Visit 18 (Week 182)		
N	9	27
Mean (SD)	0.106 (0.172)	0.206 (0.207)
Median	0.070	0.220
Min ; Max	-0.09 ; 0.48	-0.23 ; 0.71
Visit 20 (Week 208)		
N	11	36
Mean (SD)	0.124 (0.165)	0.204 (0.231)
Median	0.100	0.145

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	-0.13 ; 0.48	-0.19 ; 0.81
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	0.124 (0.165)	0.204 (0.231)
Median	0.100	0.145
Min ; Max	-0.13 ; 0.48	-0.19 ; 0.81
Overall minimum value for each subject*		
N	13	43
Mean (SD)	-0.015 (0.168)	-0.007 (0.201)
Median	-0.030	0.030
Min ; Max	-0.38 ; 0.26	-0.55 ; 0.35
Overall maximum value for each subject*		
N	13	43
Mean (SD)	0.301 (0.182)	0.390 (0.208)
Median	0.360	0.360
Min ; Max	-0.09 ; 0.62	0.06 ; 0.81
Change in Potassium (mmol/L)		
Visit 4 (Week 13)		
N	12	41
Mean (SD)	-0.17 (0.40)	0.05 (0.29)
Median	-0.15	0.00
Min ; Max	-1.2 ; 0.4	-0.5 ; 0.6
Visit 5 (Week 26)		

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
N	12	41
Mean (SD)	-0.14 (0.31)	0.09 (0.31)
Median	-0.20	0.10
Min ; Max	-0.6 ; 0.6	-0.8 ; 0.9
Visit 6 (Week 39)		
N	13	42
Mean (SD)	-0.16 (0.33)	0.05 (0.44)
Median	-0.20	0.05
Min ; Max	-1.0 ; 0.3	-1.0 ; 1.2
Visit 7 (Week 52)		
N	12	43
Mean (SD)	-0.05 (0.25)	0.09 (0.36)
Median	0.00	0.10
Min ; Max	-0.4 ; 0.4	-0.7 ; 1.0
Visit 9 (Week 78)		
N	11	40
Mean (SD)	0.14 (0.41)	0.04 (0.29)
Median	0.10	0.00
Min ; Max	-0.6 ; 1.0	-0.5 ; 0.8
Visit 11 (Week 104)		
N	11	39
Mean (SD)	-0.09 (0.39)	0.08 (0.38)
Median	-0.20	0.10
Min ; Max	-0.7 ; 0.6	-0.7 ; 1.2
Visit 13 (Week 130)		
N	11	40
Mean (SD)	0.02 (0.24)	-0.00 (0.35)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	-0.10	0.05
Min ; Max	-0.2 ; 0.6	-0.9 ; 0.7
Visit 15 (Week 156)		
N	11	38
Mean (SD)	0.03 (0.40)	-0.03 (0.37)
Median	0.10	0.00
Min ; Max	-0.9 ; 0.6	-0.8 ; 1.0
Visit 18 (Week 182)		
N	11	34
Mean (SD)	0.03 (0.41)	0.08 (0.31)
Median	0.00	0.10
Min ; Max	-0.6 ; 0.6	-0.6 ; 0.7
Visit 20 (Week 208)		
N	10	36
Mean (SD)	-0.08 (0.27)	0.10 (0.37)
Median	-0.05	0.05
Min ; Max	-0.6 ; 0.4	-0.6 ; 0.8
Visit 20 (Week 208) Treatment completers		
N	10	36
Mean (SD)	-0.08 (0.27)	0.10 (0.37)
Median	-0.05	0.05
Min ; Max	-0.6 ; 0.4	-0.6 ; 0.8
Overall minimum value for each subject*		
N	13	43
Mean (SD)	-0.41 (0.33)	-0.32 (0.30)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	-0.30	-0.30
Min ; Max	-1.2 ; 0.0	-1.0 ; 0.3
Overall maximum value for each subject*		
N	13	43
Mean (SD)	0.32 (0.35)	0.47 (0.32)
Median	0.30	0.40
Min ; Max	-0.3 ; 1.0	-0.4 ; 1.3
Change in Sodium (mmol/L)		
Visit 4 (Week 13)		
N	12	43
Mean (SD)	0.8 (1.5)	0.3 (2.2)
Median	1.0	0.0
Min ; Max	-2 ; 3	-4 ; 5
Visit 5 (Week 26)		
N	13	42
Mean (SD)	1.1 (2.1)	1.1 (2.3)
Median	2.0	1.5
Min ; Max	-3 ; 4	-5 ; 6
Visit 6 (Week 39)		
N	13	42
Mean (SD)	1.2 (1.8)	0.9 (2.3)
Median	1.0	1.0
Min ; Max	-2 ; 5	-5 ; 5
Visit 7 (Week 52)		
N	13	43

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	0.1 (4.0)	1.0 (2.2)
Median	1.0	1.0
Min ; Max	-12 ; 4	-3 ; 7
Visit 9 (Week 78)		
N	11	40
Mean (SD)	1.0 (1.7)	1.3 (2.1)
Median	2.0	2.0
Min ; Max	-2 ; 4	-2 ; 6
Visit 11 (Week 104)		
N	11	39
Mean (SD)	2.1 (2.4)	1.5 (2.1)
Median	2.0	1.0
Min ; Max	-2 ; 7	-3 ; 9
Visit 13 (Week 130)		
N	11	40
Mean (SD)	1.2 (1.8)	1.9 (2.3)
Median	1.0	2.0
Min ; Max	-2 ; 5	-3 ; 8
Visit 15 (Week 156)		
N	11	38
Mean (SD)	0.9 (1.3)	1.4 (2.5)
Median	1.0	2.0
Min ; Max	-1 ; 4	-5 ; 6
Visit 18 (Week 182)		
N	11	34
Mean (SD)	0.9 (1.6)	1.2 (2.7)
Median	0.0	1.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	-1 ; 4	-4 ; 7
Visit 20 (Week 208)		
N	11	36
Mean (SD)	0.7 (2.1)	1.0 (2.5)
Median	0.0	1.0
Min ; Max	-3 ; 4	-6 ; 6
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	0.7 (2.1)	1.0 (2.5)
Median	0.0	1.0
Min ; Max	-3 ; 4	-6 ; 6
Overall minimum value for each subject*		
N	13	43
Mean (SD)	-1.7 (3.4)	-1.1 (1.9)
Median	-1.0	-1.0
Min ; Max	-12 ; 1	-6 ; 3
Overall maximum value for each subject*		
N	13	43
Mean (SD)	3.3 (1.6)	3.6 (2.2)
Median	3.0	3.0
Min ; Max	1 ; 7	-1 ; 9
Change in Chloride (mmol/L)		
Visit 4 (Week 13)		

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
N	12	43
Mean (SD)	2.8 (2.2)	0.5 (2.3)
Median	3.0	1.0
Min ; Max	0 ; 6	-4 ; 5
Visit 5 (Week 26)		
N	13	42
Mean (SD)	1.3 (2.1)	0.2 (3.0)
Median	1.0	0.5
Min ; Max	-1 ; 5	-10 ; 6
Visit 6 (Week 39)		
N	13	42
Mean (SD)	1.8 (1.4)	0.9 (2.8)
Median	2.0	2.0
Min ; Max	-1 ; 4	-5 ; 7
Visit 7 (Week 52)		
N	13	43
Mean (SD)	0.5 (3.9)	-0.0 (2.0)
Median	1.0	0.0
Min ; Max	-10 ; 5	-5 ; 4
Visit 9 (Week 78)		
N	11	40
Mean (SD)	1.5 (1.9)	1.6 (2.0)
Median	1.0	2.0
Min ; Max	-1 ; 4	-3 ; 5
Visit 11 (Week 104)		
N	11	39
Mean (SD)	3.3 (3.2)	2.4 (2.8)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	4.0	2.0
Min ; Max	-1 ; 8	-3 ; 9
Visit 13 (Week 130)		
N	11	40
Mean (SD)	3.1 (3.2)	3.4 (3.1)
Median	3.0	3.5
Min ; Max	-3 ; 7	-3 ; 11
Visit 15 (Week 156)		
N	11	38
Mean (SD)	2.2 (3.0)	2.5 (2.9)
Median	3.0	2.0
Min ; Max	-3 ; 7	-2 ; 11
Visit 18 (Week 182)		
N	10	32
Mean (SD)	2.9 (2.8)	2.1 (2.2)
Median	3.0	2.0
Min ; Max	-2 ; 7	-3 ; 6
Visit 20 (Week 208)		
N	11	36
Mean (SD)	2.4 (2.6)	3.0 (2.5)
Median	2.0	3.0
Min ; Max	-2 ; 6	-1 ; 8
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	2.4 (2.6)	3.0 (2.5)
Median	2.0	3.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	-2 ; 6	-1 ; 8
Overall minimum value for each subject*		
N	13	43
Mean (SD)	-1.0 (3.4)	-1.5 (2.4)
Median	-1.0	-1.0
Min ; Max	-10 ; 4	-10 ; 2
Overall maximum value for each subject*		
N	13	43
Mean (SD)	5.2 (1.7)	4.7 (2.7)
Median	5.0	4.0
Min ; Max	2 ; 8	0 ; 11
Change in Uric acid (umol/L)		
Visit 4 (Week 13)		
N	12	43
Mean (SD)	-5.1 (50.4)	17.4 (43.7)
Median	3.0	24.0
Min ; Max	-143 ; 65	-107 ; 113
Visit 5 (Week 26)		
N	13	42
Mean (SD)	8.2 (70.6)	0.2 (51.7)
Median	30.0	6.0
Min ; Max	-185 ; 107	-173 ; 131
Visit 6 (Week 39)		
N	13	42

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	-14.3 (59.2)	12.9 (48.6)
Median	-12.0	21.0
Min ; Max	-185 ; 41	-89 ; 107
Visit 7 (Week 52)		
N	13	43
Mean (SD)	20.1 (79.7)	-6.0 (42.4)
Median	18.0	-6.0
Min ; Max	-179 ; 131	-119 ; 77
Visit 9 (Week 78)		
N	11	39
Mean (SD)	1.9 (35.3)	8.6 (43.3)
Median	6.0	18.0
Min ; Max	-59 ; 54	-101 ; 89
Visit 11 (Week 104)		
N	11	38
Mean (SD)	11.4 (24.5)	1.0 (48.4)
Median	12.0	6.0
Min ; Max	-30 ; 53	-125 ; 78
Visit 13 (Week 130)		
N	11	40
Mean (SD)	8.1 (23.8)	3.0 (52.5)
Median	6.0	3.0
Min ; Max	-23 ; 42	-119 ; 101
Visit 15 (Week 156)		
N	11	38
Mean (SD)	6.9 (31.1)	-4.7 (49.4)
Median	12.0	12.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	-42 ; 65	-125 ; 83
Visit 18 (Week 182)		
N	10	31
Mean (SD)	18.3 (43.9)	17.8 (56.7)
Median	29.5	23.0
Min ; Max	-77 ; 77	-90 ; 148
Visit 20 (Week 208)		
N	11	36
Mean (SD)	12.3 (50.0)	5.9 (65.0)
Median	6.0	12.0
Min ; Max	-60 ; 95	-179 ; 113
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	12.3 (50.0)	5.9 (65.0)
Median	6.0	12.0
Min ; Max	-60 ; 95	-179 ; 113
Overall minimum value for each subject*		
N	13	43
Mean (SD)	-45.8 (48.8)	-40.1 (43.3)
Median	-36.0	-35.0
Min ; Max	-185 ; 12	-179 ; 17
Overall maximum value for each subject*		
N	13	43
Mean (SD)	47.2 (66.0)	58.6 (42.3)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	53.0	60.0
Min ; Max	-143 ; 131	-30 ; 148
Change in Total protein (g/L)		
Visit 4 (Week 13)		
N	12	43
Mean (SD)	-2.8 (4.1)	-0.6 (3.8)
Median	-3.5	0.0
Min ; Max	-10 ; 4	-11 ; 7
Visit 5 (Week 26)		
N	13	42
Mean (SD)	-1.3 (3.9)	-0.8 (4.3)
Median	0.0	0.0
Min ; Max	-8 ; 4	-12 ; 8
Visit 6 (Week 39)		
N	13	42
Mean (SD)	-1.8 (2.6)	-0.4 (4.8)
Median	-2.0	1.0
Min ; Max	-8 ; 1	-11 ; 7
Visit 7 (Week 52)		
N	13	43
Mean (SD)	-4.4 (7.7)	0.2 (3.2)
Median	-2.0	1.0
Min ; Max	-28 ; 1	-10 ; 5
Visit 9 (Week 78)		
N	11	39
Mean (SD)	0.7 (5.8)	0.7 (3.5)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	-2.0	1.0
Min ; Max	-6 ; 11	-10 ; 9
Visit 11 (Week 104)		
N	11	38
Mean (SD)	-0.7 (3.7)	1.2 (3.7)
Median	-1.0	1.0
Min ; Max	-5 ; 7	-6 ; 9
Visit 13 (Week 130)		
N	11	40
Mean (SD)	-0.5 (3.8)	1.0 (4.6)
Median	1.0	1.5
Min ; Max	-7 ; 6	-8 ; 14
Visit 15 (Week 156)		
N	11	38
Mean (SD)	0.6 (3.5)	1.1 (5.0)
Median	0.0	1.0
Min ; Max	-5 ; 7	-7 ; 18
Visit 18 (Week 182)		
N	10	31
Mean (SD)	-1.5 (3.7)	1.3 (3.9)
Median	-2.0	1.0
Min ; Max	-6 ; 4	-6 ; 8
Visit 20 (Week 208)		
N	11	36
Mean (SD)	-0.5 (4.3)	2.2 (4.5)
Median	0.0	1.0
Min ; Max	-7 ; 8	-7 ; 18

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	-0.5 (4.3)	2.2 (4.5)
Median	0.0	1.0
Min ; Max	-7 ; 8	-7 ; 18
Overall minimum value for each subject*		
N	13	43
Mean (SD)	-7.0 (7.0)	-3.8 (3.4)
Median	-6.0	-4.0
Min ; Max	-28 ; 1	-12 ; 2
Overall maximum value for each subject*		
N	13	43
Mean (SD)	3.5 (4.1)	4.6 (4.7)
Median	2.0	5.0
Min ; Max	-3 ; 11	-6 ; 18
Change in Albumin (g/L)		
Visit 4 (Week 13)		
N	12	43
Mean (SD)	-2.3 (2.3)	-0.4 (2.6)
Median	-2.0	0.0
Min ; Max	-6 ; 2	-5 ; 6
Visit 5 (Week 26)		
N	13	42
Mean (SD)	-2.0 (3.1)	-1.3 (2.6)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	-1.0	-1.0
Min ; Max	-7 ; 5	-6 ; 3
Visit 6 (Week 39)		
N	13	42
Mean (SD)	-2.5 (2.9)	-1.1 (3.0)
Median	-2.0	-1.0
Min ; Max	-9 ; 2	-7 ; 6
Visit 7 (Week 52)		
N	13	43
Mean (SD)	-5.2 (7.8)	-1.4 (2.4)
Median	-4.0	-1.0
Min ; Max	-30 ; 1	-8 ; 2
Visit 9 (Week 78)		
N	11	40
Mean (SD)	-1.0 (2.5)	-0.9 (2.5)
Median	-1.0	-1.0
Min ; Max	-4 ; 3	-6 ; 5
Visit 11 (Week 104)		
N	11	39
Mean (SD)	-1.2 (2.4)	-0.7 (2.5)
Median	-2.0	0.0
Min ; Max	-5 ; 2	-7 ; 4
Visit 13 (Week 130)		
N	11	40
Mean (SD)	-1.0 (2.5)	-1.0 (3.1)
Median	-1.0	-1.0
Min ; Max	-4 ; 5	-6 ; 4

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 15 (Week 156)		
N	11	38
Mean (SD)	-0.4 (2.7)	0.3 (2.8)
Median	-1.0	0.5
Min ; Max	-3 ; 6	-4 ; 7
Visit 18 (Week 182)		
N	11	34
Mean (SD)	-0.8 (2.4)	0.2 (2.4)
Median	-1.0	0.0
Min ; Max	-6 ; 3	-6 ; 4
Visit 20 (Week 208)		
N	11	36
Mean (SD)	-1.5 (2.7)	1.1 (3.0)
Median	-1.0	1.0
Min ; Max	-7 ; 2	-5 ; 11
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	-1.5 (2.7)	1.1 (3.0)
Median	-1.0	1.0
Min ; Max	-7 ; 2	-5 ; 11
Overall minimum value for each subject*		
N	13	43
Mean (SD)	-6.5 (7.5)	-3.4 (2.3)
Median	-5.0	-4.0
Min ; Max	-30 ; 1	-8 ; 1

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Overall maximum value for each subject*		
N	13	43
Mean (SD)	0.7 (2.4)	2.5 (2.9)
Median	0.0	2.0
Min ; Max	-3 ; 6	-3 ; 11
Change in Creatine kinase (U/L)		
Visit 4 (Week 13)		
N	12	43
Mean (SD)	50.3 (46.6)	36.4 (110.6)
Median	45.5	19.0
Min ; Max	-13 ; 121	-129 ; 614
Visit 5 (Week 26)		
N	13	42
Mean (SD)	40.4 (32.6)	15.4 (64.7)
Median	32.0	12.5
Min ; Max	-12 ; 91	-96 ; 280
Visit 6 (Week 39)		
N	13	42
Mean (SD)	69.5 (129.5)	5.9 (57.8)
Median	32.0	10.0
Min ; Max	-33 ; 481	-153 ; 157
Visit 7 (Week 52)		
N	13	42
Mean (SD)	25.9 (36.1)	10.3 (49.3)
Median	21.0	5.5
Min ; Max	-32 ; 95	-86 ; 161

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 9 (Week 78)		
N	11	39
Mean (SD)	31.4 (25.3)	24.7 (96.8)
Median	37.0	11.0
Min ; Max	-14 ; 81	-131 ; 520
Visit 11 (Week 104)		
N	11	38
Mean (SD)	37.2 (42.8)	29.8 (85.2)
Median	19.0	17.5
Min ; Max	-23 ; 101	-126 ; 414
Visit 13 (Week 130)		
N	11	40
Mean (SD)	24.2 (31.5)	25.2 (80.4)
Median	24.0	7.0
Min ; Max	-29 ; 91	-93 ; 356
Visit 15 (Week 156)		
N	11	37
Mean (SD)	18.8 (37.5)	8.4 (54.2)
Median	14.0	13.0
Min ; Max	-52 ; 84	-129 ; 187
Visit 18 (Week 182)		
N	10	31
Mean (SD)	25.9 (56.5)	20.0 (102.0)
Median	16.0	8.0
Min ; Max	-38 ; 173	-109 ; 511
Visit 20 (Week 208)		
N	11	36

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Mean (SD)	14.1 (39.3)	42.7 (125.2)
Median	0.0	19.0
Min ; Max	-22 ; 94	-144 ; 616
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	14.1 (39.3)	42.7 (125.2)
Median	0.0	19.0
Min ; Max	-22 ; 94	-144 ; 616
Overall minimum value for each subject*		
N	13	43
Mean (SD)	-2.7 (27.9)	-22.8 (43.0)
Median	-6.0	-17.0
Min ; Max	-52 ; 59	-153 ; 67
Overall maximum value for each subject*		
N	13	43
Mean (SD)	117.5 (116.9)	415.7 (2262.6)
Median	92.0	58.0
Min ; Max	0 ; 481	-56 ; 14898
Change in Alkaline phosphatase (AP) (U/L)		
Visit 4 (Week 13)		
N	12	43
Mean (SD)	73.8 (54.7)	67.2 (66.1)
Median	65.5	47.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Min ; Max	11 ; 180	-27 ; 299
Visit 5 (Week 26)		
N	13	41
Mean (SD)	65.9 (56.3)	61.9 (63.7)
Median	55.0	58.0
Min ; Max	-12 ; 170	-54 ; 227
Visit 6 (Week 39)		
N	13	42
Mean (SD)	45.8 (56.0)	64.5 (70.5)
Median	43.0	51.5
Min ; Max	-41 ; 129	-56 ; 276
Visit 7 (Week 52)		
N	13	43
Mean (SD)	43.8 (46.5)	52.6 (46.5)
Median	50.0	45.0
Min ; Max	-19 ; 144	-47 ; 150
Visit 9 (Week 78)		
N	11	40
Mean (SD)	55.9 (62.0)	83.2 (59.2)
Median	68.0	82.0
Min ; Max	-39 ; 146	3 ; 303
Visit 11 (Week 104)		
N	11	39
Mean (SD)	52.6 (34.9)	66.8 (47.2)
Median	52.0	61.0
Min ; Max	-2 ; 124	-19 ; 198

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 13 (Week 130)		
N	11	40
Mean (SD)	45.4 (36.0)	62.6 (51.6)
Median	57.0	66.0
Min ; Max	-22 ; 97	-80 ; 174
Visit 15 (Week 156)		
N	11	38
Mean (SD)	46.5 (43.3)	61.1 (55.5)
Median	35.0	52.5
Min ; Max	-13 ; 128	-28 ; 210
Visit 18 (Week 182)		
N	10	32
Mean (SD)	33.6 (42.3)	56.9 (48.5)
Median	26.0	47.0
Min ; Max	-12 ; 125	-19 ; 195
Visit 20 (Week 208)		
N	11	36
Mean (SD)	60.2 (51.9)	87.3 (65.7)
Median	81.0	80.0
Min ; Max	-13 ; 132	-21 ; 267
Visit 20 (Week 208) Treatment completers		
N	11	36
Mean (SD)	60.2 (51.9)	87.3 (65.7)
Median	81.0	80.0
Min ; Max	-13 ; 132	-21 ; 267

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Overall minimum value for each subject*		
N	13	43
Mean (SD)	4.9 (32.2)	16.6 (43.8)
Median	-7.0	18.0
Min ; Max	-41 ; 70	-80 ; 126
Overall maximum value for each subject*		
N	13	43
Mean (SD)	103.1 (52.5)	117.2 (67.7)
Median	96.0	108.0
Min ; Max	19 ; 180	13 ; 303
Change in eGFR (Schwartz) (mL/min/1.73m^2)		
Visit 4 (Week 13)		
N	8	30
Mean (SD)	23.8 (42.3)	1.7 (37.1)
Median	21.6	4.8
Min ; Max	-50.4 ; 82.8	-68.7 ; 83.7
Visit 5 (Week 26)		
N	11	27
Mean (SD)	-7.8 (32.7)	4.6 (37.3)
Median	5.6	6.5
Min ; Max	-62.7 ; 41.5	-62.3 ; 84.5
Visit 6 (Week 39)		
N	10	30
Mean (SD)	1.7 (32.3)	4.4 (37.2)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	11.2	8.3
Min ; Max	-59.1 ; 44.8	-60.7 ; 94.0
Visit 7 (Week 52)		
N	12	31
Mean (SD)	-0.3 (33.3)	5.3 (40.8)
Median	11.0	10.3
Min ; Max	-57.2 ; 47.0	-78.5 ; 100.3
Visit 9 (Week 78)		
N	10	27
Mean (SD)	3.7 (31.7)	16.8 (48.4)
Median	14.5	19.7
Min ; Max	-52.3 ; 40.2	-72.7 ; 110.6
Visit 11 (Week 104)		
N	10	27
Mean (SD)	9.5 (34.6)	14.1 (39.0)
Median	19.7	19.5
Min ; Max	-47.8 ; 48.3	-41.3 ; 120.9
Visit 13 (Week 130)		
N	10	29
Mean (SD)	15.6 (34.8)	18.2 (40.9)
Median	23.7	24.4
Min ; Max	-43.2 ; 57.9	-35.7 ; 132.0
Visit 15 (Week 156)		
N	10	27
Mean (SD)	21.6 (40.6)	16.5 (37.7)
Median	32.1	26.2
Min ; Max	-40.8 ; 70.6	-66.1 ; 76.7

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 18 (Week 182)		
N	9	23
Mean (SD)	3.9 (37.3)	3.9 (38.3)
Median	0.5	8.7
Min ; Max	-50.6 ; 75.0	-64.9 ; 72.0
Visit 20 (Week 208)		
N	10	25
Mean (SD)	6.4 (34.5)	0.6 (36.5)
Median	1.5	-6.1
Min ; Max	-49.4 ; 73.7	-65.4 ; 91.3
Visit 20 (Week 208) Treatment completers		
N	10	25
Mean (SD)	6.4 (34.5)	0.6 (36.5)
Median	1.5	-6.1
Min ; Max	-49.4 ; 73.7	-65.4 ; 91.3
Overall minimum value for each subject*		
N	12	32
Mean (SD)	-23.4 (26.1)	-24.8 (30.8)
Median	-20.6	-20.4
Min ; Max	-62.7 ; 16.3	-78.5 ; 22.8
Overall maximum value for each subject*		
N	12	32
Mean (SD)	47.6 (28.3)	49.9 (32.3)
Median	53.2	50.2
Min ; Max	4.3 ; 82.8	-14.6 ; 132.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

81: Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Number of subjects	1	2	7
Change in Alanine aminotransferase (ALT) (U/L)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	3.0 (.)	-7.0 (4.2)	0.0 (1.7)
Median	3.0	-7.0	1.0
Min ; Max	3 ; 3	-10 ; -4	-2 ; 1
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	0.0 (.)	-16.0 (.)	
Median	0.0	-16.0	
Min ; Max	0 ; 0	-16 ; -16	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	0.0 (.)	-10.0 (8.5)	0.0 (1.7)
Median	0.0	-10.0	1.0
Min ; Max	0 ; 0	-16 ; -4	-2 ; 1
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	3.0 (.)	-7.0 (4.2)	0.0 (1.7)
Median	3.0	-7.0	1.0
Min ; Max	3 ; 3	-10 ; -4	-2 ; 1

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Change in Aspartate aminotransferase (AST) (U/L)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	-2.0 (.)	-5.5 (6.4)	-0.7 (3.1)
Median	-2.0	-5.5	0.0
Min ; Max	-2 ; -2	-10 ; -1	-4 ; 2
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	-6.0 (.)	-11.0 (.)	
Median	-6.0	-11.0	
Min ; Max	-6 ; -6	-11 ; -11	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	-6.0 (.)	-6.0 (7.1)	-0.7 (3.1)
Median	-6.0	-6.0	0.0
Min ; Max	-6 ; -6	-11 ; -1	-4 ; 2
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	-2.0 (.)	-5.5 (6.4)	-0.7 (3.1)
Median	-2.0	-5.5	0.0
Min ; Max	-2 ; -2	-10 ; -1	-4 ; 2
Change in Bilirubin (total) (umol/L)			

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	0.00 (.)	1.20 (2.40)	-1.70 (1.91)
Median	0.00	1.20	-1.90
Min ; Max	0.0 ; 0.0	-0.5 ; 2.9	-3.5 ; 0.3
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	0.00 (.)	-2.15 (.)	
Median	0.00	-2.15	
Min ; Max	0.0 ; 0.0	-2.2 ; -2.2	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	0.00 (.)	0.38 (3.57)	-1.70 (1.91)
Median	0.00	0.38	-1.90
Min ; Max	0.0 ; 0.0	-2.2 ; 2.9	-3.5 ; 0.3
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	0.00 (.)	1.20 (2.40)	-1.70 (1.91)
Median	0.00	1.20	-1.90
Min ; Max	0.0 ; 0.0	-0.5 ; 2.9	-3.5 ; 0.3
Change in Calcium (total) (mmol/L)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	-0.080 (.)	-0.040 (0.085)	0.150 (0.514)
Median	-0.080	-0.040	-0.030

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Min ; Max	-0.08 ; -0.08	-0.10 ; 0.02	-0.25 ; 0.73
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	-0.080 (.)	-0.060 (.)	
Median	-0.080	-0.060	
Min ; Max	-0.08 ; -0.08	-0.06 ; -0.06	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	-0.080 (.)	-0.080 (0.028)	0.150 (0.514)
Median	-0.080	-0.080	-0.030
Min ; Max	-0.08 ; -0.08	-0.10 ; -0.06	-0.25 ; 0.73
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	-0.080 (.)	-0.040 (0.085)	0.150 (0.514)
Median	-0.080	-0.040	-0.030
Min ; Max	-0.08 ; -0.08	-0.10 ; 0.02	-0.25 ; 0.73
Change in Creatinine (umol/L)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	0.0 (.)	-8.5 (0.7)	0.0 (0.0)
Median	0.0	-8.5	0.0
Min ; Max	0 ; 0	-9 ; -8	0 ; 0
Visit 20 (Week 52)			
N	1	1	

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Mean (SD)	0.0 (.)	-9.0 (.)	
Median	0.0	-9.0	
Min ; Max	0 ; 0	-9 ; -9	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	0.0 (.)	-8.5 (0.7)	0.0 (0.0)
Median	0.0	-8.5	0.0
Min ; Max	0 ; 0	-9 ; -8	0 ; 0
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	0.0 (.)	-8.5 (0.7)	0.0 (0.0)
Median	0.0	-8.5	0.0
Min ; Max	0 ; 0	-9 ; -8	0 ; 0
Change in Phosphate (mmol/L)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	0.330 (.)	0.270 (0.113)	-0.090 (0.187)
Median	0.330	0.270	-0.030
Min ; Max	0.33 ; 0.33	0.19 ; 0.35	-0.30 ; 0.06
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	-0.030 (.)	0.190 (.)	
Median	-0.030	0.190	
Min ; Max	-0.03 ; -0.03	0.19 ; 0.19	

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	-0.030 (.)	0.270 (0.113)	-0.090 (0.187)
Median	-0.030	0.270	-0.030
Min ; Max	-0.03 ; -0.03	0.19 ; 0.35	-0.30 ; 0.06
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	0.330 (.)	0.270 (0.113)	-0.090 (0.187)
Median	0.330	0.270	-0.030
Min ; Max	0.33 ; 0.33	0.19 ; 0.35	-0.30 ; 0.06
Change in Potassium (mmol/L)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	0.00 (.)	0.30 (0.14)	0.13 (0.15)
Median	0.00	0.30	0.10
Min ; Max	0.0 ; 0.0	0.2 ; 0.4	0.0 ; 0.3
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	-0.40 (.)	0.50 (.)	
Median	-0.40	0.50	
Min ; Max	-0.4 ; -0.4	0.5 ; 0.5	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	-0.40 (.)	0.30 (0.14)	0.13 (0.15)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Median	-0.40	0.30	0.10
Min ; Max	-0.4 ; -0.4	0.2 ; 0.4	0.0 ; 0.3
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	0.00 (.)	0.35 (0.21)	0.13 (0.15)
Median	0.00	0.35	0.10
Min ; Max	0.0 ; 0.0	0.2 ; 0.5	0.0 ; 0.3
Change in Sodium (mmol/L)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	-1.0 (.)	3.0 (4.2)	-3.3 (4.0)
Median	-1.0	3.0	-4.0
Min ; Max	-1 ; -1	0 ; 6	-7 ; 1
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	-1.0 (.)	5.0 (.)	
Median	-1.0	5.0	
Min ; Max	-1 ; -1	5 ; 5	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	-1.0 (.)	2.5 (3.5)	-3.3 (4.0)
Median	-1.0	2.5	-4.0
Min ; Max	-1 ; -1	0 ; 5	-7 ; 1

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	-1.0 (.)	3.0 (4.2)	-3.3 (4.0)
Median	-1.0	3.0	-4.0
Min ; Max	-1 ; -1	0 ; 6	-7 ; 1
Change in Chloride (mmol/L)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	-5.0 (.)	2.0 (1.4)	1.7 (1.5)
Median	-5.0	2.0	2.0
Min ; Max	-5 ; -5	1 ; 3	0 ; 3
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	0.0 (.)	1.0 (.)	
Median	0.0	1.0	
Min ; Max	0 ; 0	1 ; 1	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	-5.0 (.)	2.0 (1.4)	1.7 (1.5)
Median	-5.0	2.0	2.0
Min ; Max	-5 ; -5	1 ; 3	0 ; 3
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	0.0 (.)	2.0 (1.4)	1.7 (1.5)

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Median	0.0	2.0	2.0
Min ; Max	0 ; 0	1 ; 3	0 ; 3
Change in Uric acid (umol/L)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	12.0 (.)	-26.5 (105.4)	0.0 (10.4)
Median	12.0	-26.5	6.0
Min ; Max	12 ; 12	-101 ; 48	-12 ; 6
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	24.0 (.)	6.0 (.)	
Median	24.0	6.0	
Min ; Max	24 ; 24	6 ; 6	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	12.0 (.)	-26.5 (105.4)	0.0 (10.4)
Median	12.0	-26.5	6.0
Min ; Max	12 ; 12	-101 ; 48	-12 ; 6
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	24.0 (.)	27.0 (29.7)	0.0 (10.4)
Median	24.0	27.0	6.0
Min ; Max	24 ; 24	6 ; 48	-12 ; 6
Change in Total protein (g/L)			

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	2.0 (.)	-4.5 (0.7)	-4.0 (4.4)
Median	2.0	-4.5	-6.0
Min ; Max	2 ; 2	-5 ; -4	-7 ; 1
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	-4.0 (.)	-10.0 (.)	
Median	-4.0	-10.0	
Min ; Max	-4 ; -4	-10 ; -10	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	-4.0 (.)	-7.0 (4.2)	-4.0 (4.4)
Median	-4.0	-7.0	-6.0
Min ; Max	-4 ; -4	-10 ; -4	-7 ; 1
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	2.0 (.)	-4.5 (0.7)	-4.0 (4.4)
Median	2.0	-4.5	-6.0
Min ; Max	2 ; 2	-5 ; -4	-7 ; 1
Change in Albumin (g/L)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	-1.0 (.)	-4.5 (0.7)	-4.3 (2.9)
Median	-1.0	-4.5	-6.0

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Min ; Max	-1 ; -1	-5 ; -4	-6 ; -1
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	-6.0 (.)	-8.0 (.)	
Median	-6.0	-8.0	
Min ; Max	-6 ; -6	-8 ; -8	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	-6.0 (.)	-6.0 (2.8)	-4.3 (2.9)
Median	-6.0	-6.0	-6.0
Min ; Max	-6 ; -6	-8 ; -4	-6 ; -1
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	-1.0 (.)	-4.5 (0.7)	-4.3 (2.9)
Median	-1.0	-4.5	-6.0
Min ; Max	-1 ; -1	-5 ; -4	-6 ; -1
Change in Creatine kinase (U/L)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	-36.0 (.)	-52.0 (66.5)	-12.3 (42.4)
Median	-36.0	-52.0	-19.0
Min ; Max	-36 ; -36	-99 ; -5	-51 ; 33
Visit 20 (Week 52)			
N	1	1	

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Mean (SD)	-29.0 (.)	-73.0 (.)	
Median	-29.0	-73.0	
Min ; Max	-29 ; -29	-73 ; -73	
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	-36.0 (.)	-52.0 (66.5)	-12.3 (42.4)
Median	-36.0	-52.0	-19.0
Min ; Max	-36 ; -36	-99 ; -5	-51 ; 33
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	-29.0 (.)	-39.0 (48.1)	-12.3 (42.4)
Median	-29.0	-39.0	-19.0
Min ; Max	-29 ; -29	-73 ; -5	-51 ; 33
Change in Alkaline phosphatase (AP) (U/L)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	-2.0 (.)	19.0 (21.2)	80.7 (40.7)
Median	-2.0	19.0	72.0
Min ; Max	-2 ; -2	4 ; 34	45 ; 125
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	11.0 (.)	49.0 (.)	
Median	11.0	49.0	
Min ; Max	11 ; 11	49 ; 49	

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Overall minimum value for each subject*			
N	1	2	3
Mean (SD)	-2.0 (.)	19.0 (21.2)	80.7 (40.7)
Median	-2.0	19.0	72.0
Min ; Max	-2 ; -2	4 ; 34	45 ; 125
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	11.0 (.)	41.5 (10.6)	80.7 (40.7)
Median	11.0	41.5	72.0
Min ; Max	11 ; 11	34 ; 49	45 ; 125
Change in eGFR (Schwartz) (mL/min/1.73m^2)			
Visit 18 (Week 26)			
N	1	2	3
Mean (SD)	11.0 (.)	31.4 (24.8)	3.7 (1.1)
Median	11.0	31.4	4.2
Min ; Max	11.0 ; 11.0	13.9 ; 48.9	2.3 ; 4.4
Visit 20 (Week 52)			
N	1	1	
Mean (SD)	21.1 (.)	16.1 (.)	
Median	21.1	16.1	
Min ; Max	21.1 ; 21.1	16.1 ; 16.1	
Overall minimum value for each subject*			
N	1	2	3

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of change from baseline in biochemistry by visit - trial 4172 (208w) - all subjects - cohort II and III

Treatment group	Cohort II somapacitan (0.16mg/kg/week) previously treated	Cohort III somapacitan (0.16mg/kg/week) treatment naive	Cohort III somapacitan (0.16mg/kg/week) previously treated
Mean (SD)	11.0 (.)	31.4 (24.8)	3.7 (1.1)
Median	11.0	31.4	4.2
Min ; Max	11.0 ; 11.0	13.9 ; 48.9	2.3 ; 4.4
Overall maximum value for each subject*			
N	1	2	3
Mean (SD)	21.1 (.)	32.5 (23.2)	3.7 (1.1)
Median	21.1	32.5	4.2
Min ; Max	21.1 ; 21.1	16.1 ; 48.9	2.3 ; 4.4

N: Number of subjects, SD: Standard deviation, eGFR: Estimated glomerular filtration rate
*Including all scheduled and un-scheduled visits.
Post randomisation only measurements from the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until visit 20 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

ソグルーヤ皮下注 5mg
ソグルーヤ皮下注 10mg
ソグルーヤ皮下注 15mg

成長ホルモン分泌不全性低身長症及び
15 mg 製剤剤形追加

2.7.4.7 付録
2. 解析帳票（日本人集団の結果を含む）

ノボ ノルディスク ファーマ株式会社

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Clinical Summary of Safety Japanese specific

1: Summary of exposure - japanese subgroup - trial 4172 (156w) - safety analysis set

Treatment group Main + Extension / Safety extension	Norditropin (0.034mg/kg/day)	somapacitan (0.04/0.16mg/kg/week)	somapacitan (0.08/0.16mg/kg/week)	somapacitan (0.16/0.16mg/kg/week)	somapacitan pooled
Number of subjects	3	3	3	3	9
Total exposure (days)	2553	3303	3302	3302	9907
Exposure (days)					
N	3	3	3	3	9
Mean (SD)	851.0 (421.8)	1101.0 (1.7)	1100.7 (1.2)	1100.7 (1.2)	1100.8 (1.2)
Median	1093	1100	1100	1100	1100
Min ; Max	364 ; 1096	1100 ; 1103	1100 ; 1102	1100 ; 1102	1100 ; 1103

N: Number of subjects, SD: Standard deviation
Exposure days in the treatment period are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan or to week 156, which ever comes first.

2: Summary of dosing by visit (mg) - japanese subgroup - trial 4172 (156w) - safety analysis set

Treatment group	Norditropin (0.034mg/kg/day)	somapacitan (0.04/0.16mg/kg/week)	somapacitan (0.08/0.16mg/kg/week)	somapacitan (0.16/0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Number of subjects	3	3	3	3	9
Visit 2 (Week 0) - Observed dose (mg)					
N	3	3	3	3	9
Mean (SD)	0.467 (0.058)	0.467 (0.038)	1.067 (0.104)	2.667 (1.290)	1.400 (1.179)
Median	0.500	0.475	1.100	2.300	1.100
Min; Max	0.40 ; 0.50	0.43 ; 0.50	0.95 ; 1.15	1.60 ; 4.10	0.43 ; 4.10
Visit 3 (Week 4) - Observed dose (mg)					
N	3	3	3	3	9
Mean (SD)	0.469 (0.068)	0.471 (0.034)	1.067 (0.090)	2.667 (1.117)	1.476 (1.144)
Median	0.500	0.475	1.100	2.300	1.100
Min; Max	0.00 ; 0.50	0.43 ; 0.50	0.95 ; 1.15	1.60 ; 4.10	0.43 ; 4.10
Visit 4 (Week 13) - Observed dose (mg)					
N	3	3	3	3	9
Mean (SD)	0.473 (0.055)	0.475 (0.042)	1.121 (0.085)	2.742 (1.073)	1.434 (1.137)
Median	0.500	0.475	1.150	2.500	1.150
Min; Max	0.00 ; 0.50	0.43 ; 0.53	1.00 ; 1.20	1.60 ; 4.10	0.43 ; 4.10
Visit 5 (Week 26) - Observed dose (mg)					
N	3	3	3	3	9
Mean (SD)	0.484 (0.094)	0.482 (0.043)	1.136 (0.104)	2.893 (1.043)	1.496 (1.184)
Median	0.500	0.500	1.150	2.600	1.150
Min; Max	0.00 ; 0.55	0.43 ; 0.53	1.00 ; 1.25	1.80 ; 4.30	0.43 ; 4.30
Visit 6 (Week 39) - Observed dose (mg)					
N	3	3	3	3	9
Mean (SD)	0.497 (0.054)	0.495 (0.052)	1.183 (0.145)	3.054 (1.192)	1.591 (1.293)
Median	0.500	0.500	1.200	2.600	1.200
Min; Max	0.00 ; 0.55	0.43 ; 0.55	1.00 ; 1.35	1.90 ; 4.70	0.43 ; 4.70
Visit 7 (Week 52) - Observed dose (mg)					
N	3	3	3	3	9
Mean (SD)	0.526 (0.064)	0.504 (0.051)	1.230 (0.133)	3.107 (1.067)	1.614 (1.262)
Median	0.550	0.500	1.300	2.800	1.300
Min; Max	0.00 ; 0.55	0.45 ; 0.58	1.05 ; 1.35	2.00 ; 4.50	0.45 ; 4.50

N: Number of subjects, EOT: End of trial, SD: Standard deviation
Observed dose at visit 2 is the dose given on site at the randomisation visit.
*The prescribed dose from and including visit 15 are for somapacitan (0.16mg/kg/week) for all treatment arms.

Summary of dosing by visit (mg) - japanese subgroup - trial 4172 (156w) - safety analysis set

Treatment group	Norditropin (0.034mg/kg/day)	somapacitan (0.04/0.16mg/kg/week)	somapacitan (0.08/0.16mg/kg/week)	somapacitan (0.16/0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 8 (Week 65) - Observed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.532 (0.104)	2.105 (0.167)	2.568 (0.287)	3.346 (1.175)	2.663 (0.866)
Median	0.500	2.100	2.600	2.900	2.300
Min; Max	0.00 ; 0.60	1.90 ; 2.30	2.20 ; 2.90	2.20 ; 4.90	1.90 ; 4.90
Visit 9 (Week 78) - Observed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.574 (0.075)	2.300 (0.165)	2.740 (0.338)	3.433 (1.181)	2.822 (0.842)
Median	0.500	2.300	2.800	3.100	2.500
Min; Max	0.50 ; 0.65	2.10 ; 2.50	2.30 ; 3.10	2.20 ; 5.00	2.10 ; 5.00
Visit 10 (Week 91) - Observed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.570 (0.079)	2.424 (0.256)	2.861 (0.289)	3.614 (1.268)	2.974 (0.915)
Median	0.500	2.500	2.900	3.100	2.700
Min; Max	0.25 ; 0.65	2.10 ; 2.70	2.50 ; 3.30	2.40 ; 5.30	2.10 ; 5.30
Visit 11 (Week 104) - Observed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.626 (0.025)	2.540 (0.253)	3.030 (0.315)	3.656 (1.192)	3.075 (0.852)
Median	0.650	2.600	3.200	3.200	2.800
Min; Max	0.60 ; 0.65	2.20 ; 2.80	2.60 ; 3.30	2.50 ; 5.30	2.20 ; 5.30
Visit 12 (Week 117) - Observed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.648 (0.070)	2.685 (0.232)	3.203 (0.217)	3.889 (1.259)	3.277 (0.911)
Median	0.700	2.800	3.300	3.500	2.900
Min; Max	0.00 ; 0.70	2.20 ; 2.90	2.90 ; 3.40	2.60 ; 5.60	2.20 ; 5.60
Visit 13 (Week 130) - Observed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.673 (0.075)	2.868 (0.129)	3.433 (0.407)	4.005 (1.288)	3.435 (0.892)
Median	0.600	2.900	3.500	3.600	3.000
Min; Max	0.60 ; 0.75	2.70 ; 3.00	2.90 ; 3.90	2.70 ; 5.70	2.70 ; 5.70
Visit 14 (Week 143) - Observed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.672 (0.075)	2.956 (0.091)	3.545 (0.268)	4.165 (1.414)	3.544 (0.961)

N: Number of subjects, EOT: End of trial, SD: Standard deviation
Observed dose at visit 2 is the dose given on site at the randomisation visit.
*The prescribed dose from and including visit 15 are for somapacitan (0.16mg/kg/week) for all treatment arms.

Summary of dosing by visit (mg) - japanese subgroup - trial 4172 (156w) - safety analysis set

Treatment group	Norditropin (0.034mg/kg/day)	somapacitan (0.04/0.16mg/kg/week)	somapacitan (0.08/0.16mg/kg/week)	somapacitan (0.16/0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	0.600	2.900	3.700	3.600	3.200
Min; Max	0.60 ; 0.75	2.90 ; 3.10	3.20 ; 3.80	2.80 ; 6.00	2.80 ; 6.00
Visit 15 (Week 156) - Observed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.729 (0.075)	3.134 (0.128)	3.635 (0.250)	4.288 (1.349)	3.703 (0.926)
Median	0.800	3.100	3.700	3.800	3.300
Min; Max	0.65 ; 0.80	3.00 ; 3.30	3.30 ; 3.90	2.90 ; 6.10	2.90 ; 6.10
Visit 3 (Week 4) - Prescribed dose (mg)					
N	3	3	3	3	9
Mean (SD)	0.483 (0.029)	0.475 (0.050)	1.117 (0.104)	2.733 (1.266)	1.442 (1.192)
Median	0.500	0.475	1.150	2.500	1.150
Min; Max	0.45 ; 0.50	0.43 ; 0.53	1.00 ; 1.20	1.60 ; 4.10	0.43 ; 4.10
Visit 4 (Week 13) - Prescribed dose (mg)					
N	3	3	3	3	9
Mean (SD)	0.500 (0.050)	0.483 (0.052)	1.133 (0.126)	2.900 (1.277)	1.506 (1.259)
Median	0.500	0.500	1.150	2.600	1.150
Min; Max	0.45 ; 0.55	0.43 ; 0.53	1.00 ; 1.25	1.80 ; 4.30	0.43 ; 4.30
Visit 5 (Week 26) - Prescribed dose (mg)					
N	3	3	3	3	9
Mean (SD)	0.500 (0.050)	0.492 (0.063)	1.183 (0.176)	2.733 (1.710)	1.469 (1.314)
Median	0.500	0.500	1.200	1.900	1.200
Min; Max	0.45 ; 0.55	0.43 ; 0.55	1.00 ; 1.35	1.60 ; 4.70	0.43 ; 4.70
Visit 6 (Week 39) - Prescribed dose (mg)					
N	3	3	3	3	9
Mean (SD)	0.533 (0.029)	0.508 (0.063)	1.233 (0.161)	3.100 (1.277)	1.614 (1.325)
Median	0.550	0.500	1.300	2.800	1.300
Min; Max	0.50 ; 0.55	0.45 ; 0.58	1.05 ; 1.35	2.00 ; 4.50	0.45 ; 4.50
Visit 7 (Week 52) - Prescribed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.550 (0.071)	0.525 (0.050)	1.283 (0.176)	3.333 (1.401)	1.714 (1.443)
Median	0.550	0.525	1.300	2.900	1.300
Min; Max	0.50 ; 0.60	0.48 ; 0.58	1.10 ; 1.45	2.20 ; 4.90	0.48 ; 4.90

N: Number of subjects, EOT: End of trial, SD: Standard deviation
Observed dose at visit 2 is the dose given on site at the randomisation visit.
*The prescribed dose from and including visit 15 are for somapacitan (0.16mg/kg/week) for all treatment arms.

Summary of dosing by visit (mg) - japanese subgroup - trial 4172 (156w) - safety analysis set

Treatment group	Norditropin (0.034mg/kg/day)	somapacitan (0.04/0.16mg/kg/week)	somapacitan (0.08/0.16mg/kg/week)	somapacitan (0.16/0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 8 (Week 65) - Prescribed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.575 (0.106)	2.300 (0.200)	2.733 (0.404)	3.433 (1.429)	2.822 (0.898)
Median	0.575	2.300	2.800	3.100	2.500
Min; Max	0.50 ; 0.65	2.10 ; 2.50	2.30 ; 3.10	2.20 ; 5.00	2.10 ; 5.00
Visit 9 (Week 78) - Prescribed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.575 (0.106)	2.433 (0.306)	2.867 (0.351)	3.600 (1.513)	2.967 (0.942)
Median	0.575	2.500	2.900	3.100	2.700
Min; Max	0.50 ; 0.65	2.10 ; 2.70	2.50 ; 3.20	2.40 ; 5.30	2.10 ; 5.30
Visit 10 (Week 91) - Prescribed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.625 (0.035)	2.533 (0.306)	3.033 (0.379)	3.667 (1.457)	3.078 (0.912)
Median	0.625	2.600	3.200	3.200	2.800
Min; Max	0.60 ; 0.65	2.20 ; 2.80	2.60 ; 3.30	2.50 ; 5.30	2.20 ; 5.30
Visit 11 (Week 104) - Prescribed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.650 (0.071)	2.700 (0.265)	3.200 (0.265)	3.900 (1.539)	3.267 (0.949)
Median	0.650	2.800	3.300	3.500	2.900
Min; Max	0.60 ; 0.70	2.40 ; 2.90	2.90 ; 3.40	2.60 ; 5.60	2.40 ; 5.60
Visit 12 (Week 117) - Prescribed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.675 (0.106)	2.867 (0.153)	3.333 (0.379)	4.000 (1.539)	3.400 (0.937)
Median	0.675	2.900	3.500	3.600	3.000
Min; Max	0.60 ; 0.75	2.70 ; 3.00	2.90 ; 3.60	2.70 ; 5.70	2.70 ; 5.70
Visit 13 (Week 130) - Prescribed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.675 (0.106)	2.967 (0.115)	3.567 (0.321)	4.100 (1.682)	3.544 (0.989)
Median	0.675	2.900	3.700	3.500	3.200
Min; Max	0.60 ; 0.75	2.90 ; 3.10	3.20 ; 3.80	2.80 ; 6.00	2.80 ; 6.00
Visit 14 (Week 143) - Prescribed dose (mg)					
N	2	3	3	3	9
Mean (SD)	0.725 (0.106)	3.133 (0.153)	3.633 (0.306)	4.267 (1.650)	3.678 (0.976)

N: Number of subjects, EOT: End of trial, SD: Standard deviation
Observed dose at visit 2 is the dose given on site at the randomisation visit.
*The prescribed dose from and including visit 15 are for somapacitan (0.16mg/kg/week) for all treatment arms.

Summary of dosing by visit (mg) - japanese subgroup - trial 4172 (156w) - safety analysis set

Treatment group	Norditropin (0.034mg/kg/day)	somapacitan (0.04/0.16mg/kg/week)	somapacitan (0.08/0.16mg/kg/week)	somapacitan (0.16/0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Median	0.725	3.100	3.700	3.800	3.300
Min; Max	0.65 ; 0.80	3.00 ; 3.30	3.30 ; 3.90	2.90 ; 6.10	2.90 ; 6.10
Visit 15 (Week 156) - Prescribed dose (mg)*					
N	2	3	3	3	9
Mean (SD)	3.400 (0.566)	3.233 (0.115)	3.900 (0.361)	4.333 (1.595)	3.822 (0.950)
Median	3.400	3.300	4.000	3.900	3.500
Min; Max	3.00 ; 3.80	3.10 ; 3.30	3.50 ; 4.20	3.00 ; 6.10	3.00 ; 6.10
Last dose taken according to diary (mg)					
N	3	3	3	3	9
Mean (SD)	0.667 (0.126)	3.133 (0.153)	3.633 (0.306)	4.267 (1.650)	3.678 (0.976)
Median	0.650	3.100	3.700	3.800	3.300
Min; Max	0.55 ; 0.80	3.00 ; 3.30	3.30 ; 3.90	2.90 ; 6.10	2.90 ; 6.10

N: Number of subjects, EOT: End of trial, SD: Standard deviation
Observed dose at visit 2 is the dose given on site at the randomisation visit.
*The prescribed dose from and including visit 15 are for somapacitan (0.16mg/kg/week) for all treatment arms.

3: Summary of actual dose by visit (mg pr week) - japanese subgroup - trial 4172 (156w) - safety analysis set

Treatment group Main + Extension / Safety extension	Norditropin (0.034mg/kg/day)	somapacitan (0.04/0.16mg/kg/week)	somapacitan (0.08/0.16mg/kg/week)	somapacitan (0.16/0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Number of subjects	3	3	3	3	9
Average weekly dose (mg pr week)					
Visit 3 (Week 4)					
N	3	3	3	3	9
Mean (SD)	3.247 (0.175)	0.467 (0.038)	1.067 (0.104)	2.667 (1.290)	1.400 (1.179)
Median	3.325	0.475	1.100	2.300	1.100
Min; Max	3.05 ; 3.37	0.43 ; 0.50	0.95 ; 1.15	1.60 ; 4.10	0.43 ; 4.10
Visit 4 (Week 13)					
N	3	3	3	3	9
Mean (SD)	3.233 (0.240)	0.475 (0.050)	1.117 (0.104)	2.733 (1.266)	1.442 (1.192)
Median	3.167	0.475	1.150	2.500	1.150
Min; Max	3.03 ; 3.50	0.43 ; 0.53	1.00 ; 1.20	1.60 ; 4.10	0.43 ; 4.10
Visit 5 (Week 26)					
N	3	3	3	3	9
Mean (SD)	3.321 (0.207)	0.483 (0.052)	1.133 (0.126)	2.900 (1.277)	1.506 (1.259)
Median	3.364	0.500	1.150	2.600	1.150
Min; Max	3.10 ; 3.50	0.42 ; 0.53	1.00 ; 1.25	1.80 ; 4.30	0.42 ; 4.30
Visit 6 (Week 39)					
N	3	3	3	3	9
Mean (SD)	3.411 (0.324)	0.492 (0.063)	1.183 (0.176)	3.067 (1.457)	1.581 (1.368)
Median	3.323	0.500	1.200	2.600	1.200
Min; Max	3.14 ; 3.77	0.42 ; 0.55	1.00 ; 1.35	1.90 ; 4.70	0.42 ; 4.70
Visit 7 (Week 52)					
N	3	3	3	3	9
Mean (SD)	3.540 (0.063)	0.508 (0.063)	1.233 (0.161)	3.100 (1.277)	1.614 (1.325)
Median	3.575	0.500	1.300	2.800	1.300
Min; Max	3.47 ; 3.58	0.45 ; 0.58	1.05 ; 1.35	2.00 ; 4.50	0.45 ; 4.50

N: Number of subjects, SD: Standard deviation

Summary of actual dose by visit (mg pr week) - japanese subgroup - trial 4172 (156w) - safety analysis set

Treatment group Main + Extension / Safety extension	Norditropin (0.034mg/kg/day)	somapacitan (0.04/0.16mg/kg/week)	somapacitan (0.08/0.16mg/kg/week)	somapacitan (0.16/0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Visit 8 (Week 65)					
N	2	3	3	3	9
Mean (SD)	3.726 (0.341)	2.100 (0.200)	2.567 (0.351)	3.333 (1.401)	2.667 (0.907)
Median	3.726	2.100	2.600	2.900	2.300
Min; Max	3.48 ; 3.97	1.90 ; 2.30	2.20 ; 2.90	2.20 ; 4.90	1.90 ; 4.90
Visit 9 (Week 78)					
N	2	3	3	3	9
Mean (SD)	4.025 (0.742)	2.300 (0.200)	2.733 (0.404)	3.433 (1.429)	2.822 (0.898)
Median	4.025	2.300	2.800	3.100	2.500
Min; Max	3.50 ; 4.55	2.10 ; 2.50	2.30 ; 3.10	2.20 ; 5.00	2.10 ; 5.00
Visit 10 (Week 91)					
N	2	3	3	3	9
Mean (SD)	3.997 (0.782)	2.433 (0.306)	2.870 (0.356)	3.600 (1.513)	2.968 (0.942)
Median	3.997	2.500	2.900	3.100	2.700
Min; Max	3.44 ; 4.55	2.10 ; 2.70	2.50 ; 3.21	2.40 ; 5.30	2.10 ; 5.30
Visit 11 (Week 104)					
N	2	3	3	3	9
Mean (SD)	4.257 (0.217)	2.533 (0.306)	3.033 (0.379)	3.667 (1.457)	3.078 (0.912)
Median	4.257	2.600	3.200	3.200	2.800
Min; Max	4.10 ; 4.41	2.20 ; 2.80	2.60 ; 3.30	2.50 ; 5.30	2.20 ; 5.30
Visit 12 (Week 117)					
N	2	3	3	3	9
Mean (SD)	4.523 (0.456)	2.694 (0.274)	3.200 (0.265)	3.900 (1.539)	3.265 (0.951)
Median	4.523	2.800	3.300	3.500	2.900
Min; Max	4.20 ; 4.85	2.38 ; 2.90	2.90 ; 3.40	2.60 ; 5.60	2.38 ; 5.60
Visit 13 (Week 130)					
N	2	3	3	3	9
Mean (SD)	4.704 (0.772)	2.867 (0.153)	3.416 (0.479)	3.995 (1.542)	3.426 (0.947)
Median	4.704	2.900	3.500	3.585	3.000
Min; Max	4.16 ; 5.25	2.70 ; 3.00	2.90 ; 3.85	2.70 ; 5.70	2.70 ; 5.70
Visit 14 (Week 143)					

N: Number of subjects, SD: Standard deviation

Summary of actual dose by visit (mg pr week) - japanese subgroup - trial 4172 (156w) - safety analysis set

Treatment group Main + Extension / Safety extension	Norditropin (0.034mg/kg/day)	somapacitan (0.04/0.16mg/kg/week)	somapacitan (0.08/0.16mg/kg/week)	somapacitan (0.16/0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
N	2	3	3	3	9
Mean (SD)	4.702 (0.774)	2.967 (0.115)	3.567 (0.321)	4.133 (1.665)	3.556 (0.989)
Median	4.702	2.900	3.700	3.600	3.200
Min; Max	4.15 ; 5.25	2.90 ; 3.10	3.20 ; 3.80	2.80 ; 6.00	2.80 ; 6.00
Visit 15 (Week 156)					
N	2	3	3	3	9
Mean (SD)	5.075 (0.742)	3.133 (0.153)	3.633 (0.306)	4.267 (1.650)	3.678 (0.976)
Median	5.075	3.100	3.700	3.800	3.300
Min; Max	4.55 ; 5.60	3.00 ; 3.30	3.30 ; 3.90	2.90 ; 6.10	2.90 ; 6.10

N: Number of subjects, SD: Standard deviation

4: Summary of adverse events - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin (0.034mg/kg/day)			somapacitan (0.04/0.16mg/kg/week)			somapacitan (0.08/0.16mg/kg/week)			somapacitan (0.16/0.16mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	3			3			3			3			9		
Total patient years at risk	7.0			9.0			9.0			9.0			27.0		
All adverse events	3 (100.0)	32	455.0	3 (100.0)	25	278.0	3 (100.0)	54	600.6	3 (100.0)	68	756.3	9 (100.0)	147	544.9
Serious adverse events															
Yes	1 (33.3)	2	28.4	1 (33.3)	1	11.1	0			1 (33.3)	1	11.1	2 (22.2)	2	7.4
No	3 (100.0)	30	426.5	3 (100.0)	24	266.8	3 (100.0)	54	600.6	3 (100.0)	67	745.2	9 (100.0)	145	537.5
Severity															
Mild	3 (100.0)	29	412.3	3 (100.0)	24	266.8	3 (100.0)	54	600.6	3 (100.0)	64	711.8	9 (100.0)	142	526.4
Moderate	2 (66.7)	3	42.7	1 (33.3)	1	11.1	0			2 (66.7)	4	44.5	3 (33.3)	5	18.5
Severe	0			0			0			0			0		
Causality															
Probable	1 (33.3)	1	14.2	0			0			0			0		
Possible	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Unlikely	3 (100.0)	31	440.7	3 (100.0)	24	266.8	3 (100.0)	54	600.6	3 (100.0)	68	756.3	9 (100.0)	146	541.2
Missing	0			0			0			0			0		
Action taken to trial product due to AE															
Drug interrupted	0			0			0			0			0		
Drug withdrawn	1 (33.3)	1	14.2	0			0			0			0		
Dose reduced	0			0			0			0			0		
Dose increased	0			0			0			0			0		
Dose not changed	3 (100.0)	31	440.7	3 (100.0)	25	278.0	3 (100.0)	54	600.6	3 (100.0)	68	756.3	9 (100.0)	147	544.9
Unknown	0			0			0			0			0		
Missing	0			0			0			0			0		
Related to technical complaint															
Yes	0			0			0			0			0		
No	3 (100.0)	32	455.0	3 (100.0)	25	278.0	3 (100.0)	54	600.6	3 (100.0)	68	756.3	9 (100.0)	147	544.9
Injection site reaction															
Yes	1 (33.3)	1	14.2	0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until week 156 or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
AE causality is based on judgement of investigators.

Summary of adverse events - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin (0.034mg/kg/day)			somapacitan (0.04/0.16mg/kg/week)			somapacitan (0.08/0.16mg/kg/week)			somapacitan (0.16/0.16mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
No	3 (100.0)	31	440.7	3 (100.0)	25	278.0	3 (100.0)	54	600.6	3 (100.0)	68	756.3	9 (100.0)	147	544.9
Outcome															
Recovered/resolved	3 (100.0)	30	426.5	3 (100.0)	25	278.0	3 (100.0)	53	589.5	3 (100.0)	67	745.2	9 (100.0)	145	537.5
Recovering/resolving	0			0			0			0			0		
Recovered/resolved with sequelae	0			0			0			0			0		
Not recovered/not resolved	2 (66.7)	2	28.4	0			1 (33.3)	1	11.1	1 (33.3)	1	11.1	2 (22.2)	2	7.4
Fatal	0			0			0			0			0		
Unknown	0			0			0			0			0		
Missing	0			0			0			0			0		
Treatment															
Treatment discontinuations due to adverse events	1 (33.3)	1	14.2	0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until week 156 or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
AE causality is based on judgement of investigators.

5: Summary of adverse events from week 0 to 52 - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin (0.034mg/kg/day)			somapacitan (0.04/0.16mg/kg/week)			somapacitan (0.08/0.16mg/kg/week)			somapacitan (0.16/0.16mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	3			3			3			3			9		
Total patient years at risk	3.0			3.0			3.0			3.0			9.0		
All adverse events	3 (100.0)	13	432.1	3 (100.0)	8	265.6	2 (66.7)	15	498.1	3 (100.0)	28	929.7	8 (88.9)	51	564.5
Serious adverse events															
Yes	1 (33.3)	2	66.5	0			0			0			0		
No	3 (100.0)	11	365.6	3 (100.0)	8	265.6	2 (66.7)	15	498.1	3 (100.0)	28	929.7	8 (88.9)	51	564.5
Severity															
Mild	3 (100.0)	10	332.3	3 (100.0)	8	265.6	2 (66.7)	15	498.1	3 (100.0)	27	896.5	8 (88.9)	50	553.4
Moderate	2 (66.7)	3	99.7	0			0			1 (33.3)	1	33.2	1 (11.1)	1	11.1
Severe	0			0			0			0			0		
Causality															
Probable	0			0			0			0			0		
Possible	0			0			0			0			0		
Unlikely	3 (100.0)	13	432.1	3 (100.0)	8	265.6	2 (66.7)	15	498.1	3 (100.0)	28	929.7	8 (88.9)	51	564.5
Missing	0			0			0			0			0		
Action taken to trial product due to AE															
Drug interrupted	0			0			0			0			0		
Drug withdrawn	1 (33.3)	1	33.2	0			0			0			0		
Dose reduced	0			0			0			0			0		
Dose increased	0			0			0			0			0		
Dose not changed	3 (100.0)	12	398.8	3 (100.0)	8	265.6	2 (66.7)	15	498.1	3 (100.0)	28	929.7	8 (88.9)	51	564.5
Unknown	0			0			0			0			0		
Missing	0			0			0			0			0		
Related to technical complaint															
Yes	0			0			0			0			0		
No	3 (100.0)	13	432.1	3 (100.0)	8	265.6	2 (66.7)	15	498.1	3 (100.0)	28	929.7	8 (88.9)	51	564.5
Injection site reaction															
Yes	0			0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until week 156 or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
AE causality is based on judgement of investigators.

Summary of adverse events from week 0 to 52 - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin (0.034mg/kg/day)			somapacitan (0.04/0.16mg/kg/week)			somapacitan (0.08/0.16mg/kg/week)			somapacitan (0.16/0.16mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
No	3 (100.0)	13	432.1	3 (100.0)	8	265.6	2 (66.7)	15	498.1	3 (100.0)	28	929.7	8 (88.9)	51	564.5
Outcome															
Recovered/resolved	3 (100.0)	12	398.8	3 (100.0)	8	265.6	2 (66.7)	15	498.1	3 (100.0)	28	929.7	8 (88.9)	51	564.5
Recovering/resolving	0			0			0			0			0		
Recovered/resolved with sequelae	0			0			0			0			0		
Not recovered/not resolved	1 (33.3)	1	33.2	0			0			0			0		
Fatal	0			0			0			0			0		
Unknown	0			0			0			0			0		
Missing	0			0			0			0			0		
Treatment															
Treatment discontinuations due to adverse events	1 (33.3)	1	33.2	0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until week 156 or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
AE causality is based on judgement of investigators.

6: Summary of adverse events from week 52 to 156 - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin (0.034mg/kg/day)			somapacitan (0.04/0.16mg/kg/week)			somapacitan (0.08/0.16mg/kg/week)			somapacitan (0.16/0.16mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	3			3			3			3			9		
Total patient years at risk	4.0			6.0			6.0			6.0			17.9		
All adverse events	2 (66.7)	19	475.7	3 (100.0)	17	284.2	2 (66.7)	39	652.2	3 (100.0)	40	669.0	8 (88.9)	96	535.1
Serious adverse events															
Yes	0			1 (33.3)	1	16.7	0			1 (33.3)	1	16.7	2 (22.2)	2	11.1
No	2 (66.7)	19	475.7	3 (100.0)	16	267.5	2 (66.7)	39	652.2	3 (100.0)	39	652.2	8 (88.9)	94	523.9
Severity															
Mild	2 (66.7)	19	475.7	3 (100.0)	16	267.5	2 (66.7)	39	652.2	2 (66.7)	37	618.8	7 (77.8)	92	512.8
Moderate	0			1 (33.3)	1	16.7	0			2 (66.7)	3	50.2	3 (33.3)	4	22.3
Severe	0			0			0			0			0		
Causality															
Probable	1 (33.3)	1	25.0	0			0			0			0		
Possible	0			1 (33.3)	1	16.7	0			0			1 (11.1)	1	5.6
Unlikely	2 (66.7)	18	450.6	3 (100.0)	16	267.5	2 (66.7)	39	652.2	3 (100.0)	40	669.0	8 (88.9)	95	529.5
Missing	0			0			0			0			0		
Action taken to trial product due to AE															
Drug interrupted	0			0			0			0			0		
Drug withdrawn	0			0			0			0			0		
Dose reduced	0			0			0			0			0		
Dose increased	0			0			0			0			0		
Dose not changed	2 (66.7)	19	475.7	3 (100.0)	17	284.2	2 (66.7)	39	652.2	3 (100.0)	40	669.0	8 (88.9)	96	535.1
Unknown	0			0			0			0			0		
Missing	0			0			0			0			0		
Related to technical complaint															
Yes	0			0			0			0			0		
No	2 (66.7)	19	475.7	3 (100.0)	17	284.2	2 (66.7)	39	652.2	3 (100.0)	40	669.0	8 (88.9)	96	535.1
Injection site reaction															
Yes	1 (33.3)	1	25.0	0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until week 156 or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
AE causality is based on judgement of investigators.

Summary of adverse events from week 52 to 156 - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin (0.034mg/kg/day)			somapacitan (0.04/0.16mg/kg/week)			somapacitan (0.08/0.16mg/kg/week)			somapacitan (0.16/0.16mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
No	2 (66.7)	18	450.6	3 (100.0)	17	284.2	2 (66.7)	39	652.2	3 (100.0)	40	669.0	8 (88.9)	96	535.1
Outcome															
Recovered/resolved	2 (66.7)	18	450.6	3 (100.0)	17	284.2	2 (66.7)	38	635.5	3 (100.0)	39	652.2	8 (88.9)	94	523.9
Recovering/resolving	0			0			0			0			0		
Recovered/resolved with sequelae	0			0			0			0			0		
Not recovered/not resolved	1 (33.3)	1	25.0	0			1 (33.3)	1	16.7	1 (33.3)	1	16.7	2 (22.2)	2	11.1
Fatal	0			0			0			0			0		
Unknown	0			0			0			0			0		
Missing	0			0			0			0			0		
Treatment															
Treatment discontinuations due to adverse events	0			0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until week 156 or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
AE causality is based on judgement of investigators.

7: Summary of adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	3			3			3			3			9		
Total patient years at risk	7.0			9.0			9.0			9.0			27.0		
Events	3	(100.0)	32 455.0	3	(100.0)	25 278.0	3	(100.0)	54 600.6	3	(100.0)	68 756.3	9	(100.0)	147 544.9
Infections and infestations	3	(100.0)	19 270.1	3	(100.0)	12 133.4	3	(100.0)	34 378.2	3	(100.0)	33 367.0	9	(100.0)	79 292.9
Influenza	2	(66.7)	2 28.4	2	(66.7)	2 22.2	3	(100.0)	4 44.5	2	(66.7)	4 44.5	7	(77.8)	10 37.1
Nasopharyngitis	2	(66.7)	11 156.4	2	(66.7)	6 66.7	1	(33.3)	20 222.4	2	(66.7)	16 178.0	5	(55.6)	42 155.7
Pharyngitis	0			1	(33.3)	1 11.1	1	(33.3)	5 55.6	0			2	(22.2)	6 22.2
Otitis media	1	(33.3)	1 14.2	0			1	(33.3)	1 11.1	1	(33.3)	2 22.2	2	(22.2)	3 11.1
Sinusitis	0			0			0			2	(66.7)	3 33.4	2	(22.2)	3 11.1
Gastroenteritis	2	(66.7)	2 28.4	1	(33.3)	1 11.1	0			1	(33.3)	1 11.1	2	(22.2)	2 7.4
Gastroenteritis viral	0			0			0			1	(33.3)	2 22.2	1	(11.1)	2 7.4
Adenovirus infection	0			0			1	(33.3)	1 11.1	0			1	(11.1)	1 3.7
Bacterial infection	0			0			0			1	(33.3)	1 11.1	1	(11.1)	1 3.7
Bronchitis	0			0			0			1	(33.3)	1 11.1	1	(11.1)	1 3.7
Conjunctivitis	0			0			0			1	(33.3)	1 11.1	1	(11.1)	1 3.7
Conjunctivitis bacterial	0			0			1	(33.3)	1 11.1	0			1	(11.1)	1 3.7
Herpangina	0			0			1	(33.3)	1 11.1	0			1	(11.1)	1 3.7
Otitis externa	0			0			0			1	(33.3)	1 11.1	1	(11.1)	1 3.7
Pneumonia	0			0			0			1	(33.3)	1 11.1	1	(11.1)	1 3.7
Streptococcal infection	0			0			1	(33.3)	1 11.1	0			1	(11.1)	1 3.7
Upper respiratory tract infection	1	(33.3)	1 14.2	1	(33.3)	1 11.1	0			0			1	(11.1)	1 3.7
Varicella	0			1	(33.3)	1 11.1	0			0			1	(11.1)	1 3.7
Mumps	1	(33.3)	1 14.2	0			0			0			0		
Respiratory syncytial virus bronchitis	1	(33.3)	1 14.2	0			0			0			0		
Respiratory, thoracic and mediastinal disorders	2	(66.7)	2 28.4	1	(33.3)	2 22.2	1	(33.3)	1 11.1	3	(100.0)	5 55.6	5	(55.6)	8 29.7
Rhinitis allergic	2	(66.7)	2 28.4	0			1	(33.3)	1 11.1	3	(100.0)	4 44.5	4	(44.4)	5 18.5
Asthma	0			1	(33.3)	2 22.2	0			0			1	(11.1)	2 7.4
Cough	0			0			0			1	(33.3)	1 11.1	1	(11.1)	1 3.7

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
General disorders and administration site conditions	1 (33.3)	4	56.9	3 (100.0)	4	44.5	2 (66.7)	3	33.4	0			5 (55.6)	7	25.9
Pyrexia	1 (33.3)	4	56.9	3 (100.0)	4	44.5	1 (33.3)	1	11.1	0			4 (44.4)	5	18.5
Injection site bruising	0			0			1 (33.3)	2	22.2	0			1 (11.1)	2	7.4
Gastrointestinal disorders	1 (33.3)	1	14.2	1 (33.3)	2	22.2	1 (33.3)	11	122.3	2 (66.7)	12	133.5	4 (44.4)	25	92.7
Stomatitis	0			0			1 (33.3)	3	33.4	1 (33.3)	7	77.9	2 (22.2)	10	37.1
Diarrhoea	0			0			1 (33.3)	6	66.7	1 (33.3)	2	22.2	2 (22.2)	8	29.7
Constipation	0			1 (33.3)	1	11.1	0			1 (33.3)	1	11.1	2 (22.2)	2	7.4
Nausea	0			0			1 (33.3)	2	22.2	0			1 (11.1)	2	7.4
Abdominal pain	1 (33.3)	1	14.2	0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Enterocolitis	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Vomiting	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Injury, poisoning and procedural complications	0			2 (66.7)	2	22.2	0			2 (66.7)	6	66.7	4 (44.4)	8	29.7
Skin laceration	0			1 (33.3)	1	11.1	0			1 (33.3)	1	11.1	2 (22.2)	2	7.4
Contusion	0			0			0			1 (33.3)	3	33.4	1 (11.1)	3	11.1
Arthropod sting	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Head injury	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Road traffic accident	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Skin and subcutaneous tissue disorders	3 (100.0)	4	56.9	0			1 (33.3)	2	22.2	2 (66.7)	7	77.9	3 (33.3)	9	33.4
Miliaria	0			0			0			1 (33.3)	3	33.4	1 (11.1)	3	11.1
Rash	0			0			0			1 (33.3)	2	22.2	1 (11.1)	2	7.4
Dermatitis	1 (33.3)	1	14.2	0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Dermatitis allergic	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Eczema	1 (33.3)	1	14.2	0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Leukoderma	0			0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Haemorrhage subcutaneous	1 (33.3)	1	14.2	0			0			0			0		
Urticaria	1 (33.3)	1	14.2	0			0			0			0		
Immune system disorders	0			1 (33.3)	1	11.1	0			1 (33.3)	1	11.1	2 (22.2)	2	7.4
Anaphylactic reaction	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Anaphylactic shock	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Investigations	0			1 (33.3)	1	11.1	1 (33.3)	1	11.1	0			2 (22.2)	2	7.4
Blood glucose increased	0			0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Blood phosphorus increased	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Reproductive system and breast disorders	0			0			0			1 (33.3)	2	22.2	1 (11.1)	2	7.4
Balanoposthitis	0			0			0			1 (33.3)	2	22.2	1 (11.1)	2	7.4
Blood and lymphatic system disorders	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Thrombocytopenia	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Ear and labyrinth disorders	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Cerumen impaction	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Eye disorders	0			0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Conjunctivitis allergic	0			0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Skin papilloma	0			0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Nervous system disorders	1 (33.3)	1	14.2	0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Intellectual disability	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Febrile convulsion	1 (33.3)	1	14.2	0			0			0			0		
Renal and urinary disorders	1 (33.3)	1	14.2	0			0			0			0		
Nephrotic syndrome	1 (33.3)	1	14.2	0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

8: Summary of adverse events by system organ class and preferred term from week 0 to 52 - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	3			3			3			3			9		
Total patient years at risk	3.0			3.0			3.0			3.0			9.0		
Events	3	(100.0)	13 432.1	3	(100.0)	8 265.6	2	(66.7)	15 498.1	3	(100.0)	28 929.7	8	(88.9)	51 564.5
Infections and infestations	3	(100.0)	10 332.3	1	(33.3)	2 66.4	2	(66.7)	12 398.5	3	(100.0)	14 464.9	6	(66.7)	28 309.9
Nasopharyngitis	2	(66.7)	5 166.2	0			1	(33.3)	7 232.4	2	(66.7)	7 232.4	3	(33.3)	14 155.0
Influenza	1	(33.3)	1 33.2	0			1	(33.3)	1 33.2	1	(33.3)	2 66.4	2	(22.2)	3 33.2
Gastroenteritis	0			1	(33.3)	1 33.2	0			1	(33.3)	1 33.2	2	(22.2)	2 22.1
Adenovirus infection	0			0			1	(33.3)	1 33.2	0			1	(11.1)	1 11.1
Bronchitis	0			0			0			1	(33.3)	1 33.2	1	(11.1)	1 11.1
Herpangina	0			0			1	(33.3)	1 33.2	0			1	(11.1)	1 11.1
Otitis media	1	(33.3)	1 33.2	0			0			1	(33.3)	1 33.2	1	(11.1)	1 11.1
Pharyngitis	0			0			1	(33.3)	1 33.2	0			1	(11.1)	1 11.1
Pneumonia	0			0			0			1	(33.3)	1 33.2	1	(11.1)	1 11.1
Sinusitis	0			0			0			1	(33.3)	1 33.2	1	(11.1)	1 11.1
Streptococcal infection	0			0			1	(33.3)	1 33.2	0			1	(11.1)	1 11.1
Upper respiratory tract infection	1	(33.3)	1 33.2	1	(33.3)	1 33.2	0			0			1	(11.1)	1 11.1
Mumps	1	(33.3)	1 33.2	0			0			0			0		
Respiratory syncytial virus bronchitis	1	(33.3)	1 33.2	0			0			0			0		
Gastrointestinal disorders	0			0			1	(33.3)	2 66.4	2	(66.7)	7 232.4	3	(33.3)	9 99.6
Diarrhoea	0			0			1	(33.3)	2 66.4	1	(33.3)	2 66.4	2	(22.2)	4 44.3
Stomatitis	0			0			0			1	(33.3)	2 66.4	1	(11.1)	2 22.1
Abdominal pain	0			0			0			1	(33.3)	1 33.2	1	(11.1)	1 11.1
Constipation	0			0			0			1	(33.3)	1 33.2	1	(11.1)	1 11.1
Enterocolitis	0			0			0			1	(33.3)	1 33.2	1	(11.1)	1 11.1
Injury, poisoning and procedural complications	0			2	(66.7)	2 66.4	0			1	(33.3)	3 99.6	3	(33.3)	5 55.3
Contusion	0			0			0			1	(33.3)	3 99.6	1	(11.1)	3 33.2
Head injury	0			1	(33.3)	1 33.2	0			0			1	(11.1)	1 11.1
Skin laceration	0			1	(33.3)	1 33.2	0			0			1	(11.1)	1 11.1

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term from week 0 to 52 - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Respiratory, thoracic and mediastinal disorders	0			1 (33.3)	2	66.4	0			1 (33.3)	1	33.2	2 (22.2)	3	33.2
Asthma	0			1 (33.3)	2	66.4	0			0			1 (11.1)	2	22.1
Rhinitis allergic	0			0			0			1 (33.3)	1	33.2	1 (11.1)	1	11.1
Skin and subcutaneous tissue disorders	1 (33.3)	1	33.2	0			0			2 (66.7)	3	99.6	2 (22.2)	3	33.2
Miliaria	0			0			0			1 (33.3)	2	66.4	1 (11.1)	2	22.1
Dermatitis allergic	0			0			0			1 (33.3)	1	33.2	1 (11.1)	1	11.1
Eczema	1 (33.3)	1	33.2	0			0			0			0		
General disorders and administration site conditions	0			2 (66.7)	2	66.4	0			0			2 (22.2)	2	22.1
Pyrexia	0			2 (66.7)	2	66.4	0			0			2 (22.2)	2	22.1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			0			1 (33.3)	1	33.2	0			1 (11.1)	1	11.1
Skin papilloma	0			0			1 (33.3)	1	33.2	0			1 (11.1)	1	11.1
Nervous system disorders	1 (33.3)	1	33.2	0			0			0			0		
Febrile convulsion	1 (33.3)	1	33.2	0			0			0			0		
Renal and urinary disorders	1 (33.3)	1	33.2	0			0			0			0		
Nephrotic syndrome	1 (33.3)	1	33.2	0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

9: Summary of adverse events by system organ class and preferred term from week 52 to 156 - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	3			3			3			3			9		
Total patient years at risk	4.0			6.0			6.0			6.0			17.9		
Events	2 (66.7)	19	475.7	3 (100.0)	17	284.2	2 (66.7)	39	652.2	3 (100.0)	40	669.0	8 (88.9)	96	535.1
Infections and infestations	2 (66.7)	9	225.3	3 (100.0)	10	167.2	2 (66.7)	22	367.9	2 (66.7)	19	317.8	7 (77.8)	51	284.3
Nasopharyngitis	2 (66.7)	6	150.2	2 (66.7)	6	100.3	1 (33.3)	13	217.4	2 (66.7)	9	150.5	5 (55.6)	28	156.1
Influenza	1 (33.3)	1	25.0	2 (66.7)	2	33.4	2 (66.7)	3	50.2	1 (33.3)	2	33.4	5 (55.6)	7	39.0
Pharyngitis	0			1 (33.3)	1	16.7	1 (33.3)	4	66.9	0			2 (22.2)	5	27.9
Otitis media	0			0			1 (33.3)	1	16.7	1 (33.3)	1	16.7	2 (22.2)	2	11.1
Gastroenteritis viral	0			0			0			1 (33.3)	2	33.4	1 (11.1)	2	11.1
Sinusitis	0			0			0			1 (33.3)	2	33.4	1 (11.1)	2	11.1
Bacterial infection	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6
Conjunctivitis	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6
Conjunctivitis bacterial	0			0			1 (33.3)	1	16.7	0			1 (11.1)	1	5.6
Otitis externa	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6
Varicella	0			1 (33.3)	1	16.7	0			0			1 (11.1)	1	5.6
Gastroenteritis	2 (66.7)	2	50.1	0			0			0			0		
Respiratory, thoracic and mediastinal disorders	2 (66.7)	2	50.1	0			1 (33.3)	1	16.7	3 (100.0)	4	66.9	4 (44.4)	5	27.9
Rhinitis allergic	2 (66.7)	2	50.1	0			1 (33.3)	1	16.7	3 (100.0)	3	50.2	4 (44.4)	4	22.3
Cough	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6
Gastrointestinal disorders	1 (33.3)	1	25.0	1 (33.3)	2	33.4	1 (33.3)	9	150.5	1 (33.3)	5	83.6	3 (33.3)	16	89.2
Stomatitis	0			0			1 (33.3)	3	50.2	1 (33.3)	5	83.6	2 (22.2)	8	44.6
Diarrhoea	0			0			1 (33.3)	4	66.9	0			1 (11.1)	4	22.3
Nausea	0			0			1 (33.3)	2	33.4	0			1 (11.1)	2	11.1
Constipation	0			1 (33.3)	1	16.7	0			0			1 (11.1)	1	5.6
Vomiting	0			1 (33.3)	1	16.7	0			0			1 (11.1)	1	5.6
Abdominal pain	1 (33.3)	1	25.0	0			0			0			0		
General disorders and administration site conditions	1 (33.3)	4	100.1	1 (33.3)	2	33.4	2 (66.7)	3	50.2	0			3 (33.3)	5	27.9
Pyrexia	1 (33.3)	4	100.1	1 (33.3)	2	33.4	1 (33.3)	1	16.7	0			2 (22.2)	3	16.7

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term from week 52 to 156 - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Injection site bruising	0			0			1 (33.3)	2	33.4	0			1 (11.1)	2	11.1
Skin and subcutaneous tissue disorders	2 (66.7)	3	75.1	0			1 (33.3)	2	33.4	1 (33.3)	4	66.9	2 (22.2)	6	33.4
Rash	0			0			0			1 (33.3)	2	33.4	1 (11.1)	2	11.1
Dermatitis	1 (33.3)	1	25.0	0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6
Eczema	0			0			1 (33.3)	1	16.7	0			1 (11.1)	1	5.6
Leukoderma	0			0			1 (33.3)	1	16.7	0			1 (11.1)	1	5.6
Miliaria	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6
Haemorrhage subcutaneous	1 (33.3)	1	25.0	0			0			0			0		
Urticaria	1 (33.3)	1	25.0	0			0			0			0		
Injury, poisoning and procedural complications	0			0			0			2 (66.7)	3	50.2	2 (22.2)	3	16.7
Arthropod sting	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6
Road traffic accident	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6
Skin laceration	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6
Immune system disorders	0			1 (33.3)	1	16.7	0			1 (33.3)	1	16.7	2 (22.2)	2	11.1
Anaphylactic reaction	0			1 (33.3)	1	16.7	0			0			1 (11.1)	1	5.6
Anaphylactic shock	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6
Investigations	0			1 (33.3)	1	16.7	1 (33.3)	1	16.7	0			2 (22.2)	2	11.1
Blood glucose increased	0			0			1 (33.3)	1	16.7	0			1 (11.1)	1	5.6
Blood phosphorus increased	0			1 (33.3)	1	16.7	0			0			1 (11.1)	1	5.6
Reproductive system and breast disorders	0			0			0			1 (33.3)	2	33.4	1 (11.1)	2	11.1
Balanoposthitis	0			0			0			1 (33.3)	2	33.4	1 (11.1)	2	11.1
Blood and lymphatic system disorders	0			1 (33.3)	1	16.7	0			0			1 (11.1)	1	5.6
Thrombocytopenia	0			1 (33.3)	1	16.7	0			0			1 (11.1)	1	5.6
Ear and labyrinth disorders	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6
Cerumen impaction	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term from week 52 to 156 - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Eye disorders	0			0			1 (33.3)	1	16.7	0			1 (11.1)	1	5.6
Conjunctivitis allergic	0			0			1 (33.3)	1	16.7	0			1 (11.1)	1	5.6
Nervous system disorders	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6
Intellectual disability	0			0			0			1 (33.3)	1	16.7	1 (11.1)	1	5.6

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

10: Summary of serious adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	3			3			3			3			9		
Total patient years at risk	7.0			9.0			9.0			9.0			27.0		
Events	1 (33.3)	2	28.4	1 (33.3)	1	11.1	0			1 (33.3)	1	11.1	2 (22.2)	2	7.4
Immune system disorders	0			1 (33.3)	1	11.1	0			1 (33.3)	1	11.1	2 (22.2)	2	7.4
Anaphylactic reaction	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Anaphylactic shock	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Infections and infestations	1 (33.3)	1	14.2	0			0			0			0		
Respiratory syncytial virus bronchitis	1 (33.3)	1	14.2	0			0			0			0		
Renal and urinary disorders	1 (33.3)	1	14.2	0			0			0			0		
Nephrotic syndrome	1 (33.3)	1	14.2	0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:05:43 - taesocptsumx3.sas/taesaesocptsumsas4172x3.txt

11: Summary of severe adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (156w) - safety analysis set

There are no data for this output.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:05:44 - taesocptsumx3.sas/taesevaesocptsumontrsas4172x3.txt

12: Summary of moderate adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	3			3			3			3			9		
Total patient years at risk	7.0			9.0			9.0			9.0			27.0		
Events	2 (66.7)	3	42.7	1 (33.3)	1	11.1	0			2 (66.7)	4	44.5	3 (33.3)	5	18.5
Immune system disorders	0			1 (33.3)	1	11.1	0			1 (33.3)	1	11.1	2 (22.2)	2	7.4
Anaphylactic reaction	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Anaphylactic shock	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Respiratory, thoracic and mediastinal disorders	0			0			0			1 (33.3)	2	22.2	1 (11.1)	2	7.4
Rhinitis allergic	0			0			0			1 (33.3)	2	22.2	1 (11.1)	2	7.4
Injury, poisoning and procedural complications	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Road traffic accident	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Infections and infestations	1 (33.3)	1	14.2	0			0			0			0		
Respiratory syncytial virus bronchitis	1 (33.3)	1	14.2	0			0			0			0		
Nervous system disorders	1 (33.3)	1	14.2	0			0			0			0		
Febrile convulsion	1 (33.3)	1	14.2	0			0			0			0		
Renal and urinary disorders	1 (33.3)	1	14.2	0			0			0			0		
Nephrotic syndrome	1 (33.3)	1	14.2	0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

13: Summary of mild adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	3			3			3			3			9		
Total patient years at risk	7.0			9.0			9.0			9.0			27.0		
Events	3	(100.0)	29 412.3	3	(100.0)	24 266.8	3	(100.0)	54 600.6	3	(100.0)	64 711.8	9	(100.0)	142 526.4
Infections and infestations	3	(100.0)	18 255.9	3	(100.0)	12 133.4	3	(100.0)	34 378.2	3	(100.0)	33 367.0	9	(100.0)	79 292.9
Influenza	2	(66.7)	2 28.4	2	(66.7)	2 22.2	3	(100.0)	4 44.5	2	(66.7)	4 44.5	7	(77.8)	10 37.1
Nasopharyngitis	2	(66.7)	11 156.4	2	(66.7)	6 66.7	1	(33.3)	20 222.4	2	(66.7)	16 178.0	5	(55.6)	42 155.7
Pharyngitis	0			1	(33.3)	1 11.1	1	(33.3)	5 55.6	0			2	(22.2)	6 22.2
Otitis media	1	(33.3)	1 14.2	0			1	(33.3)	1 11.1	1	(33.3)	2 22.2	2	(22.2)	3 11.1
Sinusitis	0			0			0			2	(66.7)	3 33.4	2	(22.2)	3 11.1
Gastroenteritis	2	(66.7)	2 28.4	1	(33.3)	1 11.1	0			1	(33.3)	1 11.1	2	(22.2)	2 7.4
Gastroenteritis viral	0			0			0			1	(33.3)	2 22.2	1	(11.1)	2 7.4
Adenovirus infection	0			0			1	(33.3)	1 11.1	0			1	(11.1)	1 3.7
Bacterial infection	0			0			0			1	(33.3)	1 11.1	1	(11.1)	1 3.7
Bronchitis	0			0			0			1	(33.3)	1 11.1	1	(11.1)	1 3.7
Conjunctivitis	0			0			0			1	(33.3)	1 11.1	1	(11.1)	1 3.7
Conjunctivitis bacterial	0			0			1	(33.3)	1 11.1	0			1	(11.1)	1 3.7
Herpangina	0			0			1	(33.3)	1 11.1	0			1	(11.1)	1 3.7
Otitis externa	0			0			0			1	(33.3)	1 11.1	1	(11.1)	1 3.7
Pneumonia	0			0			0			1	(33.3)	1 11.1	1	(11.1)	1 3.7
Streptococcal infection	0			0			1	(33.3)	1 11.1	0			1	(11.1)	1 3.7
Upper respiratory tract infection	1	(33.3)	1 14.2	1	(33.3)	1 11.1	0			0			1	(11.1)	1 3.7
Varicella	0			1	(33.3)	1 11.1	0			0			1	(11.1)	1 3.7
Mumps	1	(33.3)	1 14.2	0			0			0			0		
General disorders and administration site conditions	1	(33.3)	4 56.9	3	(100.0)	4 44.5	2	(66.7)	3 33.4	0			5	(55.6)	7 25.9
Pyrexia	1	(33.3)	4 56.9	3	(100.0)	4 44.5	1	(33.3)	1 11.1	0			4	(44.4)	5 18.5
Injection site bruising	0			0			1	(33.3)	2 22.2	0			1	(11.1)	2 7.4
Gastrointestinal disorders	1	(33.3)	1 14.2	1	(33.3)	2 22.2	1	(33.3)	11 122.3	2	(66.7)	12 133.5	4	(44.4)	25 92.7
Stomatitis	0			0			1	(33.3)	3 33.4	1	(33.3)	7 77.9	2	(22.2)	10 37.1
Diarrhoea	0			0			1	(33.3)	6 66.7	1	(33.3)	2 22.2	2	(22.2)	8 29.7

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of mild adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Constipation	0			1 (33.3)	1	11.1	0			1 (33.3)	1	11.1	2 (22.2)	2	7.4
Nausea	0			0			1 (33.3)	2	22.2	0			1 (11.1)	2	7.4
Abdominal pain	1 (33.3)	1	14.2	0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Enterocolitis	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Vomiting	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Injury, poisoning and procedural complications	0			2 (66.7)	2	22.2	0			2 (66.7)	5	55.6	4 (44.4)	7	25.9
Skin laceration	0			1 (33.3)	1	11.1	0			1 (33.3)	1	11.1	2 (22.2)	2	7.4
Contusion	0			0			0			1 (33.3)	3	33.4	1 (11.1)	3	11.1
Arthropod sting	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Head injury	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Respiratory, thoracic and mediastinal disorders	2 (66.7)	2	28.4	1 (33.3)	2	22.2	1 (33.3)	1	11.1	2 (66.7)	3	33.4	4 (44.4)	6	22.2
Rhinitis allergic	2 (66.7)	2	28.4	0			1 (33.3)	1	11.1	2 (66.7)	2	22.2	3 (33.3)	3	11.1
Asthma	0			1 (33.3)	2	22.2	0			0			1 (11.1)	2	7.4
Cough	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Skin and subcutaneous tissue disorders	3 (100.0)	4	56.9	0			1 (33.3)	2	22.2	2 (66.7)	7	77.9	3 (33.3)	9	33.4
Miliaria	0			0			0			1 (33.3)	3	33.4	1 (11.1)	3	11.1
Rash	0			0			0			1 (33.3)	2	22.2	1 (11.1)	2	7.4
Dermatitis	1 (33.3)	1	14.2	0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Dermatitis allergic	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Eczema	1 (33.3)	1	14.2	0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Leukoderma	0			0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Haemorrhage subcutaneous	1 (33.3)	1	14.2	0			0			0			0		
Urticaria	1 (33.3)	1	14.2	0			0			0			0		
Investigations	0			1 (33.3)	1	11.1	1 (33.3)	1	11.1	0			2 (22.2)	2	7.4
Blood glucose increased	0			0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Blood phosphorus increased	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Reproductive system and breast disorders	0			0			0			1 (33.3)	2	22.2	1 (11.1)	2	7.4

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of mild adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Balanoposthitis	0			0			0			1 (33.3)	2	22.2	1 (11.1)	2	7.4
Blood and lymphatic system disorders	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Thrombocytopenia	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Ear and labyrinth disorders	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Cerumen impaction	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Eye disorders	0			0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Conjunctivitis allergic	0			0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Skin papilloma	0			0			1 (33.3)	1	11.1	0			1 (11.1)	1	3.7
Nervous system disorders	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7
Intellectual disability	0			0			0			1 (33.3)	1	11.1	1 (11.1)	1	3.7

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

14: Summary of adverse events possibly or probably related to Norditropin or somapacitan by system organ class and preferred term - japanese subgroup - trial 4172 (156w) - safety analysis set

	Norditropin(0.034mg/kg/day)			somapacitan(0.04/0.16 mg/kg/week)			somapacitan(0.08/0.16 mg/kg/week)			somapacitan(0.16/0.16 mg/kg/week)			somapacitan pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	3			3			3			3			9		
Total patient years at risk	7.0			9.0			9.0			9.0			27.0		
Events	1 (33.3)	1	14.2	1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Investigations	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Blood phosphorus increased	0			1 (33.3)	1	11.1	0			0			1 (11.1)	1	3.7
Skin and subcutaneous tissue disorders	1 (33.3)	1	14.2	0			0			0			0		
Haemorrhage subcutaneous	1 (33.3)	1	14.2	0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 23.0
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

15: Summary of exposure - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day) week 0-156	Norditropin (0.034mg/kg/day) / somapacitan (0.16mg/kg/week) week 156-208	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Number of subjects	3	2	9
Total exposure (days)	2553	727	13264
Exposure (days)			
N	3	2	9
Mean (SD)	851.0 (422)	363.5 (2.1)	1473.8 (4.5)
Median	1093.0	363.5	1473.0
Min ; Max	364 ; 1096	362 ; 365	1470 ; 1484

N: Number of subjects, SD: Standard deviation
Exposure days in the treatment period are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan or to week 208, which ever comes first.

16: Summary of dosing by visit (mg/kg) - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Number of subjects	3	9
Visit 15 (Week 156) - Observed dose (mg/kg)		
N	0	9
Mean (SD)	0	0.160 (0.001)
Median	0	0.160
Min; Max	0	0.16 ; 0.16
Visit 17 (Week 169) - Observed dose (mg/kg)		
N	2	9
Mean (SD)	0.160 (0.002)	0.160 (0.001)
Median	0.160	0.160
Min; Max	0.16 ; 0.16	0.16 ; 0.16
Visit 18 (Week 182) - Observed dose (mg/kg)		
N	2	9
Mean (SD)	0.161 (0.001)	0.160 (0.001)
Median	0.161	0.160
Min; Max	0.16 ; 0.16	0.16 ; 0.16
Visit 19 (Week 195) - Observed dose (mg/kg)		
N	2	9
Mean (SD)	0.161 (0.001)	0.159 (0.002)
Median	0.161	0.159
Min; Max	0.16 ; 0.16	0.16 ; 0.16
Visit 20 (Week 208) - Observed dose (mg/kg)		
N	2	9
Mean (SD)	0.161 (0.000)	0.160 (0.001)
Median	0.160	0.160
Min; Max	0.16 ; 0.16	0.16 ; 0.16
Visit 15 (Week 156) - Prescribed dose (mg/kg)		

N: Number of subjects, EOT: End of trial, SD: Standard deviation
Observed dose at visit 2 is the dose given on site at the randomisation visit.
At visit 15 the subjects switching to somapacitan are still receiving Norditropin.

Summary of dosing by visit (mg/kg) - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
N	2	9
Mean (SD)	0.160 (0.003)	0.160 (0.001)
Median	0.160	0.160
Min; Max	0.16 ; 0.16	0.16 ; 0.16
Visit 17 (Week 169) - Prescribed dose (mg/kg)		
N	2	9
Mean (SD)	0.130 (0.046)	0.160 (0.001)
Median	0.130	0.160
Min; Max	0.10 ; 0.16	0.16 ; 0.16
Visit 18 (Week 182) - Prescribed dose (mg/kg)		
N	2	9
Mean (SD)	0.161 (0.001)	0.159 (0.002)
Median	0.161	0.159
Min; Max	0.16 ; 0.16	0.16 ; 0.16
Visit 19 (Week 195) - Prescribed dose (mg/kg)		
N	2	9
Mean (SD)	0.161 (0.000)	0.160 (0.001)
Median	0.161	0.160
Min; Max	0.16 ; 0.16	0.16 ; 0.16
Visit 20 (Week 208) - Prescribed dose (mg/kg)		
N	2	9
Mean (SD)	0.162 (0.000)	0.160 (0.001)
Median	0.162	0.159
Min; Max	0.16 ; 0.16	0.16 ; 0.16
Last dose taken according to diary (mg/kg) in main + extension + safety extension		
N	0	9
Mean (SD)	0	0.160 (0.002)
Median	0	0.160
Min; Max	0	0.16 ; 0.16

N: Number of subjects, EOT: End of trial, SD: Standard deviation
Observed dose at visit 2 is the dose given on site at the randomisation visit.
At visit 15 the subjects switching to somapacitan are still receiving Norditropin.

Summary of dosing by visit (mg/kg) - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Last dose taken according to diary (mg/kg) in the long-term safety extension		
N	2	9
Mean (SD)	0.161 (0.000)	0.160 (0.001)
Median	0.161	0.160
Min; Max	0.16 ; 0.16	0.16 ; 0.16

N: Number of subjects, EOT: End of trial, SD: Standard deviation
Observed dose at visit 2 is the dose given on site at the randomisation visit.
At visit 15 the subjects switching to somapacitan are still receiving Norditropin.

17: Summary of actual dose by visit (mg/kg pr week) - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled
Number of subjects	3	9
Average weekly dose (mg/kg pr week)		
Visit 15 (Week 156)		
N	2	9
Mean (SD)	0.243 (0.004)	0.160 (0.002)
Median	0.243	0.160
Min; Max	0.24 ; 0.25	0.16 ; 0.16
Visit 17 (Week 169)		
N	2	9
Mean (SD)	0.160 (0.003)	0.160 (0.001)
Median	0.160	0.160
Min; Max	0.16 ; 0.16	0.16 ; 0.16
Visit 18 (Week 182)		
N	2	9
Mean (SD)	0.161 (0.002)	0.160 (0.001)
Median	0.161	0.160
Min; Max	0.16 ; 0.16	0.16 ; 0.16
Visit 19 (Week 195)		
N	2	9
Mean (SD)	0.161 (0.001)	0.159 (0.002)
Median	0.161	0.159
Min; Max	0.16 ; 0.16	0.16 ; 0.16
Visit 20 (Week 208)		
N	2	9
Mean (SD)	0.161 (0.000)	0.160 (0.001)
Median	0.161	0.160
Min; Max	0.16 ; 0.16	0.16 ; 0.16

18: Summary of adverse events - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

	Norditropin (0.034mg/kg/day) week 0-156			Norditropin (0.034mg/kg/day) / somapacitan (0.16mg/kg/week) week 156-208			somapacitan (0.04/0.08/0.16mg/kg/week) pooled			somapacitan (0.16mg/kg/week) pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	3			2			9			11		
Total patient years at risk	7.0			2.0			36.0			32.0		
All adverse events	3 (100.0)	32	455.3	2 (100.0)	5	251.2	9 (100.0)	185	513.6	9 (81.8)	166	518.7
Serious adverse events												
Yes	1 (33.3)	2	28.5	0			2 (22.2)	2	5.6	2 (18.2)	2	6.2
No	3 (100.0)	30	426.9	2 (100.0)	5	251.2	9 (100.0)	183	508.1	9 (81.8)	164	512.5
Severity												
Mild	3 (100.0)	29	412.6	2 (100.0)	4	201.0	9 (100.0)	180	499.7	9 (81.8)	160	500.0
Moderate	2 (66.7)	3	42.7	1 (50.0)	1	50.2	3 (33.3)	5	13.9	4 (36.4)	6	18.7
Severe	0			0			0			0		
Causality related to Norditropin												
Probable	1 (33.3)	1	14.2	0			0			0		
Possible	0			0			0			0		
Unlikely	3 (100.0)	31	441.1	2 (100.0)	5	251.2	0			1 (9.1)	4	12.5
Missing	0			0			9 (100.0)	185	513.6	8 (72.7)	162	506.2
Causality related to somapacitan												
Probable	0			0			0			0		
Possible	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Unlikely	0			2 (100.0)	5	251.2	9 (100.0)	184	510.8	9 (81.8)	165	515.6
Missing	3 (100.0)	32	455.3	0			0			0		
Action taken to trial product due to AE												
Drug interrupted	0			0			0			0		
Drug withdrawn	1 (33.3)	1	14.2	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
AE causality is based on judgement of investigators.
*The somapacitan (0.04/0.08/0.16mg/kg/week) pooled arm contains all subjects randomised to somapacitan in cohort I. The somapacitan (0.16mg/kg/week) pooled arm contains all subjects from cohort I from the day they receive somapacitan 0.16mg/kg/week.
For Norditropin week 156-208 action taken to trial drug, technical complaints and injection site reactions are only summarised for somapacitan.

Summary of adverse events - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

	Norditropin (0.034mg/kg/day) week 0-156			Norditropin (0.034mg/kg/day) / somapacitan (0.16mg/kg/week) week 156-208			somapacitan (0.04/0.08/0.16mg/kg/week) pooled			somapacitan (0.16mg/kg/week) pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Dose reduced	0			0			0			0		
Dose increased	0			0			0			0		
Dose not changed	3 (100.0)	31	441.1	0			9 (100.0)	185	513.6	8 (72.7)	162	506.2
Unknown	0			0			0			0		
Missing	0			0			0			0		
Related to technical complaint												
Yes	0			0			0			0		
No	3 (100.0)	32	455.3	2 (100.0)	5	251.2	9 (100.0)	185	513.6	9 (81.8)	166	518.7
Injection site reaction												
Yes	1 (33.3)	1	14.2	0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
No	3 (100.0)	31	441.1	2 (100.0)	5	251.2	9 (100.0)	184	510.8	9 (81.8)	165	515.6
Outcome												
Recovered/resolved	3 (100.0)	30	426.9	1 (50.0)	2	100.5	9 (100.0)	183	508.1	9 (81.8)	162	506.2
Recovering/resolving	0			0			0			0		
Recovered/resolved with sequelae	0			0			0			0		
Not recovered/not resolved	2 (66.7)	2	28.5	2 (100.0)	3	150.7	2 (22.2)	2	5.6	3 (27.3)	4	12.5
Fatal	0			0			0			0		
Unknown	0			0			0			0		
Missing	0			0			0			0		
Medical event of special interest												
Yes	0			0			0			0		
No	3 (100.0)	32	455.3	2 (100.0)	5	251.2	9 (100.0)	185	513.6	9 (81.8)	166	518.7
Missing	0			0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 20 (week 208) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.
AE causality is based on judgement of investigators.
*The somapacitan (0.04/0.08/0.16mg/kg/week) pooled arm contains all subjects randomised to somapacitan in cohort I. The somapacitan (0.16mg/kg/week) pooled arm contains all subjects from cohort I from the day they receive somapacitan 0.16mg/kg/week.
For Norditropin week 156-208 action taken to trial drug, technical complaints and injection site reactions are only summarised for somapacitan.

19: Summary of adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

	Norditropin (0.034mg/kg/day) week 0-156			Norditropin (0.034mg/kg/day) / somapacitan (0.16mg/kg/week) week 156-208			somapacitan (0.04/0.08/0.16mg/kg/ week) pooled			somapacitan (0.16mg/kg/week) pooled		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	3			2			9			11		
Total patient years at risk	7.0			2.0			36.0			32.0		
Events	3	(100.0)	32 455.3	2	(100.0)	5 251.2	9	(100.0)	185 513.6	9	(81.8)	166 518.7
Infections and infestations	3	(100.0)	19 270.3	1	(50.0)	2 100.5	9	(100.0)	94 261.0	9	(81.8)	82 256.2
Nasopharyngitis	2	(66.7)	11 156.5	1	(50.0)	1 50.2	5	(55.6)	51 141.6	6	(54.5)	45 140.6
Influenza	2	(66.7)	2 28.5	0			7	(77.8)	10 27.8	6	(54.5)	9 28.1
Pharyngitis	0			0			2	(22.2)	6 16.7	2	(18.2)	5 15.6
Otitis media	1	(33.3)	1 14.2	0			2	(22.2)	5 13.9	2	(18.2)	5 15.6
Sinusitis	0			0			2	(22.2)	3 8.3	2	(18.2)	3 9.4
Gastroenteritis	2	(66.7)	2 28.5	0			2	(22.2)	2 5.6	1	(9.1)	1 3.1
Upper respiratory tract infection	1	(33.3)	1 14.2	0			2	(22.2)	2 5.6	1	(9.1)	1 3.1
Gastroenteritis viral	0			0			1	(11.1)	2 5.6	1	(9.1)	2 6.2
Conjunctivitis	0			1	(50.0)	1 50.2	1	(11.1)	1 2.8	2	(18.2)	2 6.2
Varicella	0			0			1	(11.1)	1 2.8	1	(9.1)	1 3.1
Upper respiratory tract infection bacterial	0			0			1	(11.1)	1 2.8	1	(9.1)	1 3.1
Rhinitis	0			0			1	(11.1)	1 2.8	1	(9.1)	1 3.1
Pneumonia	0			0			1	(11.1)	1 2.8	1	(9.1)	1 3.1
Otitis externa	0			0			1	(11.1)	1 2.8	1	(9.1)	1 3.1
Impetigo	0			0			1	(11.1)	1 2.8	1	(9.1)	1 3.1
Conjunctivitis bacterial	0			0			1	(11.1)	1 2.8	1	(9.1)	1 3.1
Bronchitis	0			0			1	(11.1)	1 2.8	1	(9.1)	1 3.1
Bacterial infection	0			0			1	(11.1)	1 2.8	1	(9.1)	1 3.1
Streptococcal infection	0			0			1	(11.1)	1 2.8	0		
Respiratory syncytial virus bronchitis	1	(33.3)	1 14.2	0			0			0		
Mumps	1	(33.3)	1 14.2	0			0			0		
Herpangina	0			0			1	(11.1)	1 2.8	0		
Adenovirus infection	0			0			1	(11.1)	1 2.8	0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

	Norditropin (0.034mg/kg/day) week 0-156			Norditropin (0.034mg/kg/day) / somapacitan (0.16mg/kg/week) week 156-208			somapacitan (0.04/0.08/0.16mg/kg/ week) pooled			somapacitan (0.16mg/kg/week) pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Gastrointestinal disorders	1 (33.3)	1	14.2	0			5 (55.6)	30	83.3	5 (45.5)	28	87.5
Stomatitis	0			0			2 (22.2)	12	33.3	2 (18.2)	12	37.5
Diarrhoea	0			0			2 (22.2)	8	22.2	2 (18.2)	6	18.7
Abdominal pain	1 (33.3)	1	14.2	0			2 (22.2)	3	8.3	2 (18.2)	3	9.4
Constipation	0			0			3 (33.3)	3	8.3	3 (27.3)	3	9.4
Nausea	0			0			1 (11.1)	2	5.6	1 (9.1)	2	6.2
Vomiting	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Enterocolitis	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Skin and subcutaneous tissue disorders	3 (100.0)	4	56.9	2 (100.0)	2	100.5	4 (44.4)	12	33.3	5 (45.5)	13	40.6
Eczema	1 (33.3)	1	14.2	0			3 (33.3)	4	11.1	3 (27.3)	4	12.5
Miliaria	0			0			1 (11.1)	3	8.3	1 (9.1)	3	9.4
Rash	0			0			1 (11.1)	2	5.6	1 (9.1)	2	6.2
Dermatitis	1 (33.3)	1	14.2	0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Leukoderma	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Dermatitis atopic	0			1 (50.0)	1	50.2	0			1 (9.1)	1	3.1
Dermatitis allergic	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Urticaria	1 (33.3)	1	14.2	0			0			0		
Haemorrhage subcutaneous	1 (33.3)	1	14.2	0			0			0		
Eczema asteatotic	0			1 (50.0)	1	50.2	0			0		
Injury, poisoning and procedural complications	0			0			6 (66.7)	14	38.9	4 (36.4)	12	37.5
Contusion	0			0			2 (22.2)	4	11.1	2 (18.2)	4	12.5
Arthropod sting	0			0			2 (22.2)	2	5.6	2 (18.2)	2	6.2
Skin laceration	0			0			2 (22.2)	2	5.6	1 (9.1)	1	3.1
Thermal burn	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Road traffic accident	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Ligament sprain	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Heat stroke	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Arthropod bite	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Head injury	0			0			1 (11.1)	1	2.8	0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

	Norditropin (0.034mg/kg/day) week 0-156			Norditropin (0.034mg/kg/day) / somapacitan (0.16mg/kg/week) week 156-208			somapacitan (0.04/0.08/0.16mg/kg/week) pooled			somapacitan (0.16mg/kg/week) pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Respiratory, thoracic and mediastinal disorders	2 (66.7)	2	28.5	0			5 (55.6)	9	25.0	4 (36.4)	7	21.9
Rhinitis allergic	2 (66.7)	2	28.5	0			4 (44.4)	5	13.9	4 (36.4)	5	15.6
Epistaxis	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Cough	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Asthma	0			0			1 (11.1)	2	5.6	0		
General disorders and administration site conditions	1 (33.3)	4	56.9	0			5 (55.6)	8	22.2	3 (27.3)	6	18.7
Pyrexia	1 (33.3)	4	56.9	0			4 (44.4)	5	13.9	2 (18.2)	3	9.4
Injection site bruising	0			0			1 (11.1)	3	8.3	1 (9.1)	3	9.4
Musculoskeletal and connective tissue disorders	0			0			4 (44.4)	4	11.1	4 (36.4)	4	12.5
Growing pains	0			0			2 (22.2)	2	5.6	2 (18.2)	2	6.2
Myalgia	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Arthralgia	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Reproductive system and breast disorders	0			0			1 (11.1)	3	8.3	1 (9.1)	3	9.4
Balanoposthitis	0			0			1 (11.1)	3	8.3	1 (9.1)	3	9.4
Eye disorders	0			1 (50.0)	1	50.2	2 (22.2)	2	5.6	3 (27.3)	3	9.4
Conjunctivitis allergic	0			1 (50.0)	1	50.2	2 (22.2)	2	5.6	3 (27.3)	3	9.4
Investigations	0			0			2 (22.2)	2	5.6	2 (18.2)	2	6.2
Blood phosphorus increased	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Blood glucose increased	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Immune system disorders	0			0			2 (22.2)	2	5.6	2 (18.2)	2	6.2
Anaphylactic shock	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Anaphylactic reaction	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

	Norditropin (0.034mg/kg/day) week 0-156			Norditropin (0.034mg/kg/day) / somapacitan (0.16mg/kg/week) week 156-208			somapacitan (0.04/0.08/0.16mg/kg/ week) pooled			somapacitan (0.16mg/kg/week) pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Nervous system disorders	1 (33.3)	1	14.2	0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Intellectual disability	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Febrile convulsion	1 (33.3)	1	14.2	0			0			0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			0			1 (11.1)	2	5.6	1 (9.1)	1	3.1
Skin papilloma	0			0			1 (11.1)	2	5.6	1 (9.1)	1	3.1
Ear and labyrinth disorders	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Cerumen impaction	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Blood and lymphatic system disorders	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Thrombocytopenia	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Renal and urinary disorders	1 (33.3)	1	14.2	0			0			0		
Nephrotic syndrome	1 (33.3)	1	14.2	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

20: Summary of adverse events by system organ class and preferred term from week 156 to 208 - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

	Norditropin (0.034mg/kg/day) / somapacitan (0.16mg/kg/week) week 156-208			somapacitan (0.04/0.08/0.16mg/kg/week) pooled			somapacitan (0.16mg/kg/week) pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	2			9			11		
Total patient years at risk	2.0			9.1			11.1		
Events	2 (100.0)	5	251.2	6 (66.7)	39	430.1	7 (63.6)	43	388.9
Infections and infestations	1 (50.0)	2	100.5	5 (55.6)	15	165.4	6 (54.5)	17	153.7
Nasopharyngitis	1 (50.0)	1	50.2	3 (33.3)	9	99.3	4 (36.4)	10	90.4
Otitis media	0			1 (11.1)	2	22.1	1 (9.1)	2	18.1
Upper respiratory tract infection bacterial	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Upper respiratory tract infection	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Rhinitis	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Impetigo	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Conjunctivitis	1 (50.0)	1	50.2	0			1 (9.1)	1	9.0
Injury, poisoning and procedural complications	0			3 (33.3)	6	66.2	3 (27.3)	6	54.3
Thermal burn	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Ligament sprain	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Heat stroke	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Contusion	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Arthropod sting	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Arthropod bite	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Gastrointestinal disorders	0			3 (33.3)	5	55.1	3 (27.3)	5	45.2
Stomatitis	0			1 (11.1)	2	22.1	1 (9.1)	2	18.1
Abdominal pain	0			1 (11.1)	2	22.1	1 (9.1)	2	18.1
Constipation	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Skin and subcutaneous tissue disorders	2 (100.0)	2	100.5	2 (22.2)	3	33.1	3 (27.3)	4	36.2

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term from week 156 to 208 - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

	Norditropin (0.034mg/kg/day) / somapacitan (0.16mg/kg/week) week 156-208			somapacitan (0.04/0.08/0.16mg/kg/ week) pooled			somapacitan (0.16mg/kg/week) pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Eczema	0			2 (22.2)	3	33.1	2 (18.2)	3	27.1
Dermatitis atopic	1 (50.0)	1	50.2	0			1 (9.1)	1	9.0
Eczema asteatotic	1 (50.0)	1	50.2	0			0		
Musculoskeletal and connective tissue disorders	0			4 (44.4)	4	44.1	4 (36.4)	4	36.2
Growing pains	0			2 (22.2)	2	22.1	2 (18.2)	2	18.1
Myalgia	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Arthralgia	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Eye disorders	1 (50.0)	1	50.2	1 (11.1)	1	11.0	2 (18.2)	2	18.1
Conjunctivitis allergic	1 (50.0)	1	50.2	1 (11.1)	1	11.0	2 (18.2)	2	18.1
Respiratory, thoracic and mediastinal disorders	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Epistaxis	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Reproductive system and breast disorders	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Balanoposthitis	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Skin papilloma	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
General disorders and administration site conditions	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Injection site bruising	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Blood and lymphatic system disorders	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0
Thrombocytopenia	0			1 (11.1)	1	11.0	1 (9.1)	1	9.0

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

21: Summary of serious adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

	Norditropin (0.034mg/kg/day) week 0-156			Norditropin (0.034mg/kg/day) / somapacitan (0.16mg/kg/week) week 156-208			somapacitan (0.04/0.08/0.16mg/kg/ week) pooled			somapacitan (0.16mg/kg/week) pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	3			2			9			11		
Total patient years at risk	7.0			2.0			36.0			32.0		
Events	1 (33.3)	2	28.5	0			2 (22.2)	2	5.6	2 (18.2)	2	6.2
Immune system disorders	0			0			2 (22.2)	2	5.6	2 (18.2)	2	6.2
Anaphylactic shock	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Anaphylactic reaction	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Renal and urinary disorders	1 (33.3)	1	14.2	0			0			0		
Nephrotic syndrome	1 (33.3)	1	14.2	0			0			0		
Infections and infestations	1 (33.3)	1	14.2	0			0			0		
Respiratory syncytial virus bronchitis	1 (33.3)	1	14.2	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

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06APR2022:09:05:48 - taesocptsumx4C1.sas/taesaesocptsumsas4172x4C1.txt

22: Summary of severe adverse events by system organ class and preferred term - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

There are no data for this output.

23: Summary of adverse events possibly or probably related to Norditropin or somapacitan by system organ class and preferred term - japanese subgroup - trial 4172 (208w) - safety analysis set - cohort I

	Norditropin (0.034mg/kg/day) week 0-156			Norditropin (0.034mg/kg/day) / somapacitan (0.16mg/kg/week) week 156-208			somapacitan (0.04/0.08/0.16mg/kg/ week) pooled			somapacitan (0.16mg/kg/week) pooled		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Number of subjects	3			2			9			11		
Total patient years at risk	7.0			2.0			36.0			32.0		
Events	1 (33.3)	1	14.2	0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Investigations	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Blood phosphorus increased	0			0			1 (11.1)	1	2.8	1 (9.1)	1	3.1
Skin and subcutaneous tissue disorders	1 (33.3)	1	14.2	0			0			0		
Haemorrhage subcutaneous	1 (33.3)	1	14.2	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

24: Summary of exposure - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin	somapacitan
Number of subjects	11	19
Total exposure (days)	4067	7026
Exposure (days)		
N	11	19
Mean (SD)	369.7 (4.4)	369.8 (1.6)
Median	368.0	370.0
Min ; Max	368 ; 383	364 ; 371

N: Number of subjects, SD: Standard deviation
Exposure days in the treatment period are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan or to visit 7 (week 52), which ever comes first.

25: Summary of dosing by visit (mg) - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin	somapacitan
Number of subjects	11	19
Visit 3 (Week 4) - Actual dose (mg)		
N	11	19
Mean (SD)	0.512 (0.121)	2.539 (0.815)
Median	0.500	2.200
Min; Max	0.35 ; 0.70	1.70 ; 5.00
Visit 4 (Week 13) - Actual dose (mg)		
N	11	19
Mean (SD)	0.518 (0.133)	2.644 (0.839)
Median	0.500	2.250
Min; Max	0.35 ; 0.75	1.75 ; 5.20
Visit 5 (Week 26) - Actual dose (mg)		
N	11	19
Mean (SD)	0.546 (0.125)	2.795 (0.879)
Median	0.550	2.350
Min; Max	0.40 ; 0.75	1.90 ; 5.20
Visit 6 (Week 39) - Actual dose (mg)		
N	11	19
Mean (SD)	0.558 (0.132)	2.938 (0.912)
Median	0.550	2.550
Min; Max	0.40 ; 0.80	2.00 ; 5.50
Visit 7 (Week 52) - Actual dose (mg)		
N	11	19
Mean (SD)	0.594 (0.137)	3.097 (0.913)
Median	0.550	2.650
Min; Max	0.40 ; 0.85	2.15 ; 5.60
Visit 2 (Week 0) - Prescribed dose (mg)		
N	11	19
Mean (SD)	0.509 (0.128)	2.537 (0.835)
Median	0.500	2.200
Min; Max	0.35 ; 0.70	1.70 ; 5.00

N: Number of subjects, EOT: End of trial, SD: Standard deviation

Summary of dosing by visit (mg) - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin	somapacitan
Visit 3 (Week 4) - Prescribed dose (mg)		
N	11	19
Mean (SD)	0.514 (0.140)	2.655 (0.880)
Median	0.500	2.250
Min; Max	0.35 ; 0.75	1.75 ; 5.20
Visit 4 (Week 13) - Prescribed dose (mg)		
N	11	19
Mean (SD)	0.541 (0.132)	2.779 (0.882)
Median	0.550	2.350
Min; Max	0.40 ; 0.75	1.90 ; 5.20
Visit 5 (Week 26) - Prescribed dose (mg)		
N	11	19
Mean (SD)	0.559 (0.139)	2.926 (0.926)
Median	0.550	2.550
Min; Max	0.40 ; 0.80	2.00 ; 5.50
Visit 6 (Week 39) - Prescribed dose (mg)		
N	11	19
Mean (SD)	0.595 (0.139)	3.092 (0.938)
Median	0.550	2.650
Min; Max	0.45 ; 0.85	2.15 ; 5.60
Last dose taken according to diary (mg)		
N	11	19
Mean (SD)	0.586 (0.148)	3.092 (0.938)
Median	0.550	2.650
Min; Max	0.40 ; 0.85	2.15 ; 5.60

N: Number of subjects, EOT: End of trial, SD: Standard deviation

26: Summary of actual dose by visit (mg pr week) - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin	somapacitan
Number of subjects	11	19
Average weekly dose (mg pr kg pr week)		
Visit 3 (Week 4)		
N	11	19
Mean (SD)	0.236 (0.006)	0.160 (0.001)
Median	0.233	0.160
Min; Max	0.23 ; 0.25	0.16 ; 0.16
Visit 4 (Week 13)		
N	11	19
Mean (SD)	0.232 (0.007)	0.159 (0.001)
Median	0.229	0.160
Min; Max	0.22 ; 0.25	0.16 ; 0.16
Visit 5 (Week 26)		
N	11	19
Mean (SD)	0.238 (0.008)	0.160 (0.001)
Median	0.239	0.160
Min; Max	0.23 ; 0.25	0.16 ; 0.16
Visit 6 (Week 39)		
N	11	19
Mean (SD)	0.237 (0.005)	0.160 (0.001)
Median	0.239	0.160
Min; Max	0.23 ; 0.24	0.16 ; 0.16
Visit 7 (Week 52)		
N	11	19
Mean (SD)	0.239 (0.009)	0.160 (0.001)
Median	0.242	0.160
Min; Max	0.22 ; 0.25	0.16 ; 0.16

27: Summary of adverse events - on-treatment - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	11			19			30		
Total patient years at risk	11.2			19.2			30.4		
All adverse events	8	(72.7)	21 188.1	12	(63.2)	39 202.7	20	(66.7)	60 197.4
Serious adverse events									
Yes	0			2	(10.5)	3 15.6	2	(6.7)	3 9.9
No	8	(72.7)	21 188.1	12	(63.2)	36 187.1	20	(66.7)	57 187.5
Severity									
Mild	7	(63.6)	19 170.2	10	(52.6)	32 166.4	17	(56.7)	51 167.8
Moderate	1	(9.1)	2 17.9	7	(36.8)	7 36.4	8	(26.7)	9 29.6
Severe	0			0			0		
Causality									
Probable	0			0			0		
Possible	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Unlikely	8	(72.7)	20 179.1	12	(63.2)	39 202.7	20	(66.7)	59 194.1
Missing	0			0			0		
Action taken to trial product due to AE									
Drug interrupted	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Drug withdrawn	0			0			0		
Dose reduced	0			0			0		
Dose increased	0			0			0		
Dose not changed	8	(72.7)	20 179.1	12	(63.2)	39 202.7	20	(66.7)	59 194.1
Unknown	0			0			0		
Missing	0			0			0		
Related to technical complaint									
Yes	0			0			0		
No	8	(72.7)	21 188.1	12	(63.2)	39 202.7	20	(66.7)	60 197.4

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
AE causality is based on judgement of investigators.
On treatment: Measurement after first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until week 52 or 14 days after last trial drug administration, which ever comes first, for all other subjects.

Summary of adverse events - on-treatment - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Injection site reaction									
Yes	0			0			0		
No	8	(72.7)	21 188.1	12	(63.2)	39 202.7	20	(66.7)	60 197.4
Outcome									
Recovered/resolved	8	(72.7)	19 170.2	12	(63.2)	37 192.3	20	(66.7)	56 184.2
Recovering/resolving	0			0			0		
Recovered/resolved with sequelae	0			0			0		
Not recovered/not resolved	2	(18.2)	2 17.9	2	(10.5)	2 10.4	4	(13.3)	4 13.2
Fatal	0			0			0		
Unknown	0			0			0		
Missing	0			0			0		
Treatment									
Treatment discontinuations due to adverse events	0			0			0		

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, AE: Adverse event
AE causality is based on judgement of investigators.
On treatment: Measurement after first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and up until week 52 or 14 days after last trial drug administration, which ever comes first, for all other subjects.

28: Summary of adverse events by system organ class and preferred term - on-treatment - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	11			19			30		
Total patient years at risk	11.2			19.2			30.4		
Events	8	(72.7)	21 188.1	12	(63.2)	39 202.7	20	(66.7)	60 197.4
Infections and infestations	7	(63.6)	13 116.4	10	(52.6)	22 114.4	17	(56.7)	35 115.1
Nasopharyngitis	3	(27.3)	7 62.7	7	(36.8)	12 62.4	10	(33.3)	19 62.5
Bronchitis	1	(9.1)	1 9.0	1	(5.3)	1 5.2	2	(6.7)	2 6.6
Influenza	1	(9.1)	1 9.0	1	(5.3)	1 5.2	2	(6.7)	2 6.6
Otitis media	1	(9.1)	1 9.0	1	(5.3)	1 5.2	2	(6.7)	2 6.6
Enteritis infectious	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Hand-foot-and-mouth disease	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Herpangina	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Herpes dermatitis	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Hordeolum	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Impetigo	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Infection	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Molluscum contagiosum	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Sinusitis	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Streptococcal infection	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Skin and subcutaneous tissue disorders	2	(18.2)	2 17.9	3	(15.8)	3 15.6	5	(16.7)	5 16.4
Dermatitis	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Dermatitis atopic	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Miliaria	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Rash	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Urticaria	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Gastrointestinal disorders	1	(9.1)	1 9.0	3	(15.8)	4 20.8	4	(13.3)	5 16.4
Constipation	1	(9.1)	1 9.0	1	(5.3)	2 10.4	2	(6.7)	3 9.9
Umbilical hernia	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - on-treatment - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Vomiting	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Respiratory, thoracic and mediastinal disorders	1	(9.1)	2 17.9	2	(10.5)	3 15.6	3	(10.0)	5 16.4
Upper respiratory tract inflammation	0			2	(10.5)	2 10.4	2	(6.7)	2 6.6
Asthma	1	(9.1)	2 17.9	0			1	(3.3)	2 6.6
Adenoidal hypertrophy	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Injury, poisoning and procedural complications	1	(9.1)	1 9.0	1	(5.3)	2 10.4	2	(6.7)	3 9.9
Accidental overdose	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Head injury	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Skin abrasion	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Reproductive system and breast disorders	0			2	(10.5)	2 10.4	2	(6.7)	2 6.6
Balanoposthitis	0			2	(10.5)	2 10.4	2	(6.7)	2 6.6
Blood and lymphatic system disorders	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Lymphadenopathy	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Immune system disorders	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Seasonal allergy	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Skin papilloma	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Nervous system disorders	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Headache	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Psychiatric disorders	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of adverse events by system organ class and preferred term - on-treatment - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin				somapacitan				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Enuresis	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

29: Summary of serious adverse events by system organ class and preferred term - on-treatment - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin				somapacitan				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	11				19				30			
Total patient years at risk	11.2				19.2				30.4			
Events	0				2	(10.5)	3	15.6	2	(6.7)	3	9.9
Gastrointestinal disorders	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Umbilical hernia	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Infections and infestations	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Otitis media	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Respiratory, thoracic and mediastinal disorders	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Adenoidal hypertrophy	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:05:11 - taesocptsum.sas/taesaesocptsumontrsas4263.txt

30: Summary of severe adverse events by system organ class and preferred term - on-treatment - japanese subgroup - trial 4263 (52w) - safety analysis set

There are no data for this output.

nn8640/nn8640-ghd-summary/ghd_iss_20220310_er
06APR2022:09:05:11 - taesocptsum.sas/taesevaesocptsumontrsas4263.txt

31: Summary of moderate adverse events by system organ class and preferred term - on-treatment - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	11				19				30			
Total patient years at risk	11.2				19.2				30.4			
Events	1	(9.1)	2	17.9	7	(36.8)	7	36.4	8	(26.7)	9	29.6
Infections and infestations	1	(9.1)	1	9.0	4	(21.1)	4	20.8	5	(16.7)	5	16.4
Herpangina	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Influenza	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Molluscum contagiosum	1	(9.1)	1	9.0	0				1	(3.3)	1	3.3
Nasopharyngitis	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Streptococcal infection	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Immune system disorders	1	(9.1)	1	9.0	0				1	(3.3)	1	3.3
Seasonal allergy	1	(9.1)	1	9.0	0				1	(3.3)	1	3.3
Reproductive system and breast disorders	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Balanoposthitis	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Respiratory, thoracic and mediastinal disorders	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Adenoidal hypertrophy	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Skin and subcutaneous tissue disorders	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3
Dermatitis atopic	0				1	(5.3)	1	5.2	1	(3.3)	1	3.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

32: Summary of mild adverse events by system organ class and preferred term - on-treatment - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin			somapacitan			Total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R
Number of subjects	11			19			30		
Total patient years at risk	11.2			19.2			30.4		
Events	7	(63.6)	19 170.2	10	(52.6)	32 166.4	17	(56.7)	51 167.8
Infections and infestations	6	(54.5)	12 107.5	9	(47.4)	18 93.6	15	(50.0)	30 98.7
Nasopharyngitis	3	(27.3)	7 62.7	6	(31.6)	11 57.2	9	(30.0)	18 59.2
Bronchitis	1	(9.1)	1 9.0	1	(5.3)	1 5.2	2	(6.7)	2 6.6
Otitis media	1	(9.1)	1 9.0	1	(5.3)	1 5.2	2	(6.7)	2 6.6
Enteritis infectious	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Hand-foot-and-mouth disease	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Herpes dermatitis	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Hordeolum	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Impetigo	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Infection	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Influenza	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Sinusitis	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Gastrointestinal disorders	1	(9.1)	1 9.0	3	(15.8)	4 20.8	4	(13.3)	5 16.4
Constipation	1	(9.1)	1 9.0	1	(5.3)	2 10.4	2	(6.7)	3 9.9
Umbilical hernia	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Vomiting	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Skin and subcutaneous tissue disorders	2	(18.2)	2 17.9	2	(10.5)	2 10.4	4	(13.3)	4 13.2
Dermatitis	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Miliaria	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Rash	0			1	(5.3)	1 5.2	1	(3.3)	1 3.3
Urticaria	1	(9.1)	1 9.0	0			1	(3.3)	1 3.3
Respiratory, thoracic and mediastinal disorders	1	(9.1)	2 17.9	2	(10.5)	2 10.4	3	(10.0)	4 13.2

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

Summary of mild adverse events by system organ class and preferred term - on-treatment - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin			somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Upper respiratory tract inflammation	0			2 (10.5)	2	10.4	2 (6.7)	2	6.6
Asthma	1 (9.1)	2	17.9	0			1 (3.3)	2	6.6
Injury, poisoning and procedural complications	1 (9.1)	1	9.0	1 (5.3)	2	10.4	2 (6.7)	3	9.9
Accidental overdose	1 (9.1)	1	9.0	0			1 (3.3)	1	3.3
Head injury	0			1 (5.3)	1	5.2	1 (3.3)	1	3.3
Skin abrasion	0			1 (5.3)	1	5.2	1 (3.3)	1	3.3
Blood and lymphatic system disorders	0			1 (5.3)	1	5.2	1 (3.3)	1	3.3
Lymphadenopathy	0			1 (5.3)	1	5.2	1 (3.3)	1	3.3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (9.1)	1	9.0	0			1 (3.3)	1	3.3
Skin papilloma	1 (9.1)	1	9.0	0			1 (3.3)	1	3.3
Nervous system disorders	0			1 (5.3)	1	5.2	1 (3.3)	1	3.3
Headache	0			1 (5.3)	1	5.2	1 (3.3)	1	3.3
Psychiatric disorders	0			1 (5.3)	1	5.2	1 (3.3)	1	3.3
Enuresis	0			1 (5.3)	1	5.2	1 (3.3)	1	3.3
Reproductive system and breast disorders	0			1 (5.3)	1	5.2	1 (3.3)	1	3.3
Balanoposthitis	0			1 (5.3)	1	5.2	1 (3.3)	1	3.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

33: Summary of adverse events possibly or probably related to Norditropin or somapacitan by system organ class and preferred term - japanese subgroup - trial 4263 (52w) - safety analysis set

	Norditropin				somapacitan				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	11				19				30			
Total patient years at risk	11.2				19.2				30.4			
Events	1	(9.1)	1	9.0	0				1	(3.3)	1	3.3
Skin and subcutaneous tissue disorders	1	(9.1)	1	9.0	0				1	(3.3)	1	3.3
Urticaria	1	(9.1)	1	9.0	0				1	(3.3)	1	3.3

N: Number of subjects, %: Percentage, E: Number of events, R: Event rate per 100 patient years at risk, MedDRA version 24.1
Only adverse events with an onset after the first administration of trial product and up until 14 days after last trial drug administration for withdrawn subjects, and with an onset after the first administration of trial product and up until visit 7 (week 52) or 14 days after last trial drug administration, which ever comes first, for all other subjects, are included.

34: Summary of subject disposition by treatment - japanese subgroup - trial 4172 (208w) - all subjects

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week) N (%)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled N (%)	Total N (%)
Screened			39
Randomised	3 (100.0)	9 (100.0)	12 (100.0)
Exposed in main*	3 (100.0)	9 (100.0)	12 (100.0)
Discontinued trial product in main*	0	0	0
Withdrawn from trial in main*	0	0	0
Completed main trial period*	3 (100.0)	9 (100.0)	12 (100.0)
Completed main treatment period*	3 (100.0)	9 (100.0)	12 (100.0)
Exposed in extension*	3 (100.0)	9 (100.0)	12 (100.0)
Discontinued trial product in extension*	1 (33.3)	0	1 (8.3)
- Adverse event	1 (33.3)	0	1 (8.3)
Withdrawn from trial in extension*	0	0	0
Completed extension trial period*	3 (100.0)	9 (100.0)	12 (100.0)
Completed extension treatment period*	2 (66.7)	9 (100.0)	11 (91.7)
Exposed in safety extension*	2 (66.7)	9 (100.0)	11 (91.7)
Discontinued trial product in safety extension*	0	0	0

N: Number of subjects, %: Percentage
Treatment period: The period from visit 2 (Week 0) to visit 20 (Week 208) without premature discontinuation of randomised treatment.
Trial period: The period from visit 2 (Week 0) to visit 20 (Week 208).
Long-term safety extension period: The period after visit 15 (Week 156) to and including visit 20 (Week 208).
One subject is following protocol version 1, where visit 7 is last visit. This subject is a completer of all the trial and treatment periods but is not exposed to treatment after visit 7.
Re-screened subjects are counted only once.
*: Includes subjects 'as treated'.

Summary of subject disposition by treatment - japanese subgroup - trial 4172 (208w) - all subjects

Cohort I Treatment group	Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week) N (%)	somapacitan (0.04/0.08/0.16mg/kg/week) pooled N (%)	Total N (%)
Withdrawn from trial in safety extension*	1 (33.3)	0	1 (8.3)
- Protocol violation	1 (33.3)	0	1 (8.3)
Completed safety extension trial period*	2 (66.7)	9 (100.0)	11 (91.7)
Completed safety extension treatment period*	2 (66.7)	9 (100.0)	11 (91.7)
Exposed in long-term safety extension*	2 (66.7)	9 (100.0)	11 (91.7)
Discontinued trial product in long-term safety extension*	0	0	0
Withdrawn from trial in long-term safety extension*	0	0	0
Completed long-term safety extension trial period*	2 (66.7)	9 (100.0)	11 (91.7)
Completed long-term safety extension treatment period*	2 (66.7)	9 (100.0)	11 (91.7)
Full analysis set*	3 (100.0)	9 (100.0)	12 (100.0)
Safety analysis set*	3 (100.0)	9 (100.0)	12 (100.0)

N: Number of subjects, %: Percentage
Treatment period: The period from visit 2 (Week 0) to visit 20 (Week 208) without premature discontinuation of randomised treatment.
Trial period: The period from visit 2 (Week 0) to visit 20 (Week 208).
Long-term safety extension period: The period after visit 15 (Week 156) to and including visit 20 (Week 208).
One subject is following protocol version 1, where visit 7 is last visit. This subject is a completer of all the trial and treatment periods but is not exposed to treatment after visit 7.
Re-screened subjects are counted only once.
*: Includes subjects 'as treated'.

35: Listing of subject disposition - japanese subgroup - trial 4172 (208w) - randomised subjects

Treatment group/ Subject ID	Sex (M/F)/ Age (yrs)/ BMI (kg/m^2)	Randomisation date	Exposed (Y/N)	Duration of exposure (weeks)	Total no. of actual doses of Norditropin/Somapaciton	In trial (weeks)	Completed trial (Y/N)	Randomisation code broken (Y/N)
Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)/ [redacted]002	M/[redacted].0/15.6	30NOV2016	Y	52.0	348/	55.4	N	N
Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)/ [redacted]001	M/[redacted].0/14.3	21NOV2016	Y	208	1060/53	208	Y	N
Norditropin (0.034mg/kg/day)/ somapacitan (0.16mg/kg/week)/ [redacted]002	M/[redacted].0/17.5	13APR2017	Y	208	1090/52	208	Y	N
somapacitan (0.04mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]001	F/[redacted].0/14.1	20OCT2016	Y	210	/209	208	Y	N
somapacitan (0.04mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]002	M/[redacted].0/16.1	16JAN2017	Y	210	/198	209	Y	N
somapacitan (0.04mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]004	M/[redacted].0/15.1	11MAY2017	Y	210	/206	208	Y	N

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
In-trial: The period from date of randomisation and until last trial-related subject-site contact.

Listing of subject disposition - japanese subgroup - trial 4172 (208w) - randomised subjects

Treatment group/ Subject ID	Sex (M/F)/ Age (yrs)/ BMI (kg/m^2)	Randomisation date	Exposed (Y/N)	Duration of exposure (weeks)	Total no. of actual doses of Norditropin/Somapaciton	In trial (weeks)	Completed trial (Y/N)	Randomisation code broken (Y/N)
somapacitan (0.08mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]001	M/[redacted].0/14.0	02NOV2016	Y	210	/209	208	Y	N
somapacitan (0.08mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]001	M/[redacted].0/15.3	16DEC2016	Y	210	/208	209	Y	N
somapacitan (0.08mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]003	M/[redacted].0/16.5	16MAR2017	Y	210	/209	209	Y	N
somapacitan (0.16mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]001	M/[redacted].0/17.2	02MAR2017	Y	212	/209	210	Y	N
somapacitan (0.16mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]001	M/[redacted].0/16.8	26NOV2016	Y	211	/209	209	Y	N
somapacitan (0.16mg/kg/week)/ somapacitan (0.16mg/kg/week)/ [redacted]002	M/[redacted].0/16.0	12JAN2017	Y	211	/209	209	Y	N

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
In-trial: The period from date of randomisation and until last trial-related subject-site contact.

36: Summary of subject disposition by treatment - japanese subgroup - trial 4263 (52w) - all subjects

	Norditropin N (%)	somapacitan N (%)	Total N (%)
Screened			58
Randomised	11 (100.0)	19 (100.0)	30 (100.0)
Randomised in error	0	0	0
Exposed*	11 (100.0)	19 (100.0)	30 (100.0)
Discontinued trial product*	0	0	0
Withdrawn from trial	0	0	0
Completed trial period	11 (100.0)	19 (100.0)	30 (100.0)
Completed treatment period*	11 (100.0)	19 (100.0)	30 (100.0)
Full analysis set	11 (100.0)	19 (100.0)	30 (100.0)
Per protocol analysis set*	11 (100.0)	19 (100.0)	30 (100.0)
Safety analysis set*	11 (100.0)	19 (100.0)	30 (100.0)

N: Number of subjects, %: Percentage
Treatment period: The period from visit 2 (Week 0) to visit 7 (Week 52) without premature discontinuation of randomised treatment.
Trial period: The period from visit 2 (Week 0) to visit 7 (Week 52).
*: Includes subjects 'as treated'.

37: Listing of subject disposition - japanese subgroup - trial 4263 (52w) - randomised subjects

Treatment group/ Subject ID	Sex (M/F)/ Age (yrs)/ BMI (kg/m^2)	Randomisation date	Exposed (Y/N)	Duration of exposure (weeks)	Total no. of actual doses	In trial (weeks)	Completed treatment (Y/N)	Completed main trial (Y/N)
Norditropin/ [redacted]001	M/[redacted].7/14.2	29AUG2019	Y	52.6	286	52.7	Y	Y
Norditropin/ [redacted]001	M/[redacted].5/16.4	16MAR2020	Y	52.6	335	52.7	Y	Y
Norditropin/ [redacted]001	F/[redacted].5/15.2	12JUN2019	Y	52.7	343	52.9	Y	Y
Norditropin/ [redacted]005	F/[redacted].2/14.9	28OCT2020	Y	52.7	367	52.9	Y	Y
Norditropin/ [redacted]001	M/[redacted].9/14.0	27NOV2019	Y	54.7	377	54.9	Y	Y
Norditropin/ [redacted]003	F/[redacted].2/17.7	18MAY2020	Y	52.6	368	52.7	Y	Y
Norditropin/ [redacted]001	M/[redacted].5/15.6	14FEB2020	Y	52.6	359	52.7	Y	Y
Norditropin/ [redacted]003	M/[redacted].8/17.0	27NOV2019	Y	52.7	359	52.9	Y	Y
Norditropin/ [redacted]018	M/[redacted].3/16.7	23SEP2020	Y	52.7	342	52.9	Y	Y
Norditropin/ [redacted]002	M/[redacted].6/14.4	21APR2020	Y	52.6	363	52.7	Y	Y
Norditropin/ [redacted]004	F/[redacted].7/13.3	25SEP2020	Y	52.6	361	52.7	Y	Y
somapacitan/ [redacted]002	F/[redacted].8/17.6	09JUL2020	Y	52.7	53	52.7	Y	Y

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
In-trial: The period from first administration of trial product and until last trial-related subject-site contact.

Listing of subject disposition - japanese subgroup - trial 4263 (52w) - randomised subjects

Treatment group/ Subject ID	Sex (M/F)/ Age (yrs)/ BMI (kg/m^2)	Randomisation date	Exposed (Y/N)	Duration of exposure (weeks)	Total no. of actual doses	In trial (weeks)	Completed treatment (Y/N)	Completed main trial (Y/N)
somapacitan/ [redacted]001	F/[redacted].3/13.5	05AUG2020	Y	52.0	51	52.0	Y	Y
somapacitan/ [redacted]002	M/[redacted].1/15.9	12JUN2019	Y	53.0	53	53.0	Y	Y
somapacitan/ [redacted]001	M/1[redacted].8/14.8	12JUL2019	Y	52.7	53	52.7	Y	Y
somapacitan/ [redacted]003	M/[redacted].6/15.8	03JUN2020	Y	52.9	53	52.9	Y	Y
somapacitan/ [redacted]004	M/[redacted].6/16.5	10JUN2020	Y	52.9	53	52.9	Y	Y
somapacitan/ [redacted]002	M/[redacted].7/17.9	23JUL2019	Y	53.0	53	53.0	Y	Y
somapacitan/ [redacted]005	F/[redacted].4/13.9	20OCT2020	Y	53.0	53	53.0	Y	Y
somapacitan/ [redacted]002	M/1[redacted].3/20.6	15APR2020	Y	52.9	53	52.9	Y	Y
somapacitan/ [redacted]003	M/1[redacted].3/15.1	21MAY2020	Y	52.7	52	52.7	Y	Y
somapacitan/ [redacted]005	F/[redacted].2/13.9	10SEP2020	Y	52.7	47	52.7	Y	Y
somapacitan/ [redacted]001	M/[redacted].2/14.7	20NOV2019	Y	53.0	53	53.0	Y	Y
somapacitan/ [redacted]002	M/[redacted].1/16.2	13MAY2020	Y	53.0	53	53.0	Y	Y

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
In-trial: The period from first administration of trial product and until last trial-related subject-site contact.

Listing of subject disposition - japanese subgroup - trial 4263 (52w) - randomised subjects

Treatment group/ Subject ID	Sex (M/F)/ Age (yrs)/ BMI (kg/m^2)	Randomisation date	Exposed (Y/N)	Duration of exposure (weeks)	Total no. of actual doses	In trial (weeks)	Completed treatment (Y/N)	Completed main trial (Y/N)
somapacitan/ [redacted]001	F/[redacted].9/15.9	20NOV2019	Y	53.0	50	53.0	Y	Y
somapacitan/ [redacted]005	M/[redacted].9/16.2	18DEC2019	Y	52.9	53	52.9	Y	Y
somapacitan/ [redacted]009	M/[redacted].0/15.3	05FEB2020	Y	52.9	51	52.9	Y	Y
somapacitan/ [redacted]010	M/[redacted].4/17.1	19FEB2020	Y	52.9	49	52.9	Y	Y
somapacitan/ [redacted]011	M/[redacted].5/15.5	26FEB2020	Y	52.9	53	52.9	Y	Y
somapacitan/ [redacted]012	F/[redacted].4/15.2	11MAR2020	Y	52.9	53	52.9	Y	Y

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
In-trial: The period from first administration of trial product and until last trial-related subject-site contact.

ソグルーヤ皮下注 5mg
ソグルーヤ皮下注 10mg
ソグルーヤ皮下注 15mg

成長ホルモン分泌不全性低身長症及び
15 mg 製剤剤形追加

2.7.5 参考文献

ノボ ノルディスク ファーマ株式会社

2.7.5.1 参考文献

参考文献は、Module 2.5、Module 2.7.1、Module 2.7.2、Module 2.7.3 及び Module 2.7.4 の参考文献の項にそれぞれ示した。