ソマプシタン（遺伝子組換え）

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

目次

ページ

目次 2
図目次 6
表目次 6
略語一覧 10
2.7.4.1 医薬品への曝露 12
2.7.4.1.1 背景 12
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 12
2.7.4.1.2.1 本臨床概要に含める臨床試験 12
2.7.4.1.2.2 安全性の評価 16
2.7.4.1.2.3 安全性データの表示 20
2.7.4.1.2.3.1 試験別での表示 20
2.7.4.1.2.3.2 併合データでの表示 20
2.7.4.1.2.3.3 有害事象 22
2.7.4.1.2.3.4 臨床検査項目 23
2.7.4.1.2.3.5 IGF-I SD スコア 23
2.7.4.1.2.3.6 バイタルサイン、心電図及び体重 24
2.7.4.1.2.4 安全性データ及び試験の分類 24
2.7.4.1.2.4.1 安全性データの提示順序 24
2.7.4.1.2.4.2 試験別での提示 24
2.7.4.1.2.4.3 併合データでの表示 24
2.7.4.1.2.4.4 日本人被験者における安全性 25
2.7.4.1.2.4.5 臨床薬理試験 25
2.7.4.1.2.5 部分集団における安全性 25
2.7.4.1.2.6 重要な安全性に関する考察 26
2.7.4.1.2.6.1 非臨床における所見 26
2.7.4.1.2.6.2 GH の薬理的なクラスエフェクト 26
2.7.4.1.2.7 小児 GHD 患者における安全性 26
2.7.4.1.3 全般的な曝露状況 30
2.7.4.1.3.1 曝露 30
2.7.4.1.3.1.1 AGHD 患者を対象とした第 3 相試験の結果（試験別） 30
2.7.4.1.3.1.2 AGHD 患者を対象とした第 3 相試験の結果（第 3 相試験併合） 31

2.7.4.1.3.1.3 AGHD 患者を対象とした第 3 相試験の結果（ノルディトロピン/ソマプシタン併合）.....33
2.7.4.1.3.1.4 日本人被験者の結果を含む AGHD 患者を対象とした第 3 相試験の結果.....33
2.7.4.1.3.1.5 臨床薬理試験の結果.....35
2.7.4.1.3.2 試験を中止・脱落した被験者数.....36
2.7.4.1.3.3 用量レベルの調整.....38
2.7.4.1.4 試験対象集団の人口統計学的特性及びその他の特性.....39
2.7.4.1.4.1 組み入れ基準.....39
2.7.4.1.4.2 AGHD 患者を対象とした第 3 相試験の結果（試験別）.....39
2.7.4.1.4.3 AGHD 患者を対象とした第 3 相試験の結果（第 3 相試験併合）.....40
2.7.4.1.4.4 日本人被験者の結果を含む AGHD 患者を対象とした第 3 相試験の結果.....43
2.7.4.1.4.5 臨床薬理試験の結果.....43
2.7.4.2 有害事象.....44
2.7.4.2.1 比較的よく見られる有害事象.....44
2.7.4.2.1.1 AGHD 患者を対象とした第 3 相試験の結果（試験別）.....44
2.7.4.2.1.2 AGHD 患者を対象とした第 3 相試験の結果（第 3 相試験併合）.....49
2.7.4.2.1.3 日本人被験者の結果を含む AGHD 患者を対象とした第 3 相試験の結果.....54
2.7.4.2.1.4 臨床薬理試験の結果.....61
2.7.4.2.2 死亡.....63
2.7.4.2.3 その他の重篤な有害事象.....65
2.7.4.2.3.1 AGHD 患者を対象とした第 3 相試験の結果（試験別）.....65
2.7.4.2.3.2 AGHD 患者を対象とした第 3 相試験の結果（第 3 相試験併合）.....66
2.7.4.2.3.3 日本人被験者の結果を含む AGHD 患者を対象とした第 3 相試験の結果.....74
2.7.4.2.3.4 臨床薬理試験の結果.....76
2.7.4.2.4 その他の重要な有害事象.....77
2.7.4.2.4.1 試験の中止又は治験薬投与の中止に至った有害事象.....77
2.7.4.2.4.2 治験薬の投与量減量に至った有害事象.....80
2.7.4.2.5 器官別又は症候群別有害事象の解析.....80
2.7.4.2.5.1 完了した第 3 相試験の概要（試験別）.....80
2.7.4.2.5.2 内分泌障害.....83
2.7.4.2.5.3 胃腸障害.....84
2.7.4.2.5.4 一般・全身障害.....84
2.7.4.2.5.5 免疫系障害.....87
2.7.4.2.5.6 傷害、処置及び投与部位の状態.....88

2.7.4.2.5.7 臨床検査 94
2.7.4.2.5.8 代謝系障害 98
2.7.4.2.5.9 筋骨格系障害 99
2.7.4.2.5.10 新生物 100
2.7.4.2.5.11 神経系障害 105
2.7.4.2.5.12 その他の事象 106
2.7.4.2.5.13 ノルディトロピン/ソマプシタン併合での結果 106
2.7.4.2.6 Adverse drug reaction 106
2.7.4.2.7 有害事象の要約 107
2.7.4.3 臨床検査値の評価 108
2.7.4.3.1 免疫原性 108
2.7.4.3.2 血糖コントロール 108
2.7.4.3.2.1 AGHD 患者を対象とした第 3 相試験の結果 108
2.7.4.3.2.2 臨床薬理試験の結果 119
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 120
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 120
2.7.4.3.3.2 IGF-I 及び標準化された IGF-I（IGF-I SD スコア） 120
2.7.4.3.3.2.1 AGHD 患者を対象とした第 3 相試験の結果 120
2.7.4.3.3.2.2 臨床薬理試験の結果 123
2.7.4.3.4 臨床検査値の評価の要約 123
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 125
2.7.4.4.1 バイタルサイン及び体重 125
2.7.4.4.1.1 AGHD 患者を対象とした第 3 相試験の結果 125
2.7.4.4.1.2 臨床薬理試験の結果 126
2.7.4.4.2 心電図 127
2.7.4.4.2.1 概要 127
2.7.4.4.2.2 AGHD 患者を対象とした第 3 相試験の結果 127
2.7.4.4.2.3 臨床薬理試験の結果 131
2.7.4.4.3 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 131
2.7.4.5 特別な患者集団及び状況下における安全性 132
2.7.4.5.1 内因性民族的要因 132
2.7.4.5.1.1 性別（第 3 相試験併合） 132
2.7.4.5.1.2 年齢グループ（第 3 相試験併合） 132
2.7.4.5.1.3 GHD 発症型（第 3 相試験併合） 132

2.7.4.5.1.4 腎機能障害を有する患者の安全性 136
2.7.4.5.1.5 肝機能障害を有する患者の安全性 136
2.7.4.5.1.6 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 136
2.7.4.5.2 外因性民族的要因 136
2.7.4.5.3 薬物相互作用 137
2.7.4.5.4 妊娠及び授乳時の使用 138
2.7.4.5.5 過量投与 139
2.7.4.5.6 薬物乱用及び依存 139
2.7.4.5.7 離脱症状及び反跳現象 139
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 139
2.7.4.5.9 最高投与量のソマプシタンを投与した被験者の安全性 140
2.7.4.5.9.1 AGHD 患者を対象とした第 3 相試験 140
2.7.4.5.9.2 臨床薬理試験 141
2.7.4.5.10 特別な患者集団及び状況下における安全性の要約 143
2.7.4.6 市販後データ 144
参考文献 145

2.7.4.7 付録
2.7.4.7.1 第 3 相試験結果に基づく解析帳票（試験別及び併合）
2.7.4.7.2 第 3 相試験結果に基づく解析帳票（日本人集団の結果を含む）
2.7.4.7.3 小児患者を対象とした試験の解析帳票（重篤な有害事象の叙述及び一覧を含む）

図目次

ページ

図 2.7.4.2-1 有害事象の概要（第 3 相試験別）.....44
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）（4054 試験、全試験期間）.....45
図 2.7.4.2-3 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）（4043 試験）.....46
図 2.7.4.2-4 高頻度（投与群を通じて 4%以上）で報告された有害事象（基本語別）（4244 試験）.....46
図 2.7.4.2-5 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）（第 3 相試験併合）.....51
図 2.7.4.2-6 特に注目すべき安全性領域（第 3 相試験併合及び試験別）.....82
図 2.7.4.3-1 AGHD 患者における空腹時血糖値（mmol/L）の箱ひげ図（4054 試験）.....110
図 2.7.4.3-2 AGHD 患者における HbA1c（%）の箱ひげ図（4054 試験）.....111
図 2.7.4.3-3 AGHD 患者における空腹時インスリン（pmol/L）の箱ひげ図（4054 試験）.....112
図 2.7.4.3-4 ソマプシタン/ソマプシタン群で空腹時血糖値が 7.0 mmol/L 以上の値を有する被験者（4054 試験）.....115
図 2.7.4.3-5 ソマプシタン/ソマプシタン群で HbA1c が 6.5%以上の値を有する被験者（4054 試験）.....116
図 2.7.4.3-6 空腹時血糖値（mmol/L）の箱ひげ図（来院ごと）（4244 試験）.....117
図 2.7.4.3-7 HbA1c（%）の箱ひげ図（来院ごと）（4244 試験）.....118
図 2.7.4.3-8 ソマプシタン/ソマプシタン群で用量維持期間中に IGF-I SD スコアが+2 を超えた被験者（4054 試験）.....121
図 2.7.4.3-9 ノルディトロピン/ノルディトロピン群で用量維持期間中に IGF-I SD スコアが+2 を超えた被験者（4054 試験）.....122

表目次

ページ

表 2.7.4.1-1 ソマプシタンの臨床試験（健康被験者、特別な患者集団及び AGHD 患者を対象とした試験）.....14
表 2.7.4.1-2 特に注目すべき安全性領域.....18
表 2.7.4.1-3 併合した安全性データ（投与群別）（第 3 相試験併合）.....21

表 2.7.4.1-4 AGHD 患者を対象とした第 3 相試験の併合の概要 22
表 2.7.4.1-5 小児 GHD 患者を対象とした臨床試験 27
表 2.7.4.1-6 小児 GHD 患者における治験薬の投与中止に至った有害事象（4172 試験） 28
表 2.7.4.1-7 小児 GHD 患者で報告された重篤な有害事象（4172 試験、進行中） 29
表 2.7.4.1-8 AGHD 患者における平均投与量及び曝露期間（PYE）（試験別、投与群別）（4054 試験、4043 試験及び 4244 試験） 30
表 2.7.4.1-9 AGHD 患者における投与群別の曝露期間（4054 試験、主要試験期間及び主要試験期間＋延長期間） 31
表 2.7.4.1-10 AGHD 患者における曝露（第 3 相試験併合） 32
表 2.7.4.1-11 AGHD 患者における 3 ヵ月ごとの曝露（第 3 相試験併合） 32
表 2.7.4.1-12 AGHD 患者における治療遵守率（第 3 相試験併合） 33
表 2.7.4.1-13 臨床薬理試験における曝露 35
表 2.7.4.1-14 ソマプシタンの単回投与及び反復投与時の用量範囲 36
表 2.7.4.1-15 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要約 37
表 2.7.4.1-16 AGHD 患者のベースライン特性（試験別） 40
表 2.7.4.1-17 AGHD 患者のベースライン特性（第 3 相試験併合） 41
表 2.7.4.2-1 AGHD 患者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（いずれかの群で 5%以上）〔4054 試験（主要試験期間+延長期間）〕 47
表 2.7.4.2-2 AGHD 患者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（いずれかの群で 5%以上）〔4054 試験（主要試験期間）〕 47
表 2.7.4.2-3 AGHD 患者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（5%以上）（4043 試験） 48
表 2.7.4.2-4 AGHD 患者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（投与群を通じて 5%以上）（4244 試験） 49
表 2.7.4.2-5 AGHD 患者で報告された有害事象の概要（第 3 相試験併合） 50
表 2.7.4.2-6 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（器官別大分類別、基本語別）（第 3 相試験併合） 53
表 2.7.4.2-7 有害事象の概要〔4054 試験（主要試験期間）、全集団〕 55
表 2.7.4.2-8 有害事象の概要（4043 試験、全集団） 57
表 2.7.4.2-9 有害事象の概要（4244 試験） 59
表 2.7.4.2-10 AGHD 患者で報告された死亡（試験別） 64

表 2.7.4.2-11 AGHD 患者で報告された重篤な有害事象の概要（第 3 相試験併合）.....68
表 2.7.4.2-12 AGHD 患者で報告された重篤な有害事象（第 3 相試験併合）.....69
表 2.7.4.2-13 AGHD 患者で報告された 3 ヵ月ごとの重篤な有害事象の発現状況（第 3 相試験併合）.....73
表 2.7.4.2-14 日本人 AGHD 患者で報告された重篤な有害事象（4054 試験）.....74
表 2.7.4.2-15 日本人 AGHD 患者で報告された重篤な有害事象（4043 試験）.....75
表 2.7.4.2-16 日本人 AGHD 患者で報告された重篤な有害事象（4244 試験）.....76
表 2.7.4.2-17 AGHD 患者で報告された重篤な有害事象（3947 試験、反復投与）.....77
表 2.7.4.2-18 試験の中止又は治験薬投与の中止に至った有害事象を発現した被験者.....79
表 2.7.4.2-19 AGHD 患者で発現した甲状腺機能低下症の有害事象（第 3 相試験併合）.....83
表 2.7.4.2-20 AGHD 患者で発現した副腎皮質機能不全（二次性）の有害事象（第 3 相試験併合）.....84
表 2.7.4.2-21 AGHD 患者で発現した膵炎の有害事象（第 3 相試験併合）.....84
表 2.7.4.2-22 AGHD 患者で発現した末梢性浮腫の有害事象（第 3 相試験併合）.....85
表 2.7.4.2-23 AGHD 患者で発現した疲労／無力症の有害事象（第 3 相試験併合）.....86
表 2.7.4.2-24 AGHD 患者で発現した体重増加の有害事象（第 3 相試験併合）.....86
表 2.7.4.2-25 AGHD 患者で発現したアレルギー反応（非アナフィラキシー反応）の有害事象（第 3 相試験併合）.....88
表 2.7.4.2-26 AGHD 患者で発現した注射部位反応の有害事象（第 3 相試験併合）.....89
表 2.7.4.2-27 AGHD 患者で発現した脂肪肥大症／リポジストロフィーの有害事象（第 3 相試験併合）.....90
表 2.7.4.2-28 脂肪肥大症／リポジストロフィーの有害事象別の詳細.....91
表 2.7.4.2-29 AGHD 患者で発現した脂肪組織萎縮症の有害事象（第 3 相試験併合）.....92
表 2.7.4.2-30 脂肪組織萎縮症の有害事象別の詳細.....93
表 2.7.4.2-31 AGHD 患者で発現した高位グループ語「心血管系検査（酵素検査を除く）」及び高位グループ語「不整脈」に分類される有害事象（第 3 相試験併合）.....96
表 2.7.4.2-32 心電図に関連する有害事象.....97
表 2.7.4.2-33 AGHD 患者で発現した高血糖の有害事象（第 3 相試験併合）.....98
表 2.7.4.2-34 AGHD 患者で発現した 2 型糖尿病の徴候の有害事象（第 3 相試験併合）.....99
表 2.7.4.2-35 AGHD 患者で発現した関節痛の有害事象（第 3 相試験併合）.....99
表 2.7.4.2-36 AGHD 患者で発現した筋肉痛の有害事象（第 3 相試験併合）.....100
表 2.7.4.2-37 AGHD 患者で発現した良性、悪性及び詳細不明の新生物の有害事象（第 3 相試験併合）.....101
表 2.7.4.2-38 良性、悪性及び詳細不明の新生物の有害事象別の詳細.....102

表 2.7.4.2-39 AGHD 患者で発現した頭痛の有害事象（第 3 相試験併合）.....105
表 2.7.4.2-40 ソマプシタンの adverse drug reaction（AGHD 患者）.....107
表 2.7.4.3-1 ベースライン時の糖尿病の有無（4054 試験）.....113
表 2.7.4.4-1 収縮期／拡張期血圧（mmHg）のベースラインからの変化量（4054 試験、4043 試験及び 4244 試験）.....125
表 2.7.4.4-2 体重（kg）のベースラインからの変化量（4054 試験、4043 試験及び 4244 試験）.....126
表 2.7.4.4-3 心電図の判定（治験責任医師の判定に基づく）結果の要約（来院別）（4054 試験）.....128
表 2.7.4.4-4 治験責任医師により「異常／臨床的に問題あり」と判定（治験責任医師の判定に基づく）された心電図の一覧（4054 試験）.....129
表 2.7.4.5-1 男女別の有害事象の概要（第 3 相試験併合）.....133
表 2.7.4.5-2 年齢グループ別の有害事象の概要（第 3 相試験併合）.....134
表 2.7.4.5-3 GHD 発症型別の有害事象の概要（第 3 相試験併合）.....135
表 2.7.4.5-4 CCDS に提示した薬物相互作用.....137
表 2.7.4.5-5 CCDS に提示したソマプシタンの警告及び使用上の注意.....137
表 2.7.4.5-6 8 mg/週を超える用量でソマプシタンを投与した日本人及び非アジア人健康被験者の投与量及び有害事象（3915 試験、反復投与パート）.....142

略語一覧

AE	:	adverse event（有害事象）
ADA	:	The American Diabetes Association（米国糖尿病学会）
ADR	:	adverse drug reactions
AGHD	:	adult growth hormone deficiency（成人成長ホルモン分泌不全症）
AME	:	absorption, metabolism and excretion（吸収、代謝、排泄）
BMI	:	body mass index〔体容量指数：体重(kg)／身長$(m)^2$〕
CCDS	:	企業中核データシート
C_{max}	:	maximum concentration（最高血中濃度）
CMH	:	Cochran-Mantel-Haenszel
CRP	:	C-reactive protein（C 反応性タンパク）
CS	:	clinically significant（臨床的に問題あり）
ECG	:	electrocardiogram（心電図）
EOT	:	end-of-text
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）
eGFR	:	estimated glomerular filtration rate（推算糸球体濾過量）
GCP	:	good clinical practice（医薬品の臨床試験の実施の基準）
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	:	haemoglobin A1c（グリコヘモグロビン A1c）
hGH	:	growth hormone（ヒト成長ホルモン）
HLT	:	high level term（高位語）
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）
INR	:	International Normalised Ratio
JP	:	Japanese（日本人）
MedDRA	:	Medical Dictionary for Regulatory Activities（国際医薬用語集）
MD	:	multiple-dose（反復投与）
MRI	:	magnetic resonance imaging（核磁気共鳴画像）
NA	:	not applicable（該当せず）
NCS	:	not clinically significant（臨床的に問題なし）
PD	:	pharmacodynamics（薬力学的作用）
PK	:	pharmacokinetics（薬物動態）
PT	:	preferred term（基本語）
PYE	:	patient years of exposure
QTc	:	corrected QT interval
QTcF	:	Fridericia heart rate corrected QT interval
SAEc	:	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 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。

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、成人成長ホルモン分泌不全症（AGHD）患者、成長ホルモン分泌不全性低身長症（GHD）の小児患者（小児 GHD 患者）及び small for gestational age 性低身長症の小児患者に対する補充療法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を開発している。今般、AGHD の適応症の承認取得を目的として申請を行うこととした。

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）誘導体であり、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アルブミンバインダーから構成され、化学結合によりアミノ酸骨格の 101 位に結合している。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）の半減期（$t_{1/2}$）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]。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 $t_{1/2}$ 及び作用持続時間が延長する。ソマプシタンの作用機序は hGH と同様であり、GH 受容体への結合を介する直接作用及びインスリン様成長因子-I（IGF-I）を介する間接作用である。

ソマプシタンの週 1 回投与は、新たな治療選択肢であり、1 日 1 回投与の GH 製剤〔ノルディトロピン（ノボ ノルディスク社が市販しているソマトロピン製剤）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 GH 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、AGHD 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[3,4,5,6,7,8]。

本臨床概要では、AGHD 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た安全性データを提示する。また、小児 GHD 患者を対象とした 2 つの試験から得た安全性データも提示する。小児 GHD 患者を対象とした試験の安全性データのカットオフ日を 2019 年 5 月 7 日とした。

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

現在のソマプシタンの安全性情報は、AGHD 患者を対象とした 4 試験、健康被験者を対象とした 3 試験ならびに腎機能障害又は肝機能障害を有する被験者を対象とした 2 試験（これら 2 試験は健康被験者も含む）の 9 つの臨床試験から得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。

第 3 相試験（検証的試験）である 4054 試験は、hGH 製剤による治療歴がない AGHD 患者を対象として、ソマプシタンの週 1 回投与の有効性及び安全性をプラセボの週 1 回投与及びノルディトロピンの 1 日 1 回投与との比較により評価した。当該試験は、35 週間の主要試験期間（二重盲検のソマプシタン及びプラセボ投与、ならびに非盲検のノルディトロピン投与）とそれに続く 53 週間の非盲検の延長期

間で構成された。延長期間では、ソマプシタンの投与を受けていた被験者はソマプシタンの週 1 回投与を継続し、プラセボの投与を受けていた被験者はソマプシタン投与に切り替えた。ノルディトロピンの投与を受けていた被験者は、ノルディトロピンの投与継続か、ソマプシタンの投与への切り替えのいずれかに再度無作為に割り付けられた。

補足的な第 3 相試験である 4043 試験ではソマプシタンの週 1 回投与の安全性をノルディトロピンの 1 日 1 回投与と比較検討し、日本のみで実施された 4244 試験ではソマプシタンの週 1 回投与の安全性及び有効性をノルディトロピンの 1 日 1 回投与と比較検討した。両試験とも、hGH 製剤で治療中の AGHD 患者を対象とした。

日本人被験者は、AGHD 患者を対象としたすべての第 3 相試験（4054 試験、4043 試験及び 4244 試験）及び健康被験者を対象としたヒトへの初回投与試験（3915 試験）に参加した（表 2.7.4.1-1）。

ソマプシタンの投与は週 1 回皮下投与とした。AGHD 患者を対象とした第 3 相試験では、各被験者の用量を IGF-I SD スコアに基づいて調整した（目標とする IGF-I SD スコアの範囲は、4054 試験で-0.5 超+1.75 以下、4043 試験及び 4244 試験で 0 超+2 以下）。各臨床試験で適用した用量調整アルゴリズムの詳細については、Module 2.7.3.1.3.6 を参照のこと。

有効性及び安全性を評価した臨床試験の要約は、Module 2.7.3.2 に示した。

臨床試験のデザイン、対象集団、用法・用量及び対照薬の詳細は、Module 2.7.3.1（4054 試験、4043 試験及び 4244 試験）、Module 2.7.2.1.4（3915 試験、4237 試験、3947 試験、4297 試験及び 4298 試験）及び Module 2.7.1.2（4491 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 5.3.1.2、M 5.3.3.1、M 5.3.3.2、M 5.3.3.3 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[9]、関連規制要件及びヘルシンキ宣言[10]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（健康被験者、特別な患者集団及び AGHD 患者を対象とした試験）

試験 ID（実施国）	試験デザイン及び試験期間	曝露被験者数（男性／女性）、年齢	用法・用量〔曝露期間（人・年；PYE）（AGHD 患者を対象とした試験のみ）〕
第 1 相試験（健康被験者及び特別な患者集団）			
3915 試験 [a]（ドイツ）	ヒトへの初回投与 安全性、忍容性、薬物動態、薬力学的作用 無作為割り付け、単回及び反復投与、用量漸増、二重盲検、プラセボ対照 試験期間：4 週間	健康被験者計 105 例 単回投与パート 健康被験者 40 例 （40/0）、22–43 歳	単回投与パート 5 コホート ソマプシタン（0.01、0.04、0.08、0.16 及び 0.32 mg/kg）又はプラセボ単回皮下投与
		反復投与パート 日本人健康被験者 [b]32 例 （32/0）、23–38 歳 非アジア人健康被験者 [b]33 例 （33/0）、22–45 歳	反復投与パート 4 コホート ソマプシタン（0.02、0.08、0.16 及び 0.24 mg/kg）又はプラセボ週 1 回皮下投与
4237 試験（オランダ）	吸収、代謝及び排泄 単回投与、非盲検 試験期間：5 週間	健康被験者 7 例 （7/0）、45–62 歳	ソマプシタン 6 mg を含有するトリチウム標識ソマプシタン（20 MBq まで） 皮下投与
4297 試験（ドイツ）	腎機能障害を有する被験者の安全性、薬物動態、薬力学的作用 反復投与、非盲検 試験期間：約 6 週間	健康被験者 15 例 腎機能障害を有する被験者 29 例 計 44 例 （25/19）、28–74 歳	ソマプシタン 0.08 mg/kg 3 週間週 1 回皮下投与
4298 試験（スロバキア）	肝機能障害を有する被験者の安全性、薬物動態、薬力学的作用 反復投与、非盲検 試験期間：約 6 週間	健康被験者 16 例 肝機能障害を有する被験者 18 例 計 34 例 （15/19）、37–69 歳	ソマプシタン 0.08 mg/kg 3 週間週 1 回皮下投与
4491 試験（ドイツ）	2 つのソマプシタン製剤の生物学的同等性、薬物動態及び薬力的作用 単回投与、二重盲検、3 期、クロスオーバー 試験期間：約 10 週間	健康被験者 33 例 （27/5）[c]、22–45 歳 [c]	2 製剤〔5 mg/1.5 mL 製剤（5 mg 製剤）及び 10 mg/1.5 mL 製剤（10 mg 製剤）〕を用いてソマプシタン 0.04 mg/kg を等モルで単回皮下投与（5 mg 製剤の単回投与 1 回及び 10 mg 製剤の単回投与 2 回）
第 1 相試験（AGHD 患者）			
3947 試験（デンマーク、スウェーデン）	安全性、忍容性、薬物動態、薬力学的作用 無作為割り付け、反復投与、逐次用量漸増、非盲検、実薬（ノルディトロピン）対照 試験期間：4 週間	AGHD 患者 34 例 （25/9）、21–69 歳	ソマプシタン（0.02、0.04、0.08 及び 0.12 mg/kg） 週 1 回皮下投与

試験 ID （実施国）	試験デザイン及び試験期間	曝露被験者数 （男性／女性）、年齢	用法・用量 〔曝露期間（人・年；PYE） （AGHD 患者を対象とした試験のみ）〕
			〔0.4−0.5 PYE に相当（各用量群で 6−7 例づつ）、総曝露期間：1.8 PYE（26 例）〕 ノルディトロピン（試験前における用量） 1 日 1 回皮下投与 〔総曝露期間：0.6 PYE（8 例）〕
第 3 相試験（AGHD 患者）			
4054 試験 [a] （オーストラリア、ドイツ、インド、日本、ラトビア、リトアニア、マレーシア、ポーランド、ルーマニア、ロシア、南アフリカ、スウェーデン、トルコ、ウクライナ、英国、米国）	有効性及び安全性 34 週間の主要試験期間とそれに続く 52 週間の非盲検の延長期間 [f] で、ソマプシタンの週 1 回投与の有効性及び安全性をプラセボの週 1 回投与及びノルディトロピンの 1 日 1 回投与と比較する、無作為割り付け、並行群間、プラセボ対照（二重盲検）、実薬対照（非盲検、ノルディトロピン）試験 試験期間：88 週間（投与期間：86 週間）	hGH 製剤による治療歴がない AGHD 患者 300 例（日本人被験者 46 例） （145/155）、23−77 歳	主要試験期間 ソマプシタン及びプラセボ：週 1 回皮下投与 開始用量：年齢別に設定 [d] 用量調整：IGF-I SD スコアに基づき個別に実施 ノルディトロピン：1 日 1 回皮下投与 開始用量：年齢別に設定 [e] 用量調整：IGF-I SD スコアに基づき個別に実施 8 週間の用量調整期間＋26 週間の用量維持期間 延長期間 ソマプシタン：週 1 回皮下投与 ノルディトロピン：1 日 1 回皮下投与 8 週間の用量調整期間＋44 週間の用量維持期間 総試験期間 ソマプシタン平均投与量：0.040 mg/kg 総曝露期間：288.8 PYE ノルディトロピン平均投与量：0.005 mg/kg 総曝露期間：123.2 PYE
4043 試験 [a] （ドイツ、デンマーク、フランス、日本、スウェーデン、英国）	安全性 ソマプシタンの週 1 回投与及びノルディトロピンの 1 日 1 回投与の安全性を評価する、無作為割り付け、並行群間、非盲検、実薬対照（ノルディトロピン）試験 試験期間：27 週間（投与期間：26 週間）	GH 製剤で治療中の AGHD 患者 92 例（日本人被験者 17 例） （50/42）、19−77 歳	ソマプシタン：週 1 回皮下投与 開始用量：年齢別に設定 [d] 用量調整：IGF-I SD スコアに基づき個別に実施 平均投与量：0.027 mg/kg 総曝露期間：29.6 PYE ノルディトロピン：1 日 1 回皮下投与

試験 ID （実施国）	試験デザイン及び試験期間	曝露被験者数 （男性／女性）、年齢	用法・用量 〔曝露期間（人・年；PYE） （AGHD 患者を対象とした試験のみ）〕
			開始用量：年齢別に設定 [e] 用量調整：IGF-I SD スコアに基づき個別に実施 平均投与量：0.003 mg/kg 総曝露期間：14.6 PYE 8 週間の用量調整期間＋18 週間の用量維持期間
4244 試験 [a] （日本）	安全性及び有効性 ソマプシタンの週 1 回投与及びノルディトロピンの 1 日 1 回投与の安全性を評価する、無作為割り付け、並行群間、非盲検、実薬対照（ノルディトロピン）試験 試験期間：53 週間（投与期間：52 週間）	GH 製剤で治療中の日本人 AGHD 患者 62 例 （33/29）、20−75 歳	ソマプシタン：週 1 回皮下投与 開始用量：年齢別に設定 [d] 用量調整：IGF-I SD スコアに基づき個別に実施 平均投与量：0.029 mg/kg 総曝露期間：45.4 PYE ノルディトロピン：1 日 1 回皮下投与 開始用量：年齢別に設定 [e] 用量調整：IGF-I SD スコアに基づき個別に実施 平均投与量：0.003 mg/kg 総曝露期間：14.8 PYE 20 週間の用量調整期間＋32 週間の用量維持期間

[a] Trial includes Japanese subjects/patients.

[b] In trial 3915, Japanese passport and Japanese born parents was required for Japanese subjects; non-Asian born parents was required for Non-Asian subjects.

[c] In trial 4491, the number of male and female subjects and age range were based on 32 subjects who were exposed to all three treatments of somapacitan (Module 2.7.1.2).

[d] Somapacitan starting dose: patients between 23-60 years (trial 4054) or 18-60 years (trials 4043 and 4244) of age start at 1.5 mg/week; females on oral oestrogen irrespective of age start at 2.0 mg/week, and patients older than 60 years of age start at 1.0 mg/week.

[e] Norditropin starting dose: patients between 23-60 years (trial 4054) or 18-60 years (trials 4043 and 4244) of age start at 0.2 mg/day; females on oral oestrogen irrespective of age start at 0.3 mg/day; patients older than 60 years of age start at 0.1 mg/day.

[f] In the extension period, patients treated with somapacitan continued their once-weekly somapacitan treatment, patients treated with placebo were switched to somapacitan treatment and patients treated with Norditropin were re-randomised to continue Norditropin treatment or switch to somapacitan treatment.

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）
- 心電図
- 体重

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〔4054 試験（M 5.3.5.1）Section 8.5、4043 試験（M 5.3.5.1）Section 8.5、4244 試験（M 5.3.5.1）Section 8.4〕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〔4054 試験（M 5.3.5.1）Section 12.1～12.3、4043 試験（M 5.3.5.1）Section 12.1～12.3、4244 試験（M 5.3.5.1）Section 12.1～12.3〕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

特に注目すべき安全性領域を検討した。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 GH 製剤（ノルディトロピン等）と同様であることが予測されたため、特に注目すべき安全性領域には、臨床試験や公表文献で報告されている GH 製剤のクラスエフェクト及び副作用などを含めた（表 2.7.4.1-2）。

GH 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。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、GH 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障害又は糖尿病が現れることがある。そのため、耐糖能障害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（表 2.7.4.1-2）。

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 GH 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（4237 試験及び 4491 試験を除く）では、中和抗体を含めた、ソマプシタン又は GH 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。

表 2.7.4.1-2　　特に注目すべき安全性領域

評価した安全性領域	特に注目すべき安全性領域とした根拠（クラスエフェクト、他製剤の添付文書情報、臨床試験で観察された事象等）	MedDRA 検索式（SOC、SMQ 等）
内分泌障害		
甲状腺機能低下症	クラスエフェクト	SMQ 甲状腺機能低下症
副腎皮質機能不全	クラスエフェクト	HLT 副腎皮質機能低下
胃腸障害		
膵炎	クラスエフェクト（USPI）	SMQ 急性膵炎
一般・全身障害		
末梢性浮腫	クラスエフェクト	PT 末梢性浮腫 PT 末梢腫脹
疲労／無力症	Somapacitan trials[a]	HLT 無力症
体重増加	クラスエフェクト	PT 体重増加
免疫系障害		
アレルギー反応（非アナフィラキシー反応）	クラスエフェクト	SMQ 過敏症
過敏症（アナフィラキシー反応）	クラスエフェクト	SMQ アナフィラキシー反応
傷害、処置及び投与部位の状態		
注射部位反応	クラスエフェクト	HLT 注射部位反応
脂肪肥大症	Somapacitan trials[a]	PT 脂肪肥大症 PT 注射部位肥厚 PT 後天性リポジストロフィー
脂肪組織萎縮症	クラスエフェクト Somapacitan trials[a]	PT 脂肪組織萎縮症 PT 注射部位萎縮 PT 脂肪組織減少
臨床検査		
血中アルカリホスファターゼ増加（骨）	クラスエフェクト	PT 血中アルカリホスファターゼ増加
薬物特異性抗体陽性	Somapacitan trials[a]（小児）	HLT 免疫学的検査 NEC
代謝系障害		
高血糖	クラスエフェクト	HLT 高血糖 NEC HLT 炭水化物耐性検査（糖尿病を含む）
2 型糖尿病	クラスエフェクト	SMQ 高血糖／糖尿病の発症 PT 血中インスリン増加
筋骨格系障害		
関節痛	クラスエフェクト	PT 関節痛
筋肉痛	クラスエフェクト	PT 筋肉痛
側弯症	クラスエフェクト	PT 側弯症 PT 後側弯症
新生物		
新生物	クラスエフェクト	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）
神経系障害		

評価した安全性領域	特に注目すべき安全性領域とした根拠 （クラスエフェクト、他製剤の添付文書情報、臨床試験で観察された事象等）	MedDRA 検索式（SOC、SMQ 等）
頭痛	クラスエフェクト	HLT 頭痛 NEC
錯感覚	クラスエフェクト	PT 錯感覚
脳卒中	公表文献	SMQ 中枢神経系血管障害
手根管症候群	クラスエフェクト	PT 手根管症候群
良性頭蓋内圧亢進	クラスエフェクト	HLT 頭蓋内圧亢進性障害
その他		
まれな事象	N/A（当局の要求事項）	

Abbreviations: ECG = electrocardiogram; HLT = high level term; PT = preferred term; SOC = system organ class; SMQ = standard MedDRA queries; USPI = US Package Insert.

[a]somapacitan trials includes all completed clinical trials in adults and children.

ECG-related AEs (2.7.4.2.5.5) is not included in this table, because it was not considered as a “safety areas of interests” at the safety assessment period.

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した。

IGF-I

IGF-I 濃度が長期間にわたり生理的濃度の上限を超えると、安全性の懸念が生じる可能性があるため、標準的な診療として IGF-I 濃度を測定する必要がある。AGHD 患者を対象とした第 3 相試験（4054 試験、4043 試験及び 4244 試験）では、現在の AGHD 患者に対する実臨床と同様に、IGF-I 濃度が基準範囲内に維持されるよう、各被験者の用量を IGF-I SD スコアに基づいて調整した。

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[11]。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

FDA の助言及び各規制当局との協議の上（Module 2.5.3.7）、[redacted]、第 3 相試験でソマプシタン濃度が C_{max} に達すると予測される時点で心電図を測定した。

体重

これまでにも GH 製剤による治療で体重の増加と減少の両方が認められており、クラスエフェクトと考えられているため、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す。4054 試験では複数の治療（プラセボ、ノルディトロピン及びソマプシタン）を受けた被験者が存在するため、安全性データ（曝露及び有害事象のデータ）を治療別に示す（表 2.7.4.1-3）。第 3 相試験の各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。

2.7.4.1.2.3.2　併合データでの表示

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、AGHD 患者を対象とした第 3 相試験（4054 試験、4043 試験及び 4244 試験）から得られた曝露及び有害事象のデータを併合した。さらに、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。

第 3 相試験の併合データには、AGHD 患者の投与を受けた大部分のデータが含まれている。AGHD 患者を対象としたすべての第 3 相試験では、実臨床での使用に近い投与方法が用られた〔第 1 相試験における固定用量（mg/kg）に対し、各被験者の IGF-I 濃度に基づき用量調整〕。実際に投与を受けた薬剤に基づいて被験者を分類した。すなわち被験者をクロスオーバー試験と類似の考え方で取り扱った（たとえば、4054 試験で複数の治療を受けた被験者は、両方の投与群に寄与した）。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。

すべての第 3 相臨床試験は AGHD 患者を対象とし、臨床薬理試験は、3947 試験（AGHD 患者における安全性及び用量漸増試験）を除き、健康被験者及び特別な患者集団を対象とした。ソマプシタンの安全性プロファイルについて、hGH 製剤による治療歴のない AGHD 患者と治療中の AGHD 患者の間、あるいは日本人被験者と非日本人被験者の間で、明らかな違いはみられなかった（各第 3 相試験における安全性データに基づく）（図 2.7.4.2-1）。このことは、安全性データを併合することを支持するものである。

安全性データについて、以下の 2 つの異なる併合を行った。

- 安全性データの併合（調整なし）〔Pooled global data（Simple pooling）〕（当該併合によるデータを「第 3 相試験併合」とする）

- 安全性データの併合（調整あり）〔Norditropin/somapacitan pool（Cochran–Mantel–Haenszel（CMH）adjusted pooling）〕（当該併合によるデータを「ノルディトロピン/ソマプシタン併合」とする）

これらの 2 つの併合について、以下に詳細を述べる。

第 3 相試験併合

第 3 相試験併合における安全性解析対象集団は、第 3 相試験に組み入れられ、無作為割り付けされた治験薬の投与を少なくとも 1 回受けたすべての AGHD 患者からなる。併合した群のデータに含めた治療を表 2.7.4.1-3 に示す。

表 2.7.4.1-3　　併合した安全性データ（投与群別）（第 3 相試験併合）

Trial ID	Main trial	Extension	Providing data to the pooled treatment groups:		
Trial 4054	somapacitan	somapacitan			somapacitan
	Placebo	somapacitan	Placebo		somapacitan
	Norditropin	somapacitan		Norditropin	somapacitan
	Norditropin	Norditropin		Norditropin	
	Norditropin	NA		Norditropin	
Trial 4043	somapacitan	NA			somapacitan
	Norditropin	NA		Norditropin	
Trial 4244	somapacitan	NA			somapacitan
	Norditropin	NA		Norditropin	
Pooled treatment groups			Placebo	Norditropin	somapacitan

Abbreviations: NA = not applicable. In trial 4054, patients treated with somapacitan in the main phase continued their once-weekly somapacitan treatment, patients treated with placebo were switched to somapacitan treatment and patients treated with Norditropin were re-randomised to continue on Norditropin or switch to somapacitan treatment.

併合された被験者集団の投与群別の被験者の内訳及びベースライン特性は、4054 試験の主要試験期間終了後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、プラセボ/ソマプシタン群の被験者では、プラセボ群及びソマプシタン群のいずれの評価においてでも、ベースラインデータは同一である）。

ノルディトロピン/ソマプシタン併合

ソマプシタンの全体的な安全性評価を補足するため、調整を伴う安全性併合データの評価を行った。ノルディトロピン/ソマプシタン併合は、4054 試験のプラセボ群及び延長期間を除く、第 3 相試験で得られたデータ（4054 試験、4043 試験及び 4244 試験）からなる。併合データを用いてソマプシタンと 3 試験で共通の対照薬（ノルディトロピン）を比較するにあたって、上述のように併合対象のデー

タを限定することで、試験効果を調整するための標準的な方法を用いることが可能となる。ノルディトロピン/ソマプシタン併合に基づく、有害事象の単位時間あたりの発現件数（100 人・年あたりの発現件数）及び有害事象を 1 件以上発現した被験者の割合は、選択した有害事象について CMH の重み付け法を用いて調整した。

2 つの安全性データの併合の概要を表 2.7.4.1-4 に示す。

ノルディトロピン/ソマプシタン併合データでは、安全性データ（有害事象）の一部について、有害事象を発現した被験者の割合及び単位時間あたりの発現件数を、調整の有無で比較した。

表 2.7.4.1-4　　AGHD 患者を対象とした第 3 相試験の併合の概要

Trial ID (duration incl. wash-out)	**Number of exposed patients** (randomisation ratio)	**Trial population AGHD patients**	**Dose titration (IGF-I SDS)**			**Pooled global data (Simple pooling)**	**Norditropin/ somapacitan pool (CMH adjusted pooling)**
Trial 4054 (35 weeks +53 weeks extension)	N=300 (2:2:1) (in main phase)	Treatment naïve	somapacitan	Norditropin	placebo	X	X Only main phase, somapacitan and Norditropin arms
Trial 4043 (27 weeks)	N=92 (2:1)	Previously GH treated	somapacitan	Norditropin	NA	X	X
Trial 4244 (53 weeks)	N=62 (3:1)	Previously GH treated	somapacitan	Norditropin	NA	X	X

Abbreviations: AGHD = adult growth hormone deficiency; CMH = Cochran-Mantel-Haenszel; IGF-I SDS = insulin-like growth factor I standard deviation score; GH = growth hormone; NA = not applicable.

2.7.4.1.2.3.3　　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、国際医薬用語集（MedDRA）（ver. 16.0～22.0）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。併合データ、及び本申請で試験別に作成したデータの一部では、MedDRA ver. 21.0 を用いた。

有害事象及び重篤な有害事象の記述及び評価は、有害事象を発現した被験者の割合、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を用いて適切に、重症度、有害事象の種類、治験薬との因果関係及び転帰に主眼を置いて行った。

有害事象のデータは試験別に提示する。4054 試験では複数の治療（プラセボ、ノルディトロピン及びソマプシタン）を受けた被験者が存在するため、安全性データ（曝露及び有害事象のデータ）を治療別に示す（表 2.7.4.1-3）。さらに、AGHD 患者を対象とした第 3 相試験（4054 試験、4043 試験及び 4244 試験）から得られた有害事象のデータを併合して提示する。併合の手法は 2.7.4.1.2.3.2 に記載した。

国際共同試験の 4054 試験及び 4043 試験では、安全性について日本人集団と全集団での一貫性を評価するため、試験ごとに日本人集団と全集団の有害事象を提示した。両集団間の安全性の一貫性の検討は、記述統計量に基づいて実施した。当該評価に関連する図表を付録 2.7.4.7.2 に含めた。

特に注目すべき安全性領域（表 2.7.4.1-2 参照）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。MedDRA 標準検索式（SMQ）を用いて各第 3 相試験（4054 試験、4043 試験及び 4244 試験）で該当する有害事象を検索し、試験別に提示した。また、SMQ による検索は、第 3 相試験併合及びノルディトロピン/ソマプシタン併合（第 3 相試験の 4054 試験、4043 試験及び 4244 試験）でも行った。適切な SMQ がない場合は、関連する基本語（PT）又は高位語（HLT）に基づいて特定の MedDRA 検索式を構築した。事象の特定に用いた具体的な MedDRA 検索語を付録 2.7.4.7.1、Listing 111～136 に示した。

ソマプシタンの CCDS に含めた adverse drug reaction の評価は、生物学的妥当性、及びソマプシタンと有害事象との因果関係に合理的な可能性がある副作用を特定するための詳細な医学評価に基づいている。

死亡、その他の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／試験の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）。

2.7.4.1.2.3.4　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。

2.7.4.1.2.3.5　IGF-I SD スコア

年齢及び性別における正常な集団の値[12]に基づいて IGF-I SD スコアを算出した。

用量維持期間に IGF-I SD スコアが+2 超（1 回以上）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。

2.7.4.1.2.3.6　バイタルサイン、心電図及び体重

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、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）。

血圧及び脈拍数については、ベースラインからの変化量を検討した。

心電図については、FDA の助言及び各規制当局との協議の上（Module 2.5.3.7）、[redacted]、第 3 相試験でソマプシタン濃度が C_{max} に達すると予測される時点で心電図を測定した。C_{max} 時点の潜在的な QTc 間隔延長を評価するため、4054 試験の心電図データに対し QTc 間隔の絶対値の複数のカットオフ値（450 msec 超、480 msec 超及び 500 msec 超）[13]を用いた。500 msec 超の QTc 間隔延長が、特に懸念されるカットオフ値である。Bazett の補正式は成人において適切でないため、Fridericia の補正式（以下、QTcF）を適用した。

体重については、ベースラインからの変化量を検討した。

2.7.4.1.2.4　安全性データ及び試験の分類

2.7.4.1.2.4.1　安全性データの提示順序

本臨床概要では、以下の順序で安全性データを提示する。

- 第 3 相試験の結果（試験別）
- 第 3 相試験併合及びノルディトロピン/ソマプシタン併合の結果
- 日本人被験者の結果を含む第 3 相試験の結果（試験別）
- 臨床薬理試験（健康被験者を対象としたヒトへの初回投与試験、AME 試験及び生物学的同等性試験、AGHD 患者を対象とした用量探索試験、ならびに特別な患者集団を対象とした試験）

2.7.4.1.2.4.2　試験別での提示

安全性データを試験別に示す。

2.7.4.1.2.4.3　併合データでの表示

第 3 相試験併合に基づく結果（有害事象）を本文中に提示し、その後にノルディトロピン/ソマプシタン併合（調整あり）から得られた結果及び結論に基づく要約を示す。

2.7.4.1.2.4.4　日本人被験者における安全性

「国際共同治験に関する基本的考え方」のガイダンス[14]に従い（及び独立行政法人 医薬品医療機器総合機構の助言に基づき）、日本人集団と全集団との一貫性の評価を試験ごと〔4054 試験（主要試験期間）及び 4043 試験〕に実施した。安全性の結果に日本人集団と全集団で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は適切であると考えられる。

安全性について日本人集団と全集団で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）を試験ごとに要約し、全集団と比較した。日本人被験者は、日本国内の施設で組み入れられた被験者と定義した。

2.7.4.1.2.4.5　臨床薬理試験

臨床薬理試験においては、試験ごとに対象集団（健康被験者、腎機能障害を有する被験者、肝機能障害を有する被験者、AGHD 患者）、試験デザイン〔単回投与及び反復投与、体重当たりの用量（mg/kg）〕及び試験期間（4～約 10 週間）が異なるため、これら臨床薬理試験より得られた安全性データは試験別に提示する。このことから、臨床薬理試験から得られた安全性データを、第 3 相試験のデータと併合することは適切ではないと考えられる。臨床薬理試験における、関連する安全性データは各治験総括報告書に基づく。

2.7.4.1.2.5　部分集団における安全性

ICH M4E ガイドライン[15]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（男性又は女性）
- 年齢（65 歳未満又は 65 歳以上）
- GHD 発症型（小児期又は成人期発症）

これらの部分集団における安全性を検討するため、第 3 相試験の併合データに基づく有害事象の要約表を示した。

年齢による分類に際し、推奨される年齢分類の 65～74 歳及び 75～84 歳のグループでは被験者数が少なく評価が困難であるため、65 歳以上の 1 つの年齢グループとして統合した。77 歳超の被験者はいなかった（85 歳以上の年齢グループは該当なし）。

第 3 相試験に組み入れられた糖尿病患者は 17 例のみであったため、糖尿病患者の部分集団での検討は行わなかった（表 2.7.4.1-17）。

部分集団別の有害事象を 2.7.4.5.1 に示す。

2.7.4.1.2.6　重要な安全性に関する考察

2.7.4.1.2.6.1　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、Module 2.4 を参照のこと。

2.7.4.1.2.6.2　GH の薬理的なクラスエフェクト

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 GH 製剤（ノルディトロピン等）と同様であることが予測された。詳細については、ノルディトロピンの添付文書の情報〔ノルディトロピンの Summary of Product Characteristics[8]、米国添付文書[16]又は国内添付文書[17]〕を参照のこと。

したがって、特に注目すべき安全性領域に含まれる主な項目は、GH 製剤のクラスエフェクト、注射部位反応及び抗体産生とした。特に注目すべき安全性領域については表 2.7.4.1-2 に示した。

2.7.4.1.2.7　小児 GHD 患者における安全性

小児の GHD 患者を対象として 2 つの臨床試験（4042 試験及び 4172 試験）を実施している。試験デザイン、用法・用量及び対照薬の概要を表 2.7.4.1-5 に示す。4042 試験は完了し、4172 試験は進行中である（[redacted]）。

表 2.7.4.1-5　小児 GHD 患者を対象とした臨床試験

試験 ID（実施国） Status	試験デザイン及び試験期間	曝露被験者数（男性／女性）、年齢	用法・用量及び曝露期間（PYE）
第 1 相試験（小児 GHD 患者）			
4042 試験 （オーストリア、ベルギー、フランス、イスラエル、マケドニア、スロベ二ア、スペイン、スウェーデン） 完了	安全性、忍容性、薬物動態、薬力学的作用 無作為割り付け、実薬対照（ノルディトロピン）、単回投与、用量漸増 試験期間：1 週間	小児 GHD 患者 32 例 （23/9） 6.0−11.0 歳	ソマプシタン単回皮下投与 4 コホート（1 コホート 6 例、計 24 例） （0.02、0.04、0.08 及び 0.16 mg/kg） 曝露期間：0.4 PYE. ノルディトロピン 7 日間 1 日 1 回皮下投与（1 コホート 2 例、計 8 例） 0.03 mg/kg 曝露期間：0.2 PYE
第 2 相試験（小児 GHD 患者）			
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、スロベ二ア、スウェーデン、トルコ、ウクライナ、米国） 進行中 （最後の被験者の予定最終来院：[redacted]）	有効性、安全性、用量設定 無作為割り付け、非盲検、実薬対照（ノルディトロピン） 52 週 [a]＋104 週（安全性延長期間）＋208 週（長期安全性延長期間） 試験期間（合計）：364 週間又は 7 年以上	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（日本人被験者 [redacted]例） （選択基準に抵触した 2 例は最大の解析対象集団に含めなかったため 57 例を最大の解析対象集団とした） （34/23） 2.8 −9.8 歳	ソマプシタン週 1 回皮下投与 26 週間（主要試験期間）＋26 週間（延長期間）：0.04、0.08 又は 0.16 mg/kg/週 安全性延長期間及び長期安全性延長期間：0.16 mg/kg/週 ノルディトロピン 1 日 1 回皮下投与 0.034 mg/kg/日

Abbreviations: GH = growth hormone; GHD = growth hormone deficiency; PYE = patient years of exposure;

[a]Once-weekly somapacitan treatment for more than 7 years exposure of somapacitan is planned (26-week main phase + 26-week extension + 104-week safety extension + 208 weeks long-term safety extension). When the children have completed the initial 52 weeks treatment, somapacitan treated children are re-allocated to somapacitan 0.16 mg/kg/ week. Norditropin treated children continue the treatment with Norditropin 0.034 mg/kg/day. After 156 weeks all children on Norditropin are switched to somapacitan 0.16 mg/kg/week. The 26-week main phase has been reported.

小児 GHD 患者へのソマプシタン皮下投与の忍容性は、検討したすべての用量で良好であり、臨床的に問題となる安全性又は局所忍容性の新たな問題は特定されなかった。

小児患者を対象とした臨床開発プログラムにおける、重篤な有害事象及び治験薬投与の中止に至った有害事象の要約表及び叙述を以下に示す。小児患者を対象とした臨床開発プログラムでは、死亡は報告されていない。

4042 試験

4042 試験では、死亡、重篤な有害事象及び試験の中止に至った有害事象は報告されなかった。

4172 試験

4172 試験は進行中であり、死亡は報告されていない。

当該試験では、現時点において 5 例 10 件の重篤な有害事象（軽度又は中等度の重篤な有害事象 9 件及び重度の重篤な有害事象 1 件）が報告されている（表 2.7.4.1-7）。10 件中 8 件の重篤な有害事象では、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。2 件の重篤な有害事象（1 例で報告された「全身性浮腫」及び「嘔吐」）について、治験薬との因果関係は「あり」と判定された（主要試験期間：ソマプシタン 0.16 mg/kg/週群）。この被験者は、「全身性浮腫」及び「嘔吐」の発現後、ソマプシタンの投与を一時中断した。これらの有害事象の説明として全身性の感染があげられており、当該評価は妥当なものと考えられた。

[redacted]歳の[redacted]小児 GHD 患者が「アナフィラキシー反応」を発現した。本事象の発現時、当該被験者は、治験薬投与（ソマプシタン、用量は盲検下）を約 2 年間（682 日間）受けていた。当該被験者は、チョコレートを摂取した後に皮疹及び喘鳴を発現した。この被験者は食物アレルギーを有しており、入院治療を受け、その翌日には改善がみられ退院した。治験薬の投与に関する変更はなく、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。

4172 試験の現時点で報告された重篤な有害事象の叙述一覧を付録 2.7.4.7.3 に示した。

2 例が治験薬投与を中止したが、いずれもノルディトロピン群の被験者であった。表 2.7.4.1-6 に一覧を示す。ソマプシタン群では、治験薬投与を中止した被験者はいなかった。

表 2.7.4.1-6　　小児 GHD 患者における治験薬の投与中止に至った有害事象（4172 試験）

Phase	Treatment[a]	Subject ID	Preferred term	AE onset (study day)	Severity	Serious	Causality	Outcome
Main	Norditropin	651004	過敏症	45	Mild	No	Probably	Not recovered
Extension	Norditropin	750002	ネフローゼ症候群	366	Moderate	Yes	Unlikely	Not recovered

[a] Norditropin was dosed daily (0.034 mg/kg/day).

4172 試験は進行中であり、安全性データのカットオフ日を 2019 年 5 月 7 日とした。

表 2.7.4.1-7　　小児 GHD 患者で報告された重篤な有害事象（4172 試験、進行中）

Trial/ Phase	Treatment[a]	Subject ID	Preferred term	AE onset (study day)/Duration/ Period	Severity	Causality	Outcome	Case number
Trial 4172 (ongoing)	somapacitan	551005	全身性浮腫	3/9 days/ Main	Moderate	Probably	Recovered	543799
			嘔吐	4/3 days/ Main	Moderate	Probably	Recovered	543799
			扁桃炎	366/10 days/ Extension	Moderate	Unlikely	Recovered	598447
	somapacitan	603001	下垂体機能低下症	96/NA/ Main	Mild	Unlikely	Not recovered Chronic condition	539071
			胃腸炎	310/2 days/ Extension	Moderate	Unlikely	Recovered	532603
			胃腸炎	682/2 days/ Extension	Moderate	Unlikely	Recovered	587806
	Norditropin	702001	アデノイド切除	381/1 day/ Extension	Severe	Unlikely	Recovered	545308
	somapacitan	750001	アナフィラキシー反応	683/2 days/ Extension	Moderate	Unlikely	Recovered	619784
	Norditropin	750002	RS ウイルス気管支炎	290/12 days/ Extension	Moderate	Unlikely	Recovered	564514
			ネフローゼ症候群	366/NA/ Extension	Moderate	Unlikely	Not recovered Drug withdrawn	575590

[a] somapacitan was dosed once-weekly (0.04, 0.08 or 0.16 mg/kg/week). Somapacitan dose-levels are blinded in the ongoing extension trial.
Norditropin was dosed daily (0.034 mg/kg/day).

2.7.4.1.3 全般的な曝露状況

2.7.4.1.3.1 曝露

2.7.4.1.3.1.1 AGHD 患者を対象とした第 3 相試験の結果（試験別）

完了した第 3 相試験でソマプシタンの投与を受けた AGHD 患者の被験者数〔曝露期間（人・年、PYE）を含む〕を試験別に表 2.7.4.1-8 に要約する。4054 試験では、AGHD 患者を対象とした 86 週までのソマプシタンの曝露を評価した。4244 試験では 52 週までの曝露、4043 試験では 26 週までの曝露を評価した。4054 試験の投与群別の曝露を表 2.7.4.1-9 に要約する。

IGF-I SD スコアに基づく用量調整後、ソマプシタンの平均用量は 4054 試験（総試験期間）で 2.59 mg/週、4043 試験で 2.06 mg/週、4244 試験で 1.78 mg/週であった。ソマプシタンの開始用量は、23～60 歳（4054 試験）又は 18～60 歳（4043 試験及び 4244 試験）の被験者で 1.5 mg/週とした。経口エストロゲンを投与している女性被験者の開始用量は年齢によらず 2.0 mg/週とし、60 歳超の被験者の開始用量は 1.0 mg/週とした。

IGF-I SD スコアに基づく用量調整後、ノルディトロピンの平均用量は 4054 試験で 0.33 mg/日、4043 試験で 0.20 mg/日、4244 試験で 0.20 mg/日であった〔開始用量は 23～60 歳（4054 試験）又は 18～60 歳（4043 試験及び 4244 試験）の被験者で 0.2 mg/日、経口エストロゲンを投与している女性被験者で 0.3 mg/日、60 歳超の被験者で 0.1 mg/日とした〕。

AGHD 患者 61 例がプラセボの投与を受けた（4054 試験の主要試験期間内）。

表 2.7.4.1-8 AGHD 患者における平均投与量及び曝露期間（PYE）（試験別、投与群別）（4054 試験、4043 試験及び 4244 試験）

	Placebo			**somapacitan**			**Norditropin**		
Phase 3 (trial IDs)	n	mean mg/week	PYE	n	mean mg/week	PYE	n	mean mg/day	PYE
Trial 4054	61	2.20 (0.034 mg/kg/week)	38.2	226	2.59 (0.040 mg/kg/week)	288.8	119	0.33 (0.035 mg/kg/week)[a]	123.2
Trial 4043	.	.	.	61	2.06 (0.027 mg/kg/week)	29.6	31	0.20 (0.021 mg/kg/week)[b]	14.6
Trial 4244	.	.	.	46	1.78 (0.029 mg/kg/week)	45.4	16	0.20 (0.021 mg/kg/week)[b]	14.8
Total patients	61	.	38.2	333	.	363.7	166	.	152.6

Abbreviations: AGHD = adult growth hormone deficiency; '.' = not applicable; n = number of patients; PYE= patient years of exposure; Individual IGF-I dose titration. Norditropin = Norditropin FlexPro.

[a] Norditropin 0.005 mg/kg/day. [b] Norditropin 0.003 mg/kg/day.

表 2.7.4.1-9　AGHD 患者における投与群別の曝露期間（4054 試験、主要試験期間及び主要試験期間＋延長期間）

Split by treatment in main	Placebo		Somapacitan		Norditropin	
	n	PYE	n	PYE	n	PYE
Trial 4054 main	61	38.2	120	76.2	119	73.5

Split by treatment arm in main and extension	Placebo/ somapacitan		Somapacitan/ somapacitan		Norditropin/ Norditropin		Norditropin/ somapacitan		Norditropin/-	
	n	PYE	n	PYE	n	PYE	n	PYE	n	PYE
Trial 4054 main (patients)	61	38.2	120	76.2	52	33.9	51	33.2	16	6.3
Trial 4054 ext (patients)	55	53.7	114	110.9	52	49.7	51	47.9	0	.

Abbreviations: AGHD = adult growth hormone deficiency; '.' = not applicable; PYE= patient years of exposure; Individual IGF-I dose titration. Norditropin = Norditropin FlexPro. The treatment in the main/extension periods of the trial is indicated by e.g. somapacitan/somapacitan. The treatment group 'Norditropin/−' includes patients who did not participate in the extension trial and hence were not re-randomised.

試験別の曝露の詳細を治験総括報告書〔4054 試験（M 5.3.5.1）Section 10.3.1、4043 試験（M 5.3.5.1）Section 12.1、4244 試験（M 5.3.5.1）Section 10.3.1〕に示す。試験デザインの詳細は Module 2.7.6 に提示した。

2.7.4.1.3.1.2　AGHD 患者を対象とした第 3 相試験の結果（第 3 相試験併合）

第 3 相試験併合データに基づく、AGHD 患者におけるソマプシタンの曝露の要約を表 2.7.4.1-10 に示す。

完了した AGHD 患者を対象とした臨床試験では、AGHD 患者 333 例にソマプシタンを投与した。AGHD 患者を対象としたソマプシタンの 86 週までの曝露を評価した。IGF-I SD スコアに基づく用量調整後、ソマプシタンの平均投与量は 2.38 mg/週（0.036 mg/kg/週）であった。開始用量は 2.7.4.1.3.1.1 を参照のこと。

完了した AGHD 患者を対象とした臨床試験では、AGHD 患者 166 例に実薬対照としてノルディトロピンを 1 日 1 回投与した（86 週までの曝露）。ノルディトロピンの平均投与量は 0.29 mg/日（0.005 mg/kg/日）であった。

AGHD 患者 61 例がプラセボの投与を受けた。

総曝露期間はソマプシタン群が 363.7 人・年、ノルディトロピン群が 152.6 人・年、プラセボ群が 38.2 人・年であった。4054 試験では、プラセボ群の被験者及びノルディトロピン群の一部の被験者が主要試験期間終了後にソマプシタンの投与に切り替えたため、この 2 群での曝露期間は短くなった。

表 2.7.4.1-10　AGHD 患者における曝露（第 3 相試験併合）

	placebo	Norditropin	somapacitan
	once-weekly	daily	once-weekly
Number of exposed subjects	61	166	333
Days of exposure*			
Mean (SD)	228 (36.1)	336 (184.3)	399 (165.2)
Median	238	238	364
Min; Max	28; 252	1; 619	7; 623
Treatment dose** (mg)			
Mean (SD)	2.20 (0.74)	0.29 (0.19)	2.38 (1.46)
Median	2.00	0.25	2.00
Min; Max	1.00; 3.50	0.05; 1.10	0.10; 8.00
Treatment dose** (mg/kg)			
Mean (SD)	0.034 (0.016)	0.005 (0.004)	0.036 (0.027)
Median	0.032	0.003	0.027
Min; Max	0.014; 0.080	0.001; 0.044	0.001; 0.171
Total Exposure*** (years)	38.2	152.6	363.7

SD: Standard deviation;
* Exposure days are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan.
** Stable dose at last titration visit. For subjects in 4054 receiving same treatment in main and extension period, only first titration period is included.
*** Including titration period.

ソマプシタンの臨床開発プログラムを通して、319 例（95.8%）にソマプシタンを 6 ヵ月超投与し、253 例（76.0%）に 12 ヵ月超、109 例（32.7%）に 18 ヵ月超投与した（表 2.7.4.1-11）。

表 2.7.4.1-11　AGHD 患者における 3 ヵ月ごとの曝露（第 3 相試験併合）

	placebo N (%)	Norditropin N (%)	somapacitan N (%)
Number of subjects	61	166	333
Exposure period			
>0 months	61 (100.0)	166 (100.0)	333 (100.0)
>3 months	60 (98.4)	158 (95.2)	326 (97.9)
>6 months	55 (90.2)	151 (91.0)	319 (95.8)
>9 months	0	67 (40.4)	257 (77.2)
>12 months	0	66 (39.8)	253 (76.0)
>15 months	0	50 (30.1)	110 (33.0)
>18 months	0	47 (28.3)	109 (32.7)

N: Number of subjects, %: Percentage of subjects.
Subjects from 4054 switching treatment after main trial period are included for each treatment.
Exposure to placebo was only done in 4054 and for no more than 35 weeks. Month = 30 days.

治療遵守率はいずれの投与群でも高かった（ソマプシタン群：98.2%、ノルディトロピン群：96.8%、プラセボ群：98.2%）（表 2.7.4.1-12）。

表 2.7.4.1-12　　AGHD 患者における治療遵守率（第 3 相試験併合）

	placebo	Norditropin	somapacitan
Number of exposed subjects	61	166	333
Number of reported dosings	1954	53644	18708
Adherence according to diary*			
Mean (SD)	93.8 (16.6)	89.6 (23.3)	94.6 (17.2)
Median	100.0	99.2	100.0
Min; Max	11.8; 100.0	0.4; 100.0	2.9; 100.0
Adherence according to diary* for subjects completing treatment period			
Mean (SD)	98.2 (7.8)	96.8 (8.5)	98.2 (8.0)
Median	100.0	99.5	100.0
Min; Max	42.9; 100.0	22.2; 100.0	11.1; 100.0

* Number of reported dosings from diary and observed dosing visits divided by number of planned dosings multiplied by 100.

2.7.4.1.3.1.3　　AGHD 患者を対象とした第 3 相試験の結果（ノルディトロピン/ソマプシタン併合）

ノルディトロピン/ソマプシタン併合についても曝露を算出した。ソマプシタンの平均投与量は 2.26 mg/週（0.033 mg/kg）であり、第 3 相試験併合における平均投与量と同様であった。本併合では、AGHD 患者 227 例がソマプシタンの投与を受け、166 例がノルディトロピンの投与を受けた。総曝露期間はソマプシタンが 151.2 人・年、ノルディトロピンが 102.9 人・年であった。ノルディトロピン/ソマプシタン併合の曝露の要約を付録 2.7.4.7.1、Table 103 に示す。

2.7.4.1.3.1.4　　日本人被験者の結果を含む AGHD 患者を対象とした第 3 相試験の結果

日本人 AGHD 患者における曝露を試験別に要約する。国際共同試験（4054 試験及び 4043 試験）については、日本人集団における曝露と全集団における曝露（4054 試験及び 4043 試験）を要約する（各試験の要約表の参照先も併せて示す）。4244 試験（日本人被験者）における曝露の要約を表 2.7.4.1-8 に示す。

第 3 相試験では、日本人 AGHD 患者 93 例にソマプシタンを投与し（4054 試験：36 例、4043 試験：11 例、4244 試験：46 例）、日本人 AGHD 患者 40 例にノルディトロピンを投与した（4054 試験：18 例、4043 試験：6 例、4244 試験：16 例）。

被験者 79 例（84.9%）にソマプシタンを 12 ヵ月超投与し、18 例（19.4%）に 18 ヵ月超投与した。3 ヵ月ごとの曝露の要約を付録 2.7.4.7.2、Table 10 に示す。

4054 試験

4054 試験では、日本人 AGHD 患者 36 例にソマプシタンを投与し、総曝露期間は 46.7 人・年であった（プラセボ及びノルディトロピンから切り替えた被験者を含む）。ソマプシタンの平均曝露日数は日本人集団〔ソマプシタン/ソマプシタン群の平均曝露日数（標準偏差）：602（0.2）日〕と全集団

〔ソマプシタン/ソマプシタン群の平均曝露日数（標準偏差）：569（122）日〕で同様であった。ソマプシタンの平均投与量は、日本人集団〔平均の範囲：1.58～2.04 mg/週（0.028～0.036 mg/kg/週）〕の方が全集団〔平均の範囲：2.35～2.66 mg/週（0.034～0.043 mg/kg/週）〕よりもやや少なかったが、平均投与量を mg/kg/週で算出した場合には、日本人集団と第 3 相試験併合の被験者集団（2.38 mg/週、0.036 mg/kg/週）で同様であった。

日本人集団におけるノルディトロピン（ノルディトロピン/ノルディトロピン群）の平均投与量は、mg/日で算出した場合（主要試験期間：0.23 mg/日、延長期間：0.19 mg/日）では、全集団（主要試験期間：0.31 mg/日、延長期間：0.28 mg/日）と比較して少なかったが、mg/kg/日で算出した場合には同様であった（日本人集団：主要試験期間：0.004 mg/kg/日、延長期間：0.003 mg/kg/日、全集団：主要試験期間及び延長期間：0.004 mg/kg/日）。

日本人集団及び全集団における曝露を付録 2.7.4.7.2、Table 1（主要試験期間）及び 3（延長期間）（全集団）、Table 2（主要試験期間）及び 4（延長期間）（日本人集団）に要約する。

4054 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。

4043 試験

4043 試験では、日本人 AGHD 患者 11 例にソマプシタンを投与し、総曝露期間は 5.4 人・年であった。ソマプシタンの平均曝露日数（標準偏差）は日本人集団〔179（10.6）日〕と全集団〔177（28.6）日〕で同様であった。ソマプシタンの平均投与量は日本人集団（2.47 mg/週、0.038 mg/kg/週）の方が全集団（2.06 mg/週、0.027 mg/kg/週）よりもやや多かったが、第 3 相試験併合の被験者集団（2.38 mg/週、0.036 mg/kg/週）と同様であった。

ノルディトロピンの平均投与量は日本人集団で 0.13 mg/日（0.002 mg/kg/日）、全集団で 0.20 mg/日（0.003 mg/kg/日）であった。日本人集団及び全集団における曝露の要約を付録 2.7.4.7.2、Table 5（全集団）及び 6（日本人集団）に示す。

4043 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。

4244 試験

4244 試験では、日本人 AGHD 患者 46 例にソマプシタンを投与し、総曝露期間は 45.4 人・年であり、ソマプシタンの平均投与量は 1.78 mg/週（0.029 mg/kg/週）であった。

日本人 AGHD 患者 16 例にノルディトロピンを投与した。総曝露期間は 14.8 人・年であり、ノルディトロピンの平均投与量（1 日当たり）は 0.20 mg/日（0.003 mg/kg/日）であった。平均曝露日数（標準偏差）はソマプシタン〔360（25.8）日〕とノルディトロピン〔339（75.4）日〕で同様であった。

4244 試験の曝露の要約を治験総括報告書〔4244 試験（M 5.3.5.1）EOT Table 14.2.1〕に示す。

2.7.4.1.3.1.5　臨床薬理試験の結果

健康被験者、特別な患者集団及び AGHD 患者における曝露を試験別に表 2.7.4.1-13 に要約する。試験別の曝露の詳細は各試験の治験総括報告書に示す。試験デザインの詳細は Module 2.7.6 に提示した。

成人被験者を対象とする完了した臨床薬理試験では、健康被験者 150 例〔79 例（3915 試験）＋7 例（4237 試験）＋15 例（4297 試験）＋16 例（4298 試験）＋33 例（4491 試験）〕、腎機能障害を有する被験者 29 例（4297 試験）、肝機能障害を有する被験者 18 例（4298 試験）、AGHD 患者 26 例（3947 試験、第 1 相用量探索試験）にソマプシタンを投与した（表 2.7.4.1-13）。臨床薬理試験では、健康被験者（約 4 週間の曝露）及び特別な患者集団（約 3 週間の曝露）を対象としてソマプシタンを単回投与及び反復投与し、評価した。3915 試験の反復投与パートでは日本人健康被験者 24 例にソマプシタンを投与した。

表 2.7.4.1-13　臨床薬理試験における曝露

Trial ID	Population	Dose/duration	Placebo	Somapacitan	Total
Phase 1			n	n	n
Trial 3915	Healthy non-Asian	Somapacitan SD 0.01, 0.04, 0.08, 0.16 and 0.32 mg/kg	10	30	40
	Healthy non-Asian	Somapacitan MD 0.02, 0.08, 0.16, 0.24 mg/kg for 4 weeks	8	25	33
	Healthy Japanese	Somapacitan MD 0.02, 0.08, 0.16, 0.24 mg/kg for 4 weeks	8	24	32
Trial 4297	Healthy subjects	Somapacitan MD 0.08 mg/kg/week for 6 weeks		15	.
Trial 4298	Healthy subjects	Somapacitan MD 0.08 mg/kg/week for 6 weeks		16	.
Trial 4237	Healthy subjects (AME)	SD 6 mg [3H]-somapacitan up to 20 MBq	NA	7	.
Trial 4491	Healthy subjects	Somapacitan SD, equimolar doses of 0.04 mg/kg Two strengths: 5 mg/1.5 mL (one SD) and 10 mg/1.5 mL (two SDs)	NA	33	
Total	Healthy subjects		26	150	176
Trial 4297	Renal impaired	Somapacitan MD 0.08 mg/kg/week for 6 weeks	NA	29	.
Trial 4298	Hepatic impaired	Somapacitan MD 0.08 mg/kg/week for 6 weeks	NA	18	.

Trial ID	Population	Dose/duration	Placebo	Somapacitan	Total
Trial 3947	AGHD patients	Somapacitan MD 0.02, 0.04, 0.08 and 0.12 mg/kg for 4 weeks. Mean days of exposure: 25-27 days (range: 7-28 days). Norditropin MD	8 (0.6 PYE)	26 (1.8 PYE)	34

Abbreviations: AME = administration, metabolism and excretion; n = number of subjects/patients; NA = not applicable; MD = multiple-dose; PYE = patient years of exposure; SD = single dose. Dose–escalation was applied.

ソマプシタンは週 1 回皮下投与した。4237 試験（AME）以外の臨床薬理試験では、体重に基づく用量を適用した。臨床試験に用いた用量範囲を表 2.7.4.1-14 に示す。第 1 相用量探索試験（3915 試験及び 3947 試験）では用量レベルを変更した（2.7.4.1.3.3 参照）。

表 2.7.4.1-14　　ソマプシタンの単回投与及び反復投与時の用量範囲

Population	Single-dose range (mg/kg)	Multiple-dose range[a] (mg/kg)
Healthy subjects	0.01, 0.04, 0.08, 0.16 and 0.32 mg/kg	0.02, 0.08, 0.16 and 0.24 mg/kg
AGHD patients	NA	0.02, 0.04, 0.08 and 0.12 mg/kg

Abbreviations: AGHD = adult growth hormone deficiency. NA = not applicable.
[a]Multiple-dose in healthy subjects and AGHD patients: Somapacitan was dosed with intervals of 1 week at each of the 4 dose levels.

2.7.4.1.3.2　　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（健康被験者及び患者）の数を試験別に表 2.7.4.1-15 に示す。

第 3 相試験では、ソマプシタンの投与を受けた AGHD 患者での中止・脱落例の割合は、4054 試験（試験期間ごとに算出した場合）及び 4043 試験では 4.5～5.8%であったが、4244 試験（国内試験）では中止・脱落例の割合が低く、2.2%であった。国際共同試験（4054 試験及び 4043 試験）ではノルディトロピンの投与を受けた AGHD 患者での中止・脱落例の割合が高く、9.7～13.5%であった。ソマプシタンの投与を受けた被験者のうち、計 20 例が試験を中止・脱落し、7 例が有害事象のために治験薬投与を中止した。ノルディトロピンの投与を受けた被験者のうち、計 25 例が試験を中止・脱落し、6 例が有害事象のために治験薬投与を中止した。試験の中止に至った有害事象を 2.7.4.2.4.1 に示す。

第 1 相試験では、ソマプシタンの投与を受けた健康被験者（3915 試験）での中止・脱落例の割合は 3.8%であり、プラセボの投与を受けた被験者では 0%であった。4491 試験では、33 例中 1 例（3.0%）が試験を中止・脱落した。AGHD 患者を対象とした用量探索試験（3947 試験）では、中止・脱落例の割合は 15.4%であった〔被験者数が少なかったことに留意する必要がある（26 例中 4 例）〕。第 1 相試験では、ソマプシタンの投与後に 11 例、ノルディトロピンの投与後に 1 例が試験を中止・脱落した。第 1 相試験では 4 例が有害事象のために試験を中止した。

表 2.7.4.1-15　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要約

Trial ID	Number (%) of subjects/patients withdrawn of total randomised	Reason for withdrawal	Discontinued trial product
Phase 3			
Trial 4043	somapacitan: 3 of 61 (4.9%)	AEs: asthenia and disturbance in attention (1 patient). Personal reasons (2 patients) (1 JP)	
	Norditropin: 3 of 31 (9.7%)	AE: asthenia, somnolence, disturbance in attention, headache (1 patient). Personal reasons (2 patients)	
Trial 4054 Main	somapacitan: 7 of 121 (5.8%) (6 patients exposed)	Protocol violation (2 patients) violation of exclusion criteria 9 (patients with a history of pituitary adenoma or other benign intracranial tumour) Withdrawal by patient (5 patients) (of these, 1 patient was not exposed)	
	Norditropin: 14 of 119 (11.8%)	Lost to follow-up (1 patient) Other (1 patient) Withdrawal by patient (12 patients)	AEs (4 patients): diabetes mellitus; gastroenteritis; haemo-concentration; dermatitis atopic.
	Placebo: 6 of 61 (9.8%)	Other (2 patients) Withdrawal by patient (4 patients)	AE (1 patient): hepatic enzymes increased.
Trial 4054 Extension	somapacitan: 10 of 220 (4.5%)	Lost to follow-up (2 patients) Other (2 patients) Withdrawal by patient (6 patients) (1 JP)	AEs (4 patients): pituitary tumour; thyroid disorder; plasma cell myeloma[a]; fatigue. Other (2 patients)[b] Withdrawal by patient (3 patients)[c]
	Norditropin: 7 of 52 (13.5%)	Lost to follow-up (1 patient) Other (3 patients[d]) (2 JP) Withdrawal by patient (3 patients)	
Trial 4244 (JP)	somapacitan: 1 of 46 (2.2%)	Withdrawal by patient (1 patient)	
	Norditropin: 1 of 16 (6.3%)	Withdrawal by patient (1 patient)	AE (1 patient) diabetes mellitus

Trial ID	Number (%) of subjects withdrawn of total randomised	Reason for withdrawal	Comments
Phase 1			
Trial 3915	somapacitan: 3 of 79 (3.8%) subjects	0.16 mg/kg: Withdrew consent 0.24 mg/kg: AE: abnormal ECG 0.24 mg/kg: AEs: nasopharyngitis and common cold with fever	Healthy subjects, non-Asian, multiple-dose part of the trial. None in placebo.
Trial 4237	None	NA	NA
Trial 4297	somapacitan: 3 of 44 (6.8%) subjects	0.08 mg/kg: 2 withdrew consent (normal renal function group) and 1 non-compliance (mild renal impairment group)	
Trial 4298	None	NA	NA
Trial 4491	somapacitan; 1 of 33 (3.0%) subjects	0.04 mg/kg: withdrew due to personal reasons	Healthy subject
Trial 3947	somapacitan: 4 of 26 (15.4%) AGHD patients	0.02 mg/kg: SAE: gastroenteritis 0.04 mg/kg: Withdrew consent 0.08 mg/kg AE: mild weight increase and oedema 0.12 mg/kg: Dosing day exclusion criteria (consumption of alcohol within 24 hours prior to dosing)	Dose-finding in AGHD patients, dosed in mg/kg
	Norditropin: 1 of 9 (11.1%)	Other: difficult phlebotomy	

Abbreviations: AE = adverse events; AGHD = adult growth hormone deficiency; JP = Japanese; NA = not applicable; SAE = serious adverse event.

[a]The AE started in the main phase of the trial (while on Norditropin) but was first diagnosed in the extension part of the trial. The patient continued in the extension part of the trial and was treated with somapacitan in the extension trial. Somapacitan was later withdrawn in the extension trial.

[b] This included 1 patient where reason for discontinuation was reported as 'other' (pituitary tumour benign).

[c] This included 1 patient where reason for discontinuation was reported as 'withdrawn by subject' with comment due to AEs (HbA_{1c} increased and hepatic steatosis)

[d] Two (2) patients were first withdrawn in the extension trial but were not exposed in the extension trial.

Phase 1: Dosing by body weight; Phase 3: IGF-I dose titration. Number of Japanese patients withdrawn in trials 4043 and 4054 are based on 付録 2.7.4.7.2 Table 27 及び 28.

2.7.4.1.3.3 用量レベルの調整

臨床薬理試験（3915 試験及び 3947 試験）では用量レベルの変更を行った。

ヒトへの初回投与試験（3915 試験）の単回投与パートでは、計画した 6 つのソマプシタンの用量のうち 5 用量を検討した（0.01、0.04、0.08、0.16 及び 0.32 mg/kg）。この 5 用量のデータから、有害事象（末梢性浮腫、筋肉痛及び関節痛等）の発現頻度及び重症度が用量依存的に増加することが示された。0.32 mg/kg 投与時の IGF-I 濃度は、ソマプシタンを実臨床で使用する際に期待される IGF-I 反応を超えていた（Module 2.7.2.3.2.1 参照）。このため、ノボ ノルディスク社の安全性グループは 3915 試験の単回投与パートにおいて、予定された最終用量（0.64 mg/kg）への漸増を中止した。

ヒトへの初回投与試験（3915 試験）の反復投与パートでは、4 用量のソマプシタンを評価した（0.02、0.08、0.16 及び 0.24 mg/kg）。0.16 mg/kg で浮腫の増加がみられた。ノボ ノルディスク社の安全性グループは、高用量で浮腫の重症度が高くなるリスクを最小限に抑えるため、予定された最終用量（0.32 mg/kg）ではなく中間用量（0.24 mg/kg）への漸増を決定した。

AGHD 患者を対象とした反復投与試験（3947 試験）では、4 用量のソマプシタンを検討した（0.02、0.04、0.08 及び 0.12 mg/kg）。ソマプシタン 0.08 mg/kg 投与後に、2 例において軽度～中等度の浮腫が認められたため、ノボ ノルディスク社の安全性グループは、予定された最終用量（0.16 mg/kg）ではなく中間用量の 0.12 mg/kg を最終用量とした。推奨用法・用量については、Module 2.7.3.4 を参照のこと。

AGHD 患者を対象とした第 3 相試験（4043 試験、4054 試験及び 4244 試験）では、現在の AGHD 患者に対する実臨床と同様に、IGF-I 値に基づき被験者ごとに用量調整を行った。ソマプシタンの平均投与量は 0.036 mg/kg/週であった（第 3 相試験併合に基づく。表 2.7.4.1-10）。

2.7.4.1.4　試験対象集団の人口統計学的特性及びその他の特性

2.7.4.1.4.1　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　AGHD 患者を対象とした第 3 相試験の結果（試験別）

第 3 相試験に組み入れられた AGHD 患者のベースライン特性は試験間で同様であった。ベースライン特性を試験別に表 2.7.4.1-16 に要約する。

4054 試験では AGHD 患者 300 例、4043 試験では AGHD 患者 92 例、4244 試験では日本人 AGHD 患者 62 例を評価した。4054 試験及び 4043 試験では、人種の分布は国際共同試験であることを反映していた。大部分の被験者は成人期に初めて GHD と診断されたが、最大で 3 分の 1 の被験者が小児期に GHD と診断されていた。

平均年齢は試験間で同様であり、大部分の被験者（77.4～86.3%）が 18～64 歳に分類された（4054 試験では 23～64 歳）。試験別にみると、4054 試験では 13.7%、4043 試験では 20.7%、4244 試験では 22.6%が 65 歳以上であった。

4054 試験では hGH 製剤による治療歴のない AGHD 患者を、補足的な試験である 4043 試験及び 4244 試験（日本人 AGHD 患者）では hGH 製剤で治療中の AGHD 患者を対象とした。

平均 BMI から、AGHD の特徴どおり、やや過体重の集団であることが示された。平均 BMI は 4244 試験と比較して 4054 試験及び 4043 試験でやや高い傾向がみられた。17 例が糖尿病と診断されていた〔4054 試験：16 例（5.3%）、4043 試験：1 例（1.1%）〕。日本国内では糖尿病患者を組み入れなかった（4244 試験、ならびに 4054 試験及び 4043 試験の日本人被験者）。

表 2.7.4.1-16　AGHD 患者のベースライン特性（試験別）

		Trial 4054[b]	Trial 4043	Trial 4244
Number of patients		300	92	62
Treatment naive		Yes	No	No
Age (years), mean (SD)		45.1 (15.0)	49.3 (16.5%)	52.8 (12.1%)
Age group 18−64 years, n (%) (trial 4054: 23−64 years)		259 (86.3%)	73 (79.3%)	48 (77.4%)
Age group ≥65 years, n (%)		41 (13.7%)	19 (20.7%)	14 (22.6%)
Sex	Men	48.3%	54.3%	53.2%
	Women	51.7%	45.7%	46.8%
Race[a]	White	66.7%	58.7%	NA
	Asian	28.7%	19.6% (hereof 17 Japanese patients)	100% (Japanese patients)
	Black or African American	2.3%	NA	NA
BMI (kg/m^2)		27.4 (6.3)	28.6 (5.2)	26.0 (6.1)
Diabetes mellitus, n (%)		16 (5.3%)	1 (1.1%)	0
GHD adult onset, n (%)		209 (69.7%)	58 (63.0%)	51 (82.3%)
GHD childhood onset, n (%)		91 (30.3%)	34 (37.0%)	11 (17.7%)

[a] Race and ethnicity were not reported for 20 patients in France due to local regulations.

[b] Baseline characteristics by treatment for trial 4054 is provided in 付録 2.7.4.7.1 Table 137.

4054 試験では、BMI 及びウエスト周囲径がプラセボ/ソマプシタン群で明らかに低値であったこと以外は、ベースラインで投与群間に臨床的に意味のある違いは認められなかった。4043 試験及び 4244 試験では、ベースラインで投与群間に臨床的に意味のある違いは認められなかった。

試験別のベースライン特性の詳細は Module 2.7.3.3.1.2 を参照のこと。

併発疾患及び併用薬剤に関する詳細は各試験の治験総括報告書を参照のこと〔4054 試験（M 5.3.5.1）Section 16.2.4.6、4043 試験（M 5.3.5.1）Section 16.2.4.6、4244 試験（M 5.3.5.1）Section 16.2.4.6〕。

2.7.4.1.4.3　AGHD 患者を対象とした第 3 相試験の結果（第 3 相試験併合）

第 3 相試験には AGHD 患者 454 例（19～77 歳）を組み入れた（表 2.7.4.1-17）。大部分の被験者（70%）が成人期に初めて GHD と診断されたが、30%の被験者が小児期に GHD と診断されていた。平均年齢（標準偏差）は 47.0（15.2）歳であり、大部分の被験者が 18～64 歳に分類された。被験者の 16.3%が 65 歳以上であった。平均 BMI（標準偏差）が 27.5（6.1）kg/m^2 であったことから、AGHD の

特徴どおり、やや過体重の集団であることが示された。17 例（3.7%）がベースラインで糖尿病と診断されていた（日本国内では糖尿病患者は組み入れられなかった）。

人種の分布は国際共同試験であることを反映しており、55.9%が白人、36.6%がアジア人、1.5%が黒人／アフリカ系アメリカ人であった。

4054 試験では hGH 製剤による治療歴のない AGHD 患者を、補足的な試験である 4043 試験及び 4244 試験（日本人 AGHD 患者）では hGH 製剤で治療中の AGHD 患者を対象とした。

表 2.7.4.1-17　　AGHD 患者のベースライン特性（第 3 相試験併合）

	placebo	Norditropin	somapacitan	total
Number of Subjects	61	166	333	454
Age (years), N	61	166	333	454
Mean (SD)	45.0 (15.7)	47.2 (15.5)	46.5 (15.1)	47.0 (15.2)
Median	46.0	47.0	46.0	47.0
Min ; Max	23.0 ; 76.0	20.0 ; 77.0	19.0 ; 77.0	19.0 ; 77.0
Age group, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
18 - 64 years	51 (83.6)	138 (83.1)	281 (84.4)	380 (83.7)
>= 65 years	10 (16.4)	28 (16.9)	52 (15.6)	74 (16.3)
Sex, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
Female	32 (52.5)	82 (49.4)	169 (50.8)	226 (49.8)
Male	29 (47.5)	84 (50.6)	164 (49.2)	228 (50.2)
Ethnicity, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
Hispanic Or Latino	4 (6.6)	8 (4.8)	15 (4.5)	18 (4.0)
Not Hispanic Or Latino	57 (93.4)	149 (89.8)	303 (91.0)	414 (91.2)
NA	0	9 (5.4)	15 (4.5)	22 (4.8)

Continued..

Summary of baseline characteristics - full analysis set

	placebo	Norditropin	somapacitan	total
Race, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
Asian	16 (26.2)	58 (34.9)	122 (36.6)	166 (36.6)
White	42 (68.9)	94 (56.6)	188 (56.5)	254 (55.9)
Black Or African American	2 (3.3)	3 (1.8)	4 (1.2)	7 (1.5)
Native Hawaiian Or Other Pacific Islander	0	0	1 (0.3)	1 (0.2)
Other	1 (1.6)	2 (1.2)	3 (0.9)	4 (0.9)
NA	0	9 (5.4)	15 (4.5)	22 (4.8)
Country, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
Australia	7 (11.5)	10 (6.0)	26 (7.8)	30 (6.6)
Denmark	0	6 (3.6)	16 (4.8)	22 (4.8)
France	0	7 (4.2)	13 (3.9)	20 (4.4)
Germany	2 (3.3)	8 (4.8)	13 (3.9)	21 (4.6)
India	6 (9.8)	11 (6.6)	19 (5.7)	28 (6.2)
Japan	10 (16.4)	40 (24.1)	93 (27.9)	125 (27.5)
Latvia	2 (3.3)	1 (0.6)	2 (0.6)	3 (0.7)
Lithuania	4 (6.6)	3 (1.8)	7 (2.1)	8 (1.8)
Malaysia	0	3 (1.8)	5 (1.5)	7 (1.5)
Poland	1 (1.6)	2 (1.2)	8 (2.4)	11 (2.4)
Romania	2 (3.3)	14 (8.4)	21 (6.3)	28 (6.2)
Russian Federation	5 (8.2)	6 (3.6)	15 (4.5)	18 (4.0)
South Africa	1 (1.6)	4 (2.4)	7 (2.1)	9 (2.0)
Sweden	0	6 (3.6)	6 (1.8)	10 (2.2)
Turkey	3 (4.9)	1 (0.6)	7 (2.1)	8 (1.8)
Ukraine	4 (6.6)	1 (0.6)	6 (1.8)	8 (1.8)
United Kingdom	0	9 (5.4)	13 (3.9)	19 (4.2)
United States	14 (23.0)	34 (20.5)	56 (16.8)	79 (17.4)
Height (m), N	61	166	333	454
Mean (SD)	1.63 (0.10)	1.65 (0.13)	1.65 (0.11)	1.65 (0.12)
Median	1.64	1.65	1.65	1.65
Min ; Max	1.39 ; 1.83	1.07 ; 1.93	1.30 ; 1.94	1.07 ; 1.94
Body Weight (kg), N	61	166	333	454
Mean (SD)	69.8 (19.7)	76.2 (21.9)	75.0 (21.4)	75.4 (21.2)
Median	69.0	74.3	72.0	73.5
Min ; Max	38.0 ; 115	22.5 ; 151	34.5 ; 151	22.5 ; 151
BMI (kg/m^2), N	61	166	333	454
Mean (SD)	26.1 (6.4)	27.6 (5.9)	27.4 (6.2)	27.5 (6.1)
Median	25.4	26.8	26.6	26.7
Min ; Max	13.3 ; 44.3	17.0 ; 45.0	13.3 ; 51.9	13.3 ; 51.9
Waist circumference (cm), N	61	119	226	300
Mean (SD)	88.2 (14.5)	94.3 (16.6)	92.2 (15.5)	92.9 (15.7)
Median	87.7	94.6	90.8	92.8
Min ; Max	60.0 ; 123	45.3 ; 153	60.0 ; 153	45.3 ; 153
GHD Onset, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
Childhood-Idiopathic	13 (21.3)	25 (15.1)	53 (15.9)	69 (15.2)
Childhood-Organic	7 (11.5)	20 (12.0)	50 (15.0)	67 (14.8)
Adulthood	41 (67.2)	121 (72.9)	230 (69.1)	318 (70.0)
Diabetes Mellitus, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
Diabetic	3 (4.9)	7 (4.2)	11 (3.3)	17 (3.7)
Non-Diabetic	58 (95.1)	159 (95.8)	322 (96.7)	437 (96.3)

N: Number of subjects, %: Percentage of subjects, SD: Standard deviation. Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.

ノルディトロピン/ソマプシタン併合

ノルディトロピン/ソマプシタン併合のベースライン特性は、第 3 相試験併合の特性と同様であった。要約は付録 2.7.4.7.1、Table 104 を参照のこと。

2.7.4.1.4.4　日本人被験者の結果を含む AGHD 患者を対象とした第 3 相試験の結果

第 3 相臨床試験では日本人 AGHD 患者 125 例を検討した。このうち 93 例がソマプシタンの投与を受けた（4054 試験：36 例、4043 試験：11 例、4244 試験：46 例）。

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 又は各試験の治験総括報告書〔4244 試験（M 5.3.5.1）Section 10.2、4054 試験（M 5.3.5.1）Section 10.2、4043 試験（M 5.3.5.1）Section 10.2〕を参照のこと。

2.7.4.1.4.5　臨床薬理試験の結果

臨床薬理試験の対象集団における被験者背景及びベースライン特性を Module 2.7.1.2（4491 試験）及び Module 2.7.2.1.4.2（3915 試験、3947 試験、4237 試験、4297 試験及び 4298 試験）に示す。試験デザインについては Module 2.7.6 に提示した。3915 試験では、反復投与パートに日本人及び非アジア人健康男性被験者を組み入れた。

2.7.4.2 有害事象

2.7.4.2.1 比較的よく見られる有害事象

2.7.4.2.1.1 AGHD 患者を対象とした第 3 相試験の結果（試験別）

第 3 相試験では、AGHD 患者に対する 86 週まで（4054 試験）のソマプシタン週 1 回皮下投与は良好な忍容性を示し、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。治験薬の投与期間は 4043 試験では 26 週まで、4244 試験では 52 週間までであった。

4054 試験では、有害事象の単位時間あたりの発現件数はノルディトロピン群及びプラセボ群と比較してソマプシタン群でやや少ないか、同様であった。4054 試験及び 4043 試験と比較して、4244 試験では有害事象の単位時間あたりの発現件数は少なかった。試験別の有害事象の概要を図 2.7.4.2-1 に示す。

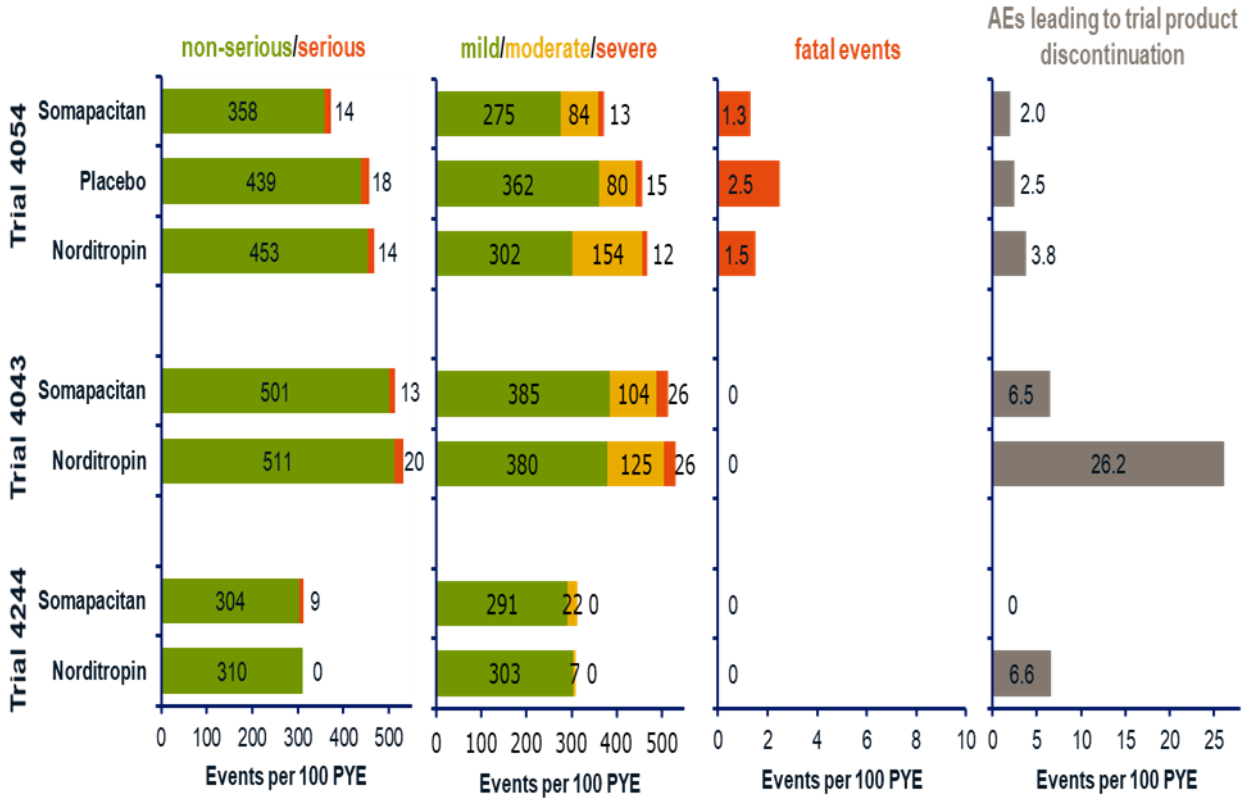


図 2.7.4.2-1 有害事象の概要（第 3 相試験別）

高頻度〔いずれかの群で 5%以上（4244 試験では投与群を通じて 4%以上）〕で報告された有害事象を試験別に図 2.7.4.2-2～図 2.7.4.2-4 に示す。有害事象のパターンは AGHD 患者で予想されるものと考えられた。ソマプシタン群において高頻度で報告された有害事象は、「上咽頭炎（鼻咽頭炎）」及び「頭痛」（すべての第 3 相試験）、「上気道感染」（4054 試験）「疲労」（4043 試験）及び「関節

痛」（4244 試験）であった。関節痛及び頭痛は GH 治療に関連する有害事象としてよく知られているものである [8,16]。

有害事象の発現頻度、重症度、種類又は発現時期に治験薬投与と関連する明らかな傾向は認められなかった。ソマプシタン週 1 回投与の安全性プロファイルはノルディトロピンの 1 日 1 回投与と同様であり、4054 試験ではプラセボと同様であった。

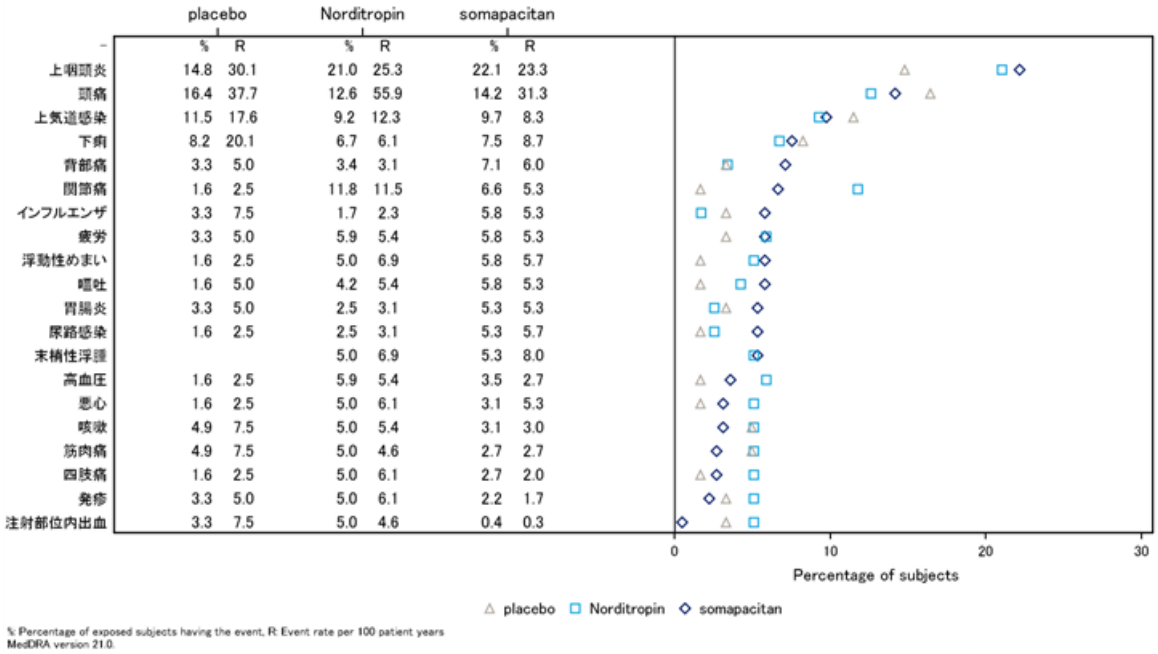


図 2.7.4.2-2　　高頻度（いずれかの群で 5%以上）で報告された有害事象（基本語別）（4054 試験、全試験期間）

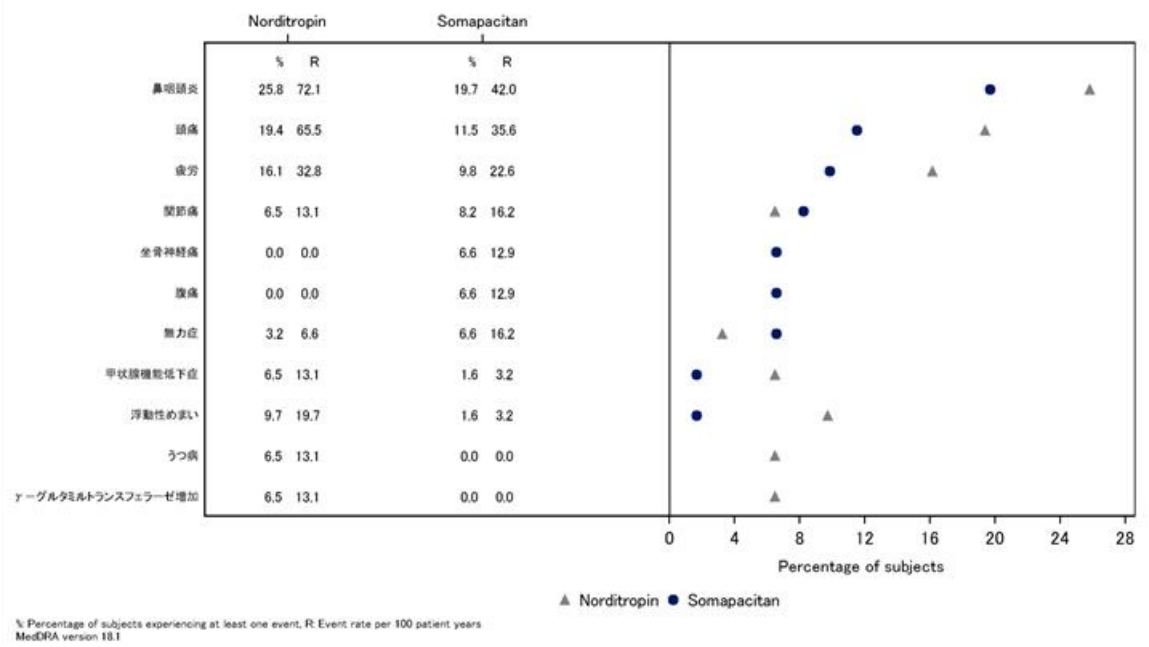


図 2.7.4.2-3　　高頻度（いずれかの群で 5%以上）で報告された有害事象（基本語別）（4043 試験）

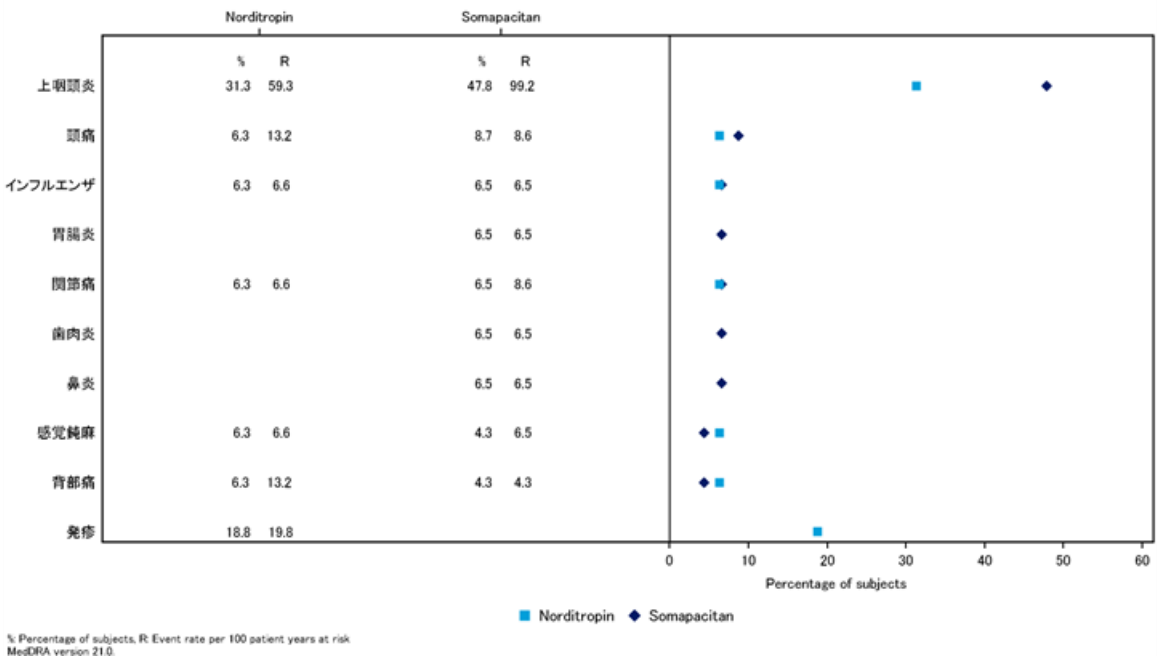


図 2.7.4.2-4　　高頻度（投与群を通じて 4%以上）で報告された有害事象（基本語別）（4244 試験）

4054 試験

有害事象を発現した被験者の割合は投与群間（総試験期間）で同様であったが（ソマプシタン群：79.2%、ノルディトロピン群：82.4%、プラセボ群：75.4%）、有害事象の単位時間あたりの発現件数は、ノルディトロピン群（467.8 件／100 人・年）及びプラセボ群（456.8 件／100 人・年）と比較してソマプシタン群（372.3 件／100 人・年）で少なかった（付録 2.7.4.7.1、Table 139）。有害事象の大部分（ソマプシタン群：96.2%、ノルディトロピン群：96.9%、プラセボ群：96.2%）は非重篤であった。

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（付録 2.7.4.7.1、Table 143 及び Figure 144）。すべての有害事象の要約を投与群別に付録 2.7.4.7.1、Table 141 に示す。

4054 試験の主要試験期間+延長期間に、高頻度（5%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を表 2.7.4.2-1 に示す。

表 2.7.4.2-1　AGHD 患者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（いずれかの群で 5%以上）〔4054 試験（主要試験期間+延長期間）〕

	Placebo/ somapacitan N (%) E R	somapacitan/ somapacitan N (%) E R	Norditropin/ Norditropin N (%) E R	Norditropin/ somapacitan N (%) E R	Nor/ - N
Patients exposed	61	120	52	51	16
Preferred term					
頭痛	2 (3.3) 7 7.4	6 (5.0) 38 19.5	2 (3.8) 6 6.9	2 (3.9) 7 8.2	0
末梢性浮腫	2 (3.3) 3 3.2	5 (4.2) 14 7.2	4 (7.7) 7 8.1	2 (3.9) 2 2.3	0
関節痛	2 (3.3) 2 2.1	4 (3.3) 4 2.1	1 (1.9) 1 1.2	5 (9.8) 7 8.2	0

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the event, or an event in the given SOC at least once, Nor = Norditropin; R: Event rate per 100 patient years at risk AE causality is based on judgement of investigators. MedDRA version 21.0. Norditropin/- group: events were only included if observed in at least 2 patients.

4054 試験の 35 週間のプラセボ対照の主要試験期間に、高頻度（いずれかの群で 5%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、主要試験期間+延長期間において認められた有害事象と同じであった（表 2.7.4.2-2 参照）。

表 2.7.4.2-2　AGHD 患者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（いずれかの群で 5%以上）〔4054 試験（主要試験期間）〕

	Placebo	somapacitan	Norditropin
Patients exposed	61	120	119

	Placebo	somapacitan	Norditropin
Preferred term:	N (%)	N (%)	N (%)
頭痛	2 (3.3)	6 (5.0)	3 (2.5)
末梢性浮腫	0	3 (2.5)	6 (5.0)
関節痛	1 (1.6)	4 (3.3)	6 (5.0)

N: Number of subjects having the given event at least once.
%: Percentage of exposed subjects having the event. AE causality is based on judgement of investigators.

4043 試験

有害事象を発現した被験者の割合は、ソマプシタン群〔53 例（86.9%）159 件〕でノルディトロピン群〔21 例（67.7%）81 件〕よりも高かったが、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（514.2 件／100 人・年）とノルディトロピン群（530.8 件／100 人・年）で同様であった。有害事象の大部分（ソマプシタン群：97.5%、ノルディトロピン群：96.3%）は非重篤であった。

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〔治験総括報告書、4043 試験（M 5.3.5.1）Table 12-5〕。すべての有害事象の要約を投与群別に治験総括報告書〔4043 試験（M 5.3.5.1）EOT Table 14.3.1.4〕に示す。

4043 試験において、高頻度（いずれかの群で 5%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を表 2.7.4.2-3 に示す。

表 2.7.4.2-3　AGHD 患者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（5%以上）（4043 試験）

	Norditropin N (%) E R	Somapacitan N (%) E R
Subjects exposed	31	61
Preferred term		
疲労	4 (12.9) 4 26.2	5 (8.2) 6 19.4
頭痛	2 (6.5) 2 13.1	2 (3.3) 2 6.5

N: Number of subjects having the given event, or an event in the given system organ class at least once; E: Number of adverse events reported, R: Event rate per 100 subject years; %: Percentage of exposed subjects having the event. AE causality is based on judgement of investigators. MedDRA version 18.1

4244 試験

有害事象を発現した被験者の割合はノルディトロピン群（68.8%）よりもソマプシタン群（93.5%）で高かったが、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（312.7 件／100 人・年）とノルディトロピン群（309.8 件／100 人・年）で同様であった。4244 試験での有害事象の単位時間あたり

の発現件数は国際共同試験（4054 試験及び 4043 試験）よりも少なかった。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。有害事象の大部分（ソマプシタン群：97.2%、ノルディトロピン群：100%）は非重篤であった。

高頻度（投与群を通じて 4%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〔治験総括報告書、4244 試験（M 5.3.5.1）Table 12-2〕。すべての有害事象の要約を投与群別に治験総括報告書〔4244 試験（M 5.3.5.1）EOT Table 14.3.1.3〕に示す。

4244 試験において、高頻度（いずれかの群で 5%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を表 2.7.4.2-4 に示す。

表 2.7.4.2-4　AGHD 患者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（投与群を通じて 5%以上）（4244 試験）

	Norditropin N (%) E R	Somapacitan N (%) E R
Subjects exposed	16	46
Preferred term		
上咽頭炎	2 (12.5) 5 33.0	2 (4.3) 2 4.3

N: Number of subjects having the given event, or an event in the given system organ class at least once; E: Number of adverse events reported, R: Event rate per 100 subject years; %: Percentage of exposed subjects having the event. AE causality is based on judgement of investigators. MedDRA version 21.0. Norditropin: events were only included if observed in at least 2 patients.

2.7.4.2.1.2　AGHD 患者を対象とした第 3 相試験の結果（第 3 相試験併合）

AGHD 患者に対する 86 週までのソマプシタン週 1 回皮下投与は良好な忍容性を示し、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。

計 382 例（84.1%）で 2344 件の有害事象が認められ、単位時間あたりの発現件数は 405.0 件／100 人・年であった（付録 2.7.4.7.1、Table 5）。有害事象を発現した被験者の割合は投与群間で同様であったが（ソマプシタン群：82.6%、ノルディトロピン群：78.3%、プラセボ群：75.4%）、有害事象の単位時間あたりの発現件数は、ノルディトロピン群（458.9 件／100 人・年）及びプラセボ群（456.8 件／100 人・年）と比較してソマプシタン群（376.6 件／100 人・年）で少なかった（表 2.7.4.2-5）。有害事象の大部分（96.6%）は非重篤であった。すべての有害事象の要約を投与群別に付録 2.7.4.7.1、Table 7 に示す。

表 2.7.4.2-5　　AGHD 患者で報告された有害事象の概要（第 3 相試験併合）

	placebo			Norditropin			somapacitan		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All adverse events	46 (75.4)	182	456.8	130 (78.3)	739	458.9	275 (82.6)	1423	376.6
Serious adverse events	5 (8.2)	7	17.6	16 (9.6)	22	13.7	29 (8.7)	50	13.2
Severity									
Mild	41 (67.2)	144	361.5	115 (69.3)	499	309.9	250 (75.1)	1081	286.1
Moderate	17 (27.9)	32	80.3	63 (38.0)	221	137.2	99 (29.7)	295	78.1
Severe	4 (6.6)	6	15.1	12 (7.2)	19	11.8	26 (7.8)	47	12.4
Causality									
Unlikely	45 (73.8)	163	409.2	125 (75.3)	629	390.6	257 (77.2)	1176	311.3
Possible	9 (14.8)	13	32.6	34 (20.5)	68	42.2	65 (19.5)	180	47.6
Probable	4 (6.6)	6	15.1	20 (12.0)	42	26.1	37 (11.1)	67	17.7
Outcome									
Recovered/Resolved	43 (70.5)	160	401.6	121 (72.9)	594	368.9	254 (76.3)	1169	309.4
Recovering/Resolving	1 (1.6)	2	5.0	13 (7.8)	19	11.8	25 (7.5)	34	9.0
Recovered/ Resolved With Sequelae	1 (1.6)	1	2.5	4 (2.4)	5	3.1	3 (0.9)	3	0.8
Not Recov/Not Resolved	13 (21.3)	18	45.2	58 (34.9)	116	72.0	108 (32.4)	212	56.1
Fatal	1 (1.6)	1	2.5	2 (1.2)	2	1.2	2 (0.6)	4	1.1
Unknown	0			1 (0.6)	3	1.9	1 (0.3)	1	0.3
Action									
Drug Interrupted	3 (4.9)	5	12.6	6 (3.6)	10	6.2	3 (0.9)	6	1.6
Drug Withdrawn	1 (1.6)	1	2.5	6 (3.6)	9	5.6	6 (1.8)	8	2.1
Dose Reduced	0			5 (3.0)	7	4.3	10 (3.0)	14	3.7
Dose Not Changed	45 (73.8)	170	426.7	126 (75.9)	689	427.9	273 (82.0)	1327	351.2
Not Applicable	3 (4.9)	6	15.1	15 (9.0)	24	14.9	38 (11.4)	68	18.0
Treatment discontinuations due to AEs[a]	1 (1.6)	1	2.5	7 (4.2)	10	6.2	6 (1.8)	8	2.1

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years. Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.AE causality is based on judgement of investigators. MedDRA version 21.0.

[a]For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

有害事象のパターンは AGHD 患者で予想されるものと考えられた。ソマプシタン群において高頻度で報告された有害事象は、「上咽頭炎」（25.2%）、「頭痛」（12.9%）及び「関節痛」（6.9%）であった。いずれかの群で 5%以上の被験者で報告された有害事象を図 2.7.4.2-5 及び付録 2.7.4.7.1、Table 21 に示す。

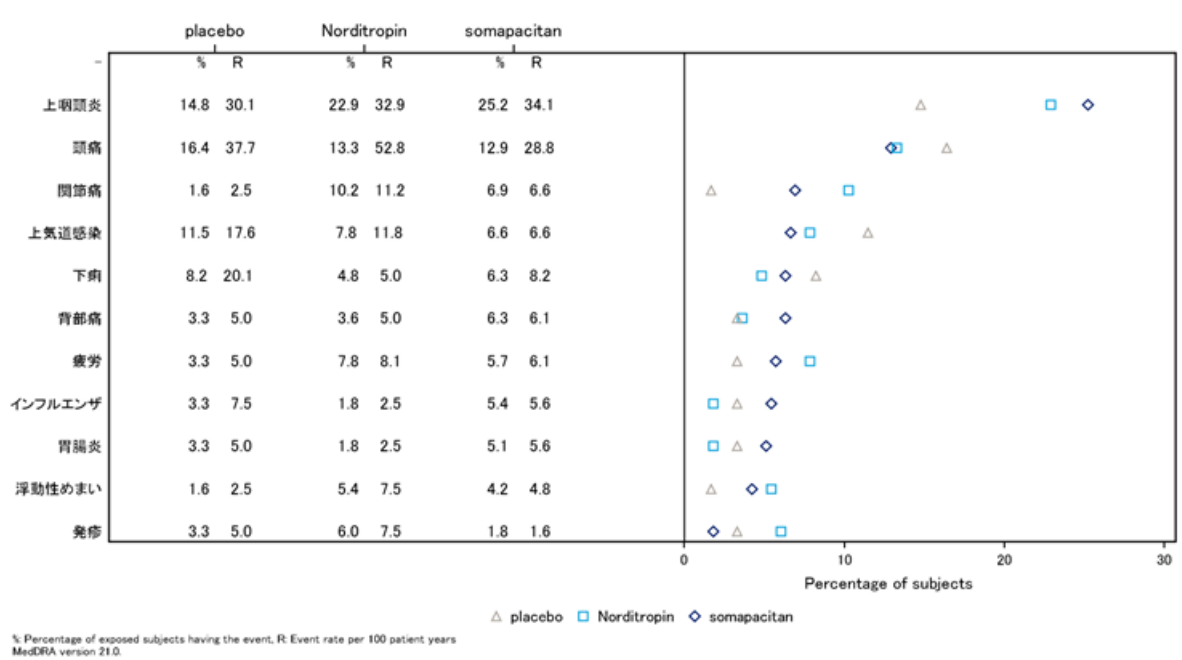


図 2.7.4.2-5　　高頻度（いずれかの群で 5%以上）で報告された有害事象（基本語別）（第 3 相試験併合）

重症度

有害事象の大部分は軽度又は中等度であったが（表 2.7.4.2-5 ならびに付録 2.7.4.7.1、Table 10 及び 11）、41 例（9.0%）で認められた 72 件の有害事象は重度と分類された（付録 2.7.4.7.1、Table 9）。

重度の有害事象の単位時間あたりの発現件数は投与群を通じて同様であった（ソマプシタン群：12.4 件／100 人・年、ノルディトロピン群：11.8 件／100 人・年、プラセボ群：15.1 件／100 人・年）（付録 2.7.4.7.1、Table 9）。

ソマプシタン群で報告された重度の有害事象 47 件中 5 件は、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〔付録 2.7.4.7.1、Table 14「頭痛」（2 件）、「無力症」、「椎間板突出」及び「膀胱移行上皮癌」（新生物の詳細は表 2.7.4.2-38 を参照のこと）〕。その他の重度の有害事象については、ソマプシタンとの因果関係は「なし」と判定された（付録 2.7.4.7.1、Table 9）。ノルディトロピン群で報告された重度の有害事象 19 件中 1 件「血液濃縮」は治験責任医師医によりノルディトロピンとの因果関係が「あり」と判定された（付録 2.7.4.7.1、Table 14）。

治験薬との因果関係

計 85 例（25.5%）で認められた有害事象 247 件が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、単位時間あたりの発現件数は 65.4 件／100 人・年であった（表 2.7.4.2-6）。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のパターンはノルディトロピン群と同様であった。一方、プラセボ群では単位時間あたりの発現件数は少なかっ

た。ソマプシタンとの因果関係が「可能性あり」又は「あり」と判定された有害事象の大部分は非重篤であり、軽度又は中等度であった（付録 2.7.4.7.1、Table 12～14）。

治験責任医師により因果関係が「可能性あり」又は「あり」と判定された有害事象で、ソマプシタン群及びノルディトロピン群において高頻度（いずれかの群で 2%以上）で報告された事象の中でも「頭痛」、「疲労」、「関節痛」及び「末梢性浮腫」は、いずれも GH による治療後に認められる有害事象としてよく知られているものである [8,16]（表 2.7.4.2-6）。「疲労」、「末梢性浮腫」及び「関節痛」を発現した被験者の割合は、ノルディトロピン群よりもソマプシタン群で低い傾向がみられた。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「頭痛」を発現した被験者の割合は投与群を通じて同様であったが（ソマプシタン群：3.3%、ノルディトロピン群：3.0%、プラセボ群：3.3%）、単位時間あたりの発現件数は、ノルディトロピン群（6.2 件／100 人・年）及びプラセボ群（5.0 件／100 人・年）よりもソマプシタン群（13.2 件／100 人・年）で多かった。その他、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」と判定された事象は様々な器官別大分類及び基本語に分類され、1～4 例で報告された（付録 2.7.4.7.1、Table 12）。

表 2.7.4.2-6 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（器官別大分類別、基本語別）（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All possibly or probably related adverse events	12 (19.7)	19	47.7	48 (28.9)	110	68.3	85 (25.5)	247	65.4	133 (29.3)	376	65.0
一般・全身障害および投与部位の状態												
疲労	1 (1.6)	1	2.5	7 (4.2)	7	4.3	9 (2.7)	11	2.9	17 (3.7)	19	3.3
末梢性浮腫	0			6 (3.6)	9	5.6	7 (2.1)	17	4.5	13 (2.9)	26	4.5
注射部位内出血	2 (3.3)	3	7.5	4 (2.4)	4	2.5	1 (0.3)	1	0.3	7 (1.5)	8	1.4
筋骨格系および結合組織障害												
関節痛	1 (1.6)	1	2.5	6 (3.6)	6	3.7	9 (2.7)	11	2.9	15 (3.3)	18	3.1
神経系障害												
頭痛	2 (3.3)	2	5.0	5 (3.0)	10	6.2	11 (3.3)	50	13.2	16 (3.5)	62	10.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

ノルディトロピン/ソマプシタン併合

有害事象のプロファイルは、第 3 相試験併合とノルディトロピン/ソマプシタン併合で同様であった。ノルディトロピン/ソマプシタン併合において有害事象を発現した被験者の割合及び単位時間あたりの発現件数を調整の有無で比較した要約表を付録 2.7.4.7.1、Table 105～110 に示す。

2.7.4.2.1.3　日本人被験者の結果を含む AGHD 患者を対象とした第 3 相試験の結果

4054 試験

全集団（4054 試験、主要試験期間）では、有害事象の単位時間あたりの発現件数はノルディトロピン群よりもソマプシタン群で少なかった（ソマプシタン群：485.7 件／100 人・年、ノルディトロピン群：559.7 件／100 人・年）（表 2.7.4.2-7）。有害事象の大部分は治験薬との因果関係が「なし」と判定され（815 件、81%）、軽度又は中等度に分類された（977 件、97%）。因果関係が「可能性あり」及び「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、ソマプシタン群（それぞれ、88.9 件／100 人・年及び 28.8 件／100 人・年）及びノルディトロピン群（それぞれ、65.8 件／100 人・年及び 32.2 件／100 人・年）で同様であった。大部分の被験者（71.3%）は有害事象から回復した。

日本人集団でも同様のパターンがみられ、有害事象の単位時間あたりの発現件数はノルディトロピン群（379.4 件／100 人・年）よりもソマプシタン群（313.4 件／100 人・年）で少なかった。日本人集団における有害事象の単位時間あたりの発現件数は少なく、有害事象のためにソマプシタン投与の中止に至った被験者はいなかった。4054 試験に組み入れられた日本人 AGHD 患者で報告された有害事象の概要を付録 2.7.4.7.2、Table 12 に示す。

日本人集団で最も高頻度で報告された有害事象は「上咽頭炎」であった〔付録 2.7.4.7.2、Table 15（全集団）、Table 16（日本人集団）〕。日本人集団では、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がソマプシタン群の 4 例で 9 件報告され、うち 2 件は「末梢性浮腫」であった。因果関係が「可能性あり」又は「あり」と判定された有害事象の単位時間あたりの発現件数は、日本人集団で 74.2 件／100 人・年、全集団で 117.7 件／100 人・年であった〔付録 2.7.4.7.2、Table 19（全集団）、Table 20（日本人集団）〕。

延長期間では、主要試験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 Module 2.7.6.7〔4054 試験（延長期間）〕及び治験総括報告書〔4054 試験（延長期間）（M 5.3.5.1）〕を参照のこと。

4054 試験における日本人集団と全集団の一貫性の評価

国際共同試験である 4054 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〔付録 2.7.4.7.2、Table 11（全集団）、Table 12（日本人集団）〕。

表 2.7.4.2-7　有害事象の概要〔4054 試験（主要試験期間）、全集団〕

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	61			119			120			300		
Total patient years	39.8			77.5			79.9			197.2		
All adverse events	46 (75.4)	182	457.0	96 (80.7)	434	559.7	87 (72.5)	388	485.7	229 (76.3)	1004	509.0
Serious adverse events	5 (8.2)	7	17.6	11 (9.2)	13	16.8	7 (5.8)	12	15.0	23 (7.7)	32	16.2
Severity												
Mild	41 (67.2)	144	361.6	82 (68.9)	287	370.1	75 (62.5)	276	345.5	198 (66.0)	707	358.5
Moderate	17 (27.9)	32	80.4	42 (35.3)	137	176.7	34 (28.3)	101	126.4	93 (31.0)	270	136.9
Severe	4 (6.6)	6	15.1	9 (7.6)	10	12.9	7 (5.8)	11	13.8	20 (6.7)	27	13.7
Causality												
Unlikely	45 (73.8)	163	409.3	90 (75.6)	358	461.7	79 (65.8)	294	368.1	214 (71.3)	815	413.2
Possible	9 (14.8)	13	32.6	27 (22.7)	51	65.8	23 (19.2)	71	88.9	59 (19.7)	135	68.4
Probable	4 (6.6)	6	15.1	15 (12.6)	25	32.2	14 (11.7)	23	28.8	33 (11.0)	54	27.4
Outcome												
Recovered/Resolved	43 (70.5)	160	401.8	89 (74.8)	367	473.3	82 (68.3)	358	448.2	214 (71.3)	885	448.7
Recovering/Resolving	1 (1.6)	2	5.0	2 (1.7)	2	2.6	0			3 (1.0)	4	2.0
Recovered/Resolved With Sequelae	1 (1.6)	1	2.5	2 (1.7)	3	3.9	1 (0.8)	1	1.3	4 (1.3)	5	2.5
Not Recovered/Not Resolved	13 (21.3)	18	45.2	36 (30.3)	59	76.1	19 (15.8)	29	36.3	68 (22.7)	106	53.7
Fatal	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Unknown	0			1 (0.8)	3	3.9	0			1 (0.3)	3	1.5
Action												
Drug Interrupted	3 (4.9)	5	12.6	5 (4.2)	8	10.3	0			8 (2.7)	13	6.6
Drug Withdrawn	1 (1.6)	1	2.5	4 (3.4)	4	5.2	0			5 (1.7)	5	2.5
Dose Reduced	0			5 (4.2)	6	7.7	2 (1.7)	3	3.8	7 (2.3)	9	4.6
Dose Not Changed	45 (73.8)	170	426.9	93 (78.2)	407	524.9	87 (72.5)	371	464.5	225 (75.0)	948	480.6
Not Applicable	3 (4.9)	6	15.1	6 (5.0)	9	11.6	6 (5.0)	14	17.5	15 (5.0)	29	14.7
Treatment discontinuations due to adverse events	1 (1.6)	1	2.5	5 (4.2)	5	6.4	0			6 (2.0)	6	3.0

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years. AE causality is based on judgement of investigators. MedDRA version 21.0.

4043 試験

全集団（4043 試験）では、有害事象を発現した被験者の割合はノルディトロピン群よりもソマプシタン群で多かった〔ソマプシタン群：53 例（86.9%）159 件、ノルディトロピン群：21 例（67.7%）81 件〕。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同様であった（ソマプシタン群：514.2 件／100 人・年、ノルディトロピン群：530.8 件／100 人・年）（表 2.7.4.2-8）。有害事象の大部分は 1～2 例でそれぞれ 1 件の発現であり、軽度又は中等度であった。有害事象の大部分（198 件、83%）は、治験薬との因果関係が「なし」と判定された。

日本人集団では、ソマプシタン群の 11 例（100%）で 36 件、ノルディトロピン群の 1 例（16.7%）で 4 件の有害事象が報告された。解釈にあたり、治験薬の総曝露期間がノルディトロピン群（3.1 人・年）よりもソマプシタン群（5.7 人・年）で長く、日本人被験者数が少なかった（17 例）ことを考慮すべきである。日本人集団では有害事象のためにソマプシタン投与の中止に至った被験者はいなかった。4043 試験に組み入れられた日本人 AGHD 患者で報告された有害事象の概要を付録 2.7.4.7.2、Table 14 に示す。

日本人被験者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〔付録 2.7.4.7.2、Table 17（全集団）、Table 18（日本人集団）〕。日本人集団では、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、ソマプシタン群の 2 例（18.2%）のみで認められたが、特別に懸念される事象はなかった（「下痢」、「倦怠感」、「関節痛」及び「浮動性めまい」）〔付録 2.7.4.7.2、Table 21（全集団）、Table 22（日本人集団）〕。

4043 試験における日本人集団と全集団の一貫性の評価

国際共同試験である 4043 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〔付録 2.7.4.7.2、Table 13（全集団）、Table 14（日本人集団）〕。

表 2.7.4.2-8 有害事象の概要（4043 試験、全集団）

	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All adverse events	21 (67.7)	81	530.8	53 (86.9)	159	514.2	74 (80.4)	240	519.7
Serious adverse events	2 (6.5)	3	19.7	4 (6.6)	4	12.9	6 (6.5)	7	15.2
Severity									
Mild	18 (58.1)	58	380.1	44 (72.1)	119	384.8	62 (67.4)	177	383.3
Moderate	8 (25.8)	19	124.5	16 (26.2)	32	103.5	24 (26.1)	51	110.4
Severe	2 (6.5)	4	26.2	5 (8.2)	8	25.9	7 (7.6)	12	26.0
Causality									
Unlikely	21 (67.7)	68	445.6	46 (75.4)	130	420.4	67 (72.8)	198	428.7
Possible	3 (9.7)	5	32.8	9 (14.8)	15	48.5	12 (13.0)	20	43.3
Probable	4 (12.9)	8	52.4	8 (13.1)	14	45.3	12 (13.0)	22	47.6
Outcome									
Recovered/Resolved	20 (64.5)	57	373.5	46 (75.4)	109	352.5	66 (71.7)	166	359.4
Recovering/Resolving	4 (12.9)	6	39.3	9 (14.8)	10	32.3	13 (14.1)	16	34.6
Recovered/Resolved With Sequelae	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Not Recovered/Not Resolved	10 (32.3)	17	111.4	22 (36.1)	39	126.1	32 (34.8)	56	121.3
Unknown	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Action									
Drug Withdrawn	1 (3.2)	4	26.2	1 (1.6)	2	6.5	2 (2.2)	6	13.0
Dose Not Changed	20 (64.5)	74	484.9	52 (85.2)	146	472.2	72 (78.3)	220	476.4
Not Applicable	3 (9.7)	3	19.7	9 (14.8)	11	35.6	12 (13.0)	14	30.3
Treatment discontinuations due to adverse events	1 (3.2)	4	26.2	1 (1.6)	2	6.5	2 (2.2)	6	13.0

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years. AE causality is based on judgement of investigators. MedDRA version 21.0.

4244 試験

4244 試験（すべて日本人被験者）では、有害事象を発現した被験者の割合はノルディトロピン群（68.8%）よりもソマプシタン群（93.5%）で高かった（表 2.7.4.2-9）。

すべて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（312.7 件／100 人・年）とノルディトロピン群（309.8 件／100 人・年）で同様であった。有害事象の発現頻度、重症度、種類又は発現時期に治験薬投与と関連する明らかな傾向は認められなかった。ソマプシタン週 1 回投与の安全性プロファイルはノルディトロピンの 1 日 1 回投与と同様であった。

4244 試験における有害事象の単位時間あたりの発現件数は国際共同試験（4054 試験及び 4043 試験）よりも少なく、有害事象のためにソマプシタン投与を中止した被験者はいなかった。4244 試験に組み入れられた AGHD 患者で報告された有害事象の概要を示す（表 2.7.4.2-9）。

最も高頻度で報告された有害事象は「上咽頭炎」であった〔治験総括報告書、4244 試験（M 5.3.5.1）Table 12-2〕。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、ソマプシタン群で「上咽頭炎」及び「関節痛」がそれぞれ 2 例、ノルディトロピン群で「上咽頭炎」が 2 例で報告されたことを除き、1 例での報告であった〔治験総括報告書、4244 試験（M 5.3.5.1）Table 12-3〕。

表 2.7.4.2-9 有害事象の概要（4244 試験）

	Norditropin N (%) E R	Somapacitan N (%) E R	Total N (%) E R
Number of exposed subjects	16	46	62
Total patient years at risk	15.2	46.4	61.5
All adverse events	11 (68.8) 47 309.8	43 (93.5) 145 312.7	54 (87.1) 192 312.0
Serious adverse events	0	4 (8.7) 4 8.6	4 (6.5) 4 6.5
Severity			
Mild	11 (68.8) 46 303.2	42 (91.3) 135 291.1	53 (85.5) 181 294.1
Moderate	1 (6.3) 1 6.6	8 (17.4) 10 21.6	9 (14.5) 11 17.9
Severe	0	0	0
Causality			
Probable	1 (6.3) 7 46.1	3 (6.5) 4 8.6	4 (6.5) 11 17.9
Possible	2 (12.5) 2 13.2	6 (13.0) 8 17.3	8 (12.9) 10 16.2
Unlikely	11 (68.8) 38 250.4	41 (89.1) 133 286.8	52 (83.9) 171 277.8
Outcome			
Recovered/resolved	10 (62.5) 35 230.7	41 (89.1) 123 265.3	51 (82.3) 158 256.7
Recovering/resolving	1 (6.3) 1 6.6	6 (13.0) 9 19.4	7 (11.3) 10 16.2
Recovered/resolved with sequelae	0	0	0
Not recovered/not resolved	6 (37.5) 11 72.5	11 (23.9) 13 28.0	17 (27.4) 24 39.0
Fatal	0	0	0
Unknown	0	0	0

	Norditropin N (%) E R	Somapacitan N (%) E R	Total N (%) E R
Action taken to trial product due to AE			
Drug interrupted	0	0	0
Drug withdrawn	1 (6.3) 1 6.6	0	1 (1.6) 1 1.6
Dose reduced	0	2 (4.3) 4 8.6	2 (3.2) 4 6.5
Dose increased	0	0	0
Dose not changed	11 (68.8) 44 290.0	43 (93.5) 132 284.7	54 (87.1) 176 286.0
Unknown	0	0	0
NA	2 (12.5) 2 13.2	8 (17.4) 9 19.4	10 (16.1) 11 17.9
Related to a technical complaint	0	0	0
Injection site reaction	1 (6.3) 1 6.6	1 (2.2) 1 2.2	2 (3.2) 2 3.2
Treatment discontinued due to adverse event	1 (6.3) 1 6.6	0	1 (1.6) 1 1.6

N: Number of subjects, %: Percentage of subjects, AE: Adverse event, E: Number of events, NA: Not applicable, R: Event rate per 100 patient years at risk
AE causality is based on judgement of investigators.

2.7.4.2.1.4　臨床薬理試験の結果

健康被験者を対象としたヒトへの初回投与試験（3915 試験）

健康男性被験者（79 例、日本人被験者を含む）に対するソマプシタンの単回投与及び週 1 回反復投与は、検討したすべての用量（単回投与：0.01～0.32 mg/kg 皮下投与、反復投与：0.02～0.24 mg/kg 皮下投与）で良好な忍容性を示し、臨床的に重大な安全性又は局所忍容性の懸念は認められなかった。健康被験者で報告された有害事象は GH 製剤を 1 日 1 回投与した臨床試験で認められた有害事象と同様であり、大部分は GH 治療の有害事象としてよく知られているものであった（「末梢性浮腫」、「筋肉痛」、「関節痛」及び「頭痛」）[8,16]。非アジア人健康被験者で認められた有害事象を器官別大分類及び基本語別に要約し、治験総括報告書〔3915 試験（M 5.3.3.1）Section 12.2、Table 12-7〕に示す。日本人被験者で認められた有害事象を器官別大分類及び基本語別に要約し、治験総括報告書〔3915 試験（M 5.3.3.1）Section 12.2、Table 12-6〕に示す。

有害事象（「末梢性浮腫」、「筋肉痛」及び「関節痛」等）の発現頻度及び重症度に用量依存的な増加がみられた〔治験総括報告書、3915 試験（M 5.3.3.1）Section 12.2、Table 12-5～12-7〕。有害事象は主に高用量のソマプシタン（単回投与：0.16 及び 0.32 mg/kg、反復投与：0.16 及び 0.24 mg/kg）で発現し、これらの用量は、成人患者において予定されている臨床用量の範囲（0.08 mg/kg 以下）を超えていると考えられる。用量のレベルの変更の詳細は 2.7.4.1.3.3 を参照のこと。

AGHD 患者を対象とした第 1 相、安全性、用量探索〔体重当たりの用量（mg/kg）〕試験（3947 試験）

AGHD 患者に対するソマプシタンの週 1 回反復皮下投与は、検討した 4 つの用量（0.02、0.04、0.08 及び 0.12 mg/kg）で良好な忍容性を示し、臨床的に重大な安全性又は局所忍容性の懸念は認められなかった。ソマプシタンの投与後に AGHD 患者で発現した有害事象はノルディトロピンの投与後に発現した有害事象と同様であり、その一部は GH 治療の有害事象としてよく知られているものであった（空腹時血糖値の上昇、浮腫、末梢性浮腫及び体重増加等）。有害事象を器官別大分類及び基本語別に要約し、治験総括報告書〔3947 試験（M 5.3.3.2）EOT Table 14.3.1.3〕に示す。

本試験では有害事象の発現頻度及び重症度に用量依存的な増加がみられた〔治験総括報告書、3947 試験（M 5.3.3.2）Table 12-2〕。有害事象及び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高用量のソマプシタン（0.08 及び 0.12 mg/kg）において高頻度で発現したことは重要である。用量のレベルの調整の詳細は 2.7.4.1.3.3 を参照のこと。

AGHD 患者では、有害事象の 3 分の 1（24 件、ソマプシタン群 26 例中 8 例で発現）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」と判定された（0.02 mg/kg：1 件、0.08 mg/kg：7 件、0.12 mg/kg：16 件）。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で、高頻度で発現した事象は「体重増加」（5 例 6 件）、「血中ブドウ糖増加」（4 例 5

件）及び浮腫（「浮腫」：3 例 3 件、「末梢性浮腫」：1 例 2 件）であった〔治験総括報告書、3947 試験（M 5.3.3.2）Section 12.3.2.2、Table 12-5〕。

多くの被験者が有害事象から回復した。4 例 6 件の軽度で非重篤な有害事象が「未回復」であった〔0.12 mg/kg：「体重増加」（3 件）、「第一度房室ブロック」、「C－反応性蛋白増加」、「血中ブドウ糖増加」〕〔治験総括報告書、3947 試験（M 5.3.3.2）Section 12.3.2.1、Table 12-4〕。

健康被験者を対象とした単回投与、AME 試験（4237 試験）

2 例 6 件の有害事象が認められたが、いずれも軽度であり、これらは治験責任医師により治験薬（ソマプシタン）との因果関係は「なし」と判定された（基本語：「口内乾燥」、「歯痛」、「錯感覚」、「傾眠」、「口腔咽頭痛」及び「皮膚刺激」）〔治験総括報告書、4237 試験（M 5.3.3.1）Section 12.3.2、Table 12-2〕。2 例ともこれらの有害事象から回復した。

腎機能障害を有する被験者を対象とした反復投与試験（4297 試験）

腎機能障害を有する被験者に対するソマプシタンの週 1 回反復皮下投与は、検討した用量（ソマプシタン 0.08 mg/kg）で良好な忍容性を示し、臨床的に重大な安全性又は局所忍容性の懸念は認められなかった。

24 例（54.5%）65 件の有害事象が報告された。いずれも軽度又は中等度であった。腎機能障害を有する被験者と正常な腎機能を有する被験者で有害事象の分布に明らかな違いは認められなかった。高頻度で発現した有害事象は「頭痛」〔10 例（22.7%）14 件〕、「末梢性浮腫」〔5 例（11.4%）6 件〕、「関節痛」〔4 例（9.1%）6 件〕であった〔治験総括報告書、4297 試験（M 5.3.3.3）Table 12-2〕。

ソマプシタンとの因果関係が「なし」と判定された有害事象が 17 例（38.6%）28 件報告され、因果関係が「可能性あり」又は「あり」と判定された有害事象が 18 例（40.9%）37 件報告された。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のうち、高頻度で発現した有害事象は、「末梢性浮腫」〔5 例（11.4%）6 件〕、「頭痛」〔7 例（15.9%）10 件〕、「関節痛」〔4 例（9.1%）6 件〕であった〔治験総括報告書、4297 試験（M 5.3.3.3）EOT Table 14.3.1.8〕。

有害事象の概要を治験総括報告書〔4297 試験（M 5.3.3.3）Table 12-1〕に示す。有害事象を器官別大分類及び基本語別に要約し、治験総括報告書〔4297 試験（M 5.3.3.3）Table 12-2〕に示す。

肝機能障害を有する被験者を対象とした反復投与試験（4298 試験）

肝機能障害を有する被験者に対するソマプシタンの週 1 回反復皮下投与は、検討した用量（ソマプシタン 0.08 mg/kg）で良好な忍容性を示し、臨床的に重大な安全性又は局所忍容性の懸念は認められなかった。

ソマプシタンの安全性及び忍容性は 3 つの肝機能別のグループ（軽度及び中等度の肝機能障害、ならびに正常な肝機能を有する被験者）で同様であった。

5 例（14.7%）9 件の有害事象が報告された（正常な肝機能を有する被験者：1 例 1 件、軽度の肝機能障害の被験者：2 例 3 件、中等度の肝機能障害の被験者：2 例 5 件）。有害事象は軽度又は中等度であり、全例が回復した。有害事象 4 件（2 例）はソマプシタンとの因果関係が「あり」と判定され、いずれも軽度の注射部位反応に関する事象であった〔治験総括報告書、4298 試験（M 5.3.3.3）Section 12.1.2.2〕。このほかに報告された 5 件の有害事象は、「皮膚炎」、「皮膚変色」、「歯痛」、「眼刺激」及び「眼そう痒症」であった〔治験総括報告書、4298 試験（M 5.3.3.3）Section 12.1.2.1〕。

有害事象の概要を治験総括報告書〔4298 試験（M 5.3.3.3）Table 12-1〕に示す。有害事象を器官別大分類及び基本語別に要約し、治験総括報告書〔4298 試験（M 5.3.3.3）Table 12-2〕に示す。

健康成人被験者を対象とした生物学的同等性試験（4491 試験）

被験者は、ソマプシタン 0.04 mg/kg を等モルで、5 mg 製剤を用いて 1 回及び 10 mg 製剤を用いて 2 回単回投与した。臨床的に重大な新規の安全性又は忍容性の懸念は認められなかった。有害事象の単位時間あたりの発現件数は 5 mg 製剤と 10 mg 製剤で同程度であり、安全性プロファイルは同様であった。

17 例（51.5%）34 件の有害事象が発現した。すべての有害事象は軽度又は中等度に分類され、すべての被験者が有害事象から回復した〔治験総括報告書、4491 試験（M 5.3.1.2）Table 12-1〕。高頻度で報告された有害事象は、「頭痛」〔5 例（15.2%）8 件〕、「背部痛」〔3 例（9.1%）3 件〕及び「嘔吐」〔2 例（6.1%）2 件〕であった〔治験総括報告書、4491 試験（M 5.3.1.2）Table 12-2、EOT Table 14.3.1.5〕。

治験責任医師によりソマプシタンとの因果関係が「なし」と判定された有害事象は 10 例（30.3%）12 件であり、「可能性あり」又は「あり」と判定された有害事象は 9 例（27.3%）22 件であった〔治験総括報告書、4491 試験（M 5.3.1.2）EOT Table 14.3.1.7〕。高頻度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」〔3 例（9.1%）5 件〕、「背部痛」〔3 例（9.1%）3 件〕及び「嘔吐」〔2 例（6.1%）2 件〕であった。

有害事象の概要を治験総括報告書〔4491 試験（M 5.3.1.2）Table 12-1〕に示す。有害事象を器官別大分類及び基本語別に要約し、治験総括報告書〔4298 試験（M 5.3.1.2）Table 12-2〕に示す。

2.7.4.2.2　死亡

4054 試験では 5 例（1.3%）の死亡が報告された。5 例とも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（ソマプシタン群 2 例、ノルディトロピン群 2 例、プラセボ群 1 例）。報告された 5 例の死亡に関する詳細を表 2.7.4.2-10 に示す。死亡した被験者のうち 2 例は日本人であった（表 2.7.4.2-10 において#を付した被験者。付録 2.7.4.7.2、Listing 23）。

死亡した被験者における有害事象の種類及び発現時期に特定の傾向はみられなかった。治療を受けた AGHD 患者の年齢を考慮すると、死亡は予想されないものではなかった。5 例の死亡に関する叙述を治験総括報告書〔4054 試験（延長期間）（M 5.3.5.1）Section 12.2.1 及び 14.3.3〕に示す。

4043 試験及び 4244 試験では死亡の報告はなかった〔治験総括報告書、4043 試験（M 5.3.5.1）Section 12.4.1 及び 4244 試験（M 5.3.5.1）Section 12.2.1〕。

表 2.7.4.2-10　AGHD 患者で報告された死亡（試験別）

Phase/ Trial	Subject ID	Sex/Age/ BMI	Preferred term	AE onset after exposure	Causality (Main/ extension)	Case number[a]
Phase 3						
Trial 4054 AGHD patients						
somapacitan[b]	601003	M/66/32.4	心室細動、心原性ショック、誤嚥性肺炎	Week 51 (Day 363)	Unlikely/ unlikely	484141
somapacitan[c]	116006	M/73/39.9	死亡（報告された用語：原因不明）	Week 65 (Day 458)	Unlikely/ unlikely	529346
Norditropin	204012[#]	M/70/25.8	肺炎	Week 51 (Day 360)	Unlikely/ unlikely	527452
Norditropin	216003[#]	M/60/28.0	インフルエンザ	Week 70 (Day 493)	Unlikely/ -[d]	581052
Placebo	702005	F/76/29.9	急性副腎皮質機能不全	Week 23 (Day 163)	Unlikely	486651
Trial 4043 AGHD patients		Not applicable				
Trial 4244 AGHD patients		Not applicable				

Abbreviations: M = Male; F = Female; Age in years; BMI: Body mass index (kg/m^2) at baseline; [#] Japanese patient. AE causality to trial product given in main/extension respectively, based on judgement of investigators.

[a] Internal case number. [b] Treated with placebo in the main phase of trial 4054; [c] Treated with Norditropin in the main phase of trial 4054.

[d] The patient was withdrawn after completing main phase of the trial and the event occurred after the patient withdrew.

4054 試験の延長期間において、プラセボ/ソマプシタン群の被験者（被験者 ID：601003）が「心室細動」、「心原性ショック」及び「誤嚥性肺炎」により死亡した（死亡時の年齢は 68 歳）。当該被験者は既往歴として、2 型糖尿病（1972 年）、高血圧（2003 年）、狭心症（2005 年）、下垂体の良性腫瘍（2007 年）、下垂体性甲状腺機能低下症（2007 年）を有していた。投与後 363 日に自宅で呼吸困難を訴え、意識を消失した。救急車内で心肺蘇生が施行された。心調律は心室細動であった。救急車内で除細動を施行したところ心室粗動を呈した。心原性ショックにて集中治療室に入院した。当該被験者は、誤嚥により誤嚥性肺炎をきたした。治験薬の最終投与は当該事象発現の 5 日前であった。入院中

は治験薬の投与は中断された。当該事象発現後 12 日に、「心室細動」、「心原性ショック」及び「誤嚥性肺炎」により死亡した。これらの有害事象と治験薬との因果関係は「なし」と判定された。

臨床薬理試験（3915 試験、3947 試験、4237 試験、4297 試験、4298 試験及び 4491 試験）では死亡の報告はなかった。

2.7.4.2.3　その他の重篤な有害事象

2.7.4.2.3.1　AGHD 患者を対象とした第 3 相試験の結果（試験別）

AGHD 患者で認められた重篤な有害事象のパターンは第 3 相試験を通じて同様であった。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及び 4054 試験のプラセボ群で同様であった。重篤な有害事象の大部分は様々な器官別大分類に分類され、1～2 例でそれぞれ 1 件ずつ報告された。

4054 試験

37 例（12.3%）68 件の重篤な有害事象が報告され、このうち 66 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（付録 2.7.4.7.1 Table 140）。

重篤な有害事象を発現した被験者の割合はソマプシタン群（9.3%）、ノルディトロピン群（11.8%）及びプラセボ群（8.2%）で同様であった（付録 2.7.4.7.1 Table 140）。重篤な有害事象の単位時間あたりの発現件数も同様であった（ソマプシタン群 14.0 件／100 人・年、ノルディトロピン群 14.5 件／100 人・年、プラセボ群 17.6 件／100 人・年）。

重篤な有害事象の概要を投与群別に付録 2.7.4.7.1 Table 140 に示す。重篤な有害事象の器官別大分類及び基本語別の要約を投与群別に付録 2.7.4.7.1 Table 142 に示す。

4043 試験

重篤な有害事象を発現した被験者の割合はソマプシタン群（6.6%）とノルディトロピン群（6.5%）で同様であった。重篤な有害事象の単位時間あたりの発現件数も同様であった（ソマプシタン群 12.9 件／100 人・年、ノルディトロピン群 19.7 件／100 人・年）。重篤な有害事象は、ソマプシタン群で 4 例 4 件（「膝蓋骨骨折」、「処置合併症」、「乳房形成」及び「胆石症」）、ノルディトロピン群で 2 例 3 件（「腸管虚血」、「短腸症候群」及び「腎結石症」）報告された。重篤な有害事象はいずれも治験責任医師により治験薬との因果関係は「なし」と判定された。重篤な有害事象の概要を治験総括報告書〔4043 試験（M5.3.5.1）EOT Table 14.3.1.2〕に示す。重篤な有害事象の器官別大分類及び基本語別の要約を治験総括報告書〔4043 試験（M5.3.5.1）Table 12-8〕に示す。

4244 試験

重篤な有害事象がソマプシタン群で 4 例（8.7%）4 件報告されたが（単位時間あたりの発現件数：8.6 件／100 人・年）、いずれも明らかに GH 治療に関連する有害事象ではなかった（「鼠径ヘルニア」、「大腸ポリープ」、「胃腸炎」及び「頭部損傷」）。ノルディトロピン群では重篤な有害事象の報告はなかった。いずれの重篤な有害事象も、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。重篤な有害事象の概要を治験総括報告書〔4244 試験（M5.3.5.1）EOT Table 14.3.1.2〕に示す。重篤な有害事象の器官別大分類及び基本語別の要約を治験総括報告書〔4244 試験（M5.3.5.1）EOT Table 14.3.1.4〕に示す。

重篤な有害事象の詳細を治験総括報告書に示す〔4054 試験（延長期間）（M 5.3.5.1）Section 12.2.2、4043 試験（M 5.3.5.1）Section 12.4.2 及び 4244 試験（M 5.3.5.1）Section 12.2.2〕。

重篤な有害事象に関する叙述の一覧を治験総括報告書に示す〔4054 試験（M 5.3.5.1）Section 14.3.3、4054 試験（延長期間）（M 5.3.5.1）Section 14.3.3、4043 試験（M 5.3.5.1）Section 14.3.3 及び 4244 試験（M 5.3.5.1）Section 14.3.3〕。

2.7.4.2.3.2　AGHD 患者を対象とした第 3 相試験の結果（第 3 相試験併合）

第 3 相試験併合における重篤な有害事象の概要を表 2.7.4.2-11 に、要約を表 2.7.4.2-12（器官別大分類及び基本語別）に示す。

AGHD 患者を対象とした第 3 相試験では、47 例（10.4%）79 件の重篤な有害事象が報告され、このうち 77 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（表 2.7.4.2-11）。

重篤な有害事象を発現した被験者の割合はソマプシタン群（8.7%）、ノルディトロピン群（9.6%）及びプラセボ群（8.2%）で同様であった。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とノルディトロピン群で同様であり、プラセボ群より少なかった（ソマプシタン群 13.2 件／100 人・年、ノルディトロピン群 13.7 件／100 人・年、プラセボ群 17.6 件／100 人・年）。

重篤な有害事象の大部分は様々な器官別大分類に分類され、1～2 例でそれぞれ 1 件ずつ報告された（表 2.7.4.2-12 及び付録 2.7.4.7.1 Table 8）。ソマプシタン群では「胃腸炎」が 3 例で報告された。

2 件の重篤な有害事象（4054 試験）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」と判定された（付録 2.7.4.7.1 Table 13）。

- ソマプシタン群「膀胱移行上皮癌」。因果関係は「可能性あり」。治験薬投与について変更はなかった。慢性状態となり、転帰は「未回復」。詳細を表 2.7.4.2-38 に示す。注目すべきこととして、当該被験者には 30 年にわたる喫煙歴があり、当該有害事象の治験薬投与以外の説明として、この喫煙歴が考えられた。

- ノルディトロピン群「血液濃縮」。因果関係は「あり」。治験薬投与を中止した。転帰は「回復」。

3 例が重篤な有害事象のために治験薬投与を中止した（2.7.4.2.4）。

死亡に至った被験者は 5 例であった（2.7.4.2.2）。各試験のカットオフ日までに回復しなかった事象は 4 件であった〔ソマプシタン群「睡眠時無呼吸症候群」、「脊椎圧迫骨折」及び「膀胱移行上皮癌」。ノルディトロピン群「形質細胞性骨髄腫」。治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）Listing 16.2.7.1〕。また、転帰が「不明」であった事象は 1 件であった〔ソマプシタン群「処置合併症」。なお、本事象は術中（予定関節半月板手術）に発現した合併症であった。総括報告書、4043 試験（M 5.3.5.1）Section 12.4.2〕。これ以外の事象は、各試験のカットオフ日時点で「回復」又は「軽快」と報告された（表 2.7.4.2-11）。

3 ヵ月ごとの重篤な有害事象の発現状況を表 2.7.4.2-13 に示す。有害事象の発現状況には群間で違いがみられたが、試験デザインに起因していずれの群でも長期の曝露を受けた被験者数はより少なくなったことを考慮する必要がある。

表 2.7.4.2-11　AGHD 患者で報告された重篤な有害事象の概要（第 3 相試験併合）

	placebo			Norditropin			somapacitan			total		
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Subjects Exposed	61				166				333				454			
Total patient years	39.8				161.0				377.8				578.7			
All SAEs	5	(8.2)	7	17.6	16	(9.6)	22	13.7	29	(8.7)	50	13.2	47	(10.4)	79	13.7
Severity																
Mild	1	(1.6)	1	2.5	1	(0.6)	1	0.6	6	(1.8)	6	1.6	7	(1.5)	8	1.4
Moderate	1	(1.6)	1	2.5	7	(4.2)	7	4.3	11	(3.3)	15	4.0	18	(4.0)	23	4.0
Severe	3	(4.9)	5	12.6	10	(6.0)	14	8.7	15	(4.5)	29	7.7	27	(5.9)	48	8.3
Causality																
Unlikely	5	(8.2)	7	17.6	16	(9.6)	21	13.0	28	(8.4)	49	13.0	46	(10.1)	77	13.3
Possible	0				0				1	(0.3)	1	0.3	1	(0.2)	1	0.2
Probable	0				1	(0.6)	1	0.6	0				1	(0.2)	1	0.2
Outcome																
Recovered/Resolved	3	(4.9)	5	12.6	13	(7.8)	18	11.2	22	(6.6)	41	10.9	36	(7.9)	64	11.1
Recovering/Resolving	0				0				1	(0.3)	1	0.3	1	(0.2)	1	0.2
Recovered/ Resolved with sequelae	1	(1.6)	1	2.5	1	(0.6)	1	0.6	0				2	(0.4)	2	0.3
Not Recovered/Not Resolved	0				1	(0.6)	1	0.6	3	(0.9)	3	0.8	4	(0.9)	4	0.7
Fatal	1	(1.6)	1	2.5	2	(1.2)	2	1.2	2	(0.6)	4	1.1	5	(1.1)	7	1.2
Unknown	0				0				1	(0.3)	1	0.3	1	(0.2)	1	0.2
Action																
Drug Interrupted	1	(1.6)	1	2.5	4	(2.4)	6	3.7	1	(0.3)	3	0.8	6	(1.3)	10	1.7
Drug Withdrawn	0				2	(1.2)	2	1.2	0				2	(0.4)	2	0.3
Dose Reduced	0				1	(0.6)	1	0.6	0				1	(0.2)	1	0.2
Dose Not Changed	3	(4.9)	5	12.6	9	(5.4)	11	6.8	25	(7.5)	39	10.3	35	(7.7)	55	9.5
Not Applicable	1	(1.6)	1	2.5	2	(1.2)	2	1.2	4	(1.2)	8	2.1	7	(1.5)	11	1.9
Treatment discont due AEs	0				3	(1.8)	3	1.9	0				3	(0.7)	3	0.5

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years; Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054. AE causality is based on judgement of investigators. MedDRA version 21.0.

表 2.7.4.2-12　AGHD 患者で報告された重篤な有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All serious adverse events	5 (8.2)	7	17.6	16 (9.6)	22	13.7	29 (8.7)	50	13.2	47 (10.4)	79	13.7
感染症および寄生虫症	1 (1.6)	1	2.5	5 (3.0)	7	4.3	8 (2.4)	11	2.9	13 (2.9)	19	3.3
胃腸炎	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
ウイルス性胃腸炎	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
虫垂炎	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
尿路感染	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
インフルエンザ	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
ウイルス感染	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
ウイルス性上気道感染	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
ウイルス性肺炎	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
クロストリジウム・ディフィシレ感染	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
単純ヘルペス	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
尿路性敗血症	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
敗血症	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
肺炎	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
胃腸障害	2 (3.3)	3	7.5	2 (1.2)	4	2.5	6 (1.8)	7	1.9	10 (2.2)	14	2.4
嘔吐	1 (1.6)	1	2.5	0			2 (0.6)	2	0.5	3 (0.7)	3	0.5
急性膵炎	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
単径ヘルニア	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
下痢	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
口内炎	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
歯嚢胞	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
大腸ポリープ	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
短腸症候群	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
腸管虚血	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
腹痛	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
傷害、中毒および処置合併症	0			2 (1.2)	3	1.9	6 (1.8)	6	1.6	8 (1.8)	9	1.6
各種物質毒性[a]	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
歯牙破折	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
処置合併症	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
脊椎圧迫骨折	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
調剤過誤	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
転倒	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
頭部損傷	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
膝蓋骨骨折	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
脛骨骨折	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
内分泌障害	1 (1.6)	1	2.5	1 (0.6)	1	0.6	4 (1.2)	4	1.1	6 (1.3)	6	1.0
急性副腎皮質機能不全	1 (1.6)	1	2.5	0			2 (0.6)	2	0.5	3 (0.7)	3	0.5
下垂体機能低下症	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
続発性副腎皮質機能不全	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
尿崩症	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
一般・全身障害および投与部位の状態	0			0			5 (1.5)	5	1.3	5 (1.1)	5	0.9
疲労	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
死亡	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
発熱	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
非心臓性胸痛	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
呼吸器、胸郭および縦隔障害	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
誤嚥性肺炎	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
睡眠時無呼吸症候群	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
労作性呼吸困難	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
腎および尿路障害	0			3 (1.8)	3	1.9	0			3 (0.7)	3	0.5
腎結石症	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
慢性腎臓病	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
臨床検査	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5
血中テストステロン増加	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
心電図異常T波	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
胆管造影	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
外科および内科処置	0			0			2 (0.6)	4	1.1	2 (0.4)	4	0.7
胆嚢切除	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
動脈ステント挿入	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
乳房形成	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
臍ヘルニア修復	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
心臓障害	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
心原性ショック	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
心室細動	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
心室性期外収縮	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
形質細胞性骨髄腫	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
膀胱移行上皮癌	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
肝胆道系障害	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
胆石症	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
血液およびリンパ系障害	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
血液濃縮	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
血管障害	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
高血圧	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
神経系障害	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
意識レベルの低下	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
頭痛	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
精神障害	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
譫妄	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
代謝および栄養障害	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
低ナトリウム血症	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
皮膚および皮下組織障害	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
アトピー性皮膚炎	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

[a]Drug toxicity secondary to anti-tuberculous therapy (trial 4054-ext, case no. 526437).

表 2.7.4.2-13 AGHD 患者で報告された 3 ヵ月ごとの重篤な有害事象の発現状況（第 3 相試験併合）

	placebo N (%)	E	Norditropin N (%)	E	somapacitan N (%)	E	total N (%)	E
Subjects Exposed	61		166		333		454	
All serious adverse events	5 (100.0)	7	16 (100.0)	22	29 (100.0)	50	47 (100.0)	79
Time after start of exposure								
0-<3 months	1 (20.0)	3	7 (43.8)	9	7 (24.1)	11	15 (31.9)	23
3-<6 months	4 (80.0)	4	5 (31.3)	5	8 (27.6)	11	16 (34.0)	20
6-<9 months	0		1 (6.3)	2	6 (20.7)	7	7 (14.9)	9
9-<12 months	0		1 (6.3)	1	7 (24.1)	13	8 (17.0)	14
12-<15 months	0		2 (12.5)	4	1 (3.4)	2	3 (6.4)	6
15-<18 months	0		1 (6.3)	1	3 (10.3)	3	4 (8.5)	4
18-<21 months	0		0		1 (3.4)	3	1 (2.1)	3

N: Number of subjects, %: Percentage of subjects having serious adverse events, E: Number of events
For subjects in 4054 time is calculated from start of current treatment.
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
Exposure to placebo was only done in 4054 and for no more than 35 weeks.
Month = 30 days.

ノルディトロピン/ソマプシタン併合

重篤な有害事象のプロファイルは、第 3 相試験併合とノルディトロピン/ソマプシタン併合で同様であった。ノルディトロピン/ソマプシタン併合において有害事象を発現した被験者の割合及び単位時間あたりの発現件数を調整の有無で比較した要約表を付録 2.7.4.7.1、Table 106 に示す。

2.7.4.2.3.3　日本人被験者の結果を含む AGHD 患者を対象とした第 3 相試験の結果

4054 試験

全集団（主要試験期間+延長期間）では、37 例（12.3%）68 件の重篤な有害事象が報告され、このうち 66 件が治験責任医師により治験薬との因果関係が「なし」と判定された。重篤な有害事象を発現した被験者の割合はソマプシタン/ソマプシタン群〔13 例（10.8%）24 件〕とノルディトロピン/ノルディトロピン群〔5 例（9.6%）9 件〕で同様であった〔治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）Table 14.3.1.5〕。プラセボ/ソマプシタン群〔8 例（13.1%）21 件〕、ノルディトロピン/ソマプシタン群〔7 例（13.7%）9 件〕及びノルディトロピン/ー群〔4 例（25.0%）5 件〕では、重篤な有害事象を発現した被験者の割合がやや高かった。

重篤な有害事象の大部分はそれぞれ 1 件の報告であったが、ソマプシタン/ソマプシタン群では「胃腸炎」が 2 件、プラセボ/ソマプシタン群では「嘔吐」が 2 件、「急性副腎皮質機能不全」が 2 件、ノルディトロピン/ノルディトロピン群では「尿路性敗血症」が 2 件（1 例）報告された。

日本人集団では、6 例 7 件の重篤な有害事象が報告された（表 2.7.4.2-14）。いずれも治験薬との因果関係は「なし」と判定された。

表 2.7.4.2-14　日本人 AGHD 患者で報告された重篤な有害事象（4054 試験）

Treatment	Sex/Age/ BMI	Preferred term	Onset day/ phase/ duration (days)	Severity/Causality	Action taken	Outcome
Placebo/ somapacitan	M/52/29.2	心電図異常 T 波	176/main/63	Mild/unlikely	Drug interrupted	Recovered
		睡眠時無呼吸症候群	315/ext/-	Mild/unlikely	None	Not recovered
Placebo/ somapacitan	F/72/18.1	尿路感染	583/ext/10	Moderate/unlikely	None	Recovered
Placebo/ somapacitan	M/56/27.3	低ナトリウム血症	177/main/6	Moderate/unlikely	None	Recovered
Norditropin/so mapacitan	M/68/23.3	形質細胞性骨髄腫 [a]	146/main/-	Severe/unlikely	Drug withdrawn in extension	Not recovered
Norditropin/No rditropin	M/70/25.8	肺炎	360/ext/14	Severe/unlikely	None	Fatal

Treatment	Sex/Age/ BMI	Preferred term	Onset day/ phase/ duration (days)	Severity/Causality	Action taken	Outcome
Norditropin/No treatment	M/60/28.0	インフルエンザ	493/ext/7	Moderate/unlikely	NA	Fatal

Abbreviations: M = Male; F = Female; Age in years; BMI = Body mass index (kg/m^2) at baseline;
[a] AE onset in main and drug withdrawn in extension. Main = main phase of the trial; ext = extension phase of the trial.

心電図に関連する有害事象の詳細は表 2.7.4.2-32 を参照のこと。「形質細胞性骨髄腫」の詳細は表 2.7.4.2-38 を参照のこと。

ノルディトロピン群では死亡に至った重篤な有害事象が 2 件（「肺炎」及び「インフルエンザ」）報告された（詳細は 2.7.4.2.2 を参照のこと）。

4054 試験（主要試験期間+延長期間）では、重篤な有害事象のプロファイルについて、日本人集団と全集団間で明らかな違いはみられなかった。

重篤な有害事象に関する叙述の一覧を治験総括報告書〔4054 試験（延長期間）（M 5.3.5.1）Section 14.3.3〕に示す。主要試験期間+延長期間の重篤な有害事象については、付録 2.7.4.7.2 Listing 25（日本人集団）及び治験総括報告書〔4054 試験（延長期間）（M 5.3.5.1）Table 14.3.1.5 及び 14.3.1.11〕（全集団）を参照のこと。

4043 試験

全集団で報告された重篤な有害事象を 2.7.4.2.3.1 に示す。

4043 試験では、ソマプシタン群の日本人被験者 1 例で 1 件の重篤な有害事象「膝蓋骨骨折」が報告された（表 2.7.4.2-15）。

4043 試験では、重篤な有害事象のプロファイルについて、日本人集団と全集団間で明らかな違いはみられなかった。

表 2.7.4.2-15　　日本人 AGHD 患者で報告された重篤な有害事象（4043 試験）

Treatment	Sex/Age/BMI	Preferred term	Onset day/ duration (days)	Severity/Causality	Action taken	Outcome
somapacitan	M/63/31.0	膝蓋骨骨折	26/165	Moderate/unlikely	No change in dose	Recovering

Abbreviations: M = Male; Age in years; BMI = Body mass index (kg/m^2) at baseline;

重篤な有害事象に関する叙述の一覧を治験総括報告書〔4043 試験（M 5.3.5.1）Section 14.3.3〕に示す。重篤な有害事象については、付録 2.7.4.7.2 Listing 26（日本人集団）及び治験総括報告書〔4043 試験（M 5.3.5.1）Section 12.4.2 Table 12-8〕（全集団）を参照のこと。

4244 試験

4244 試験では、ソマプシタン群の日本人被験者 4 例で 4 件の重篤な有害事象が報告された（表 2.7.4.2-16）。4 件の重篤な有害事象に関する叙述の一覧を治験総括報告書〔4244 試験（M 5.3.5.1）Section 14.3.3〕に示す。

表 2.7.4.2-16　　日本人 AGHD 患者で報告された重篤な有害事象（4244 試験）

Treatment	Sex/Age/BMI	Preferred term	Onset day/ duration (days)	Severity/Causality	Action taken	Outcome
somapacitan	M/54.3/28.0	頭部損傷	295/3	Mild/unlikely	None	Recovered
somapacitan	M/44.8/20.8	大腸ポリープ	89/120	Mild/unlikely	None	Recovered
somapacitan	M/60.7/20.5	鼠径ヘルニア	82/148	Mild/unlikely	None	Recovered
somapacitan	F/37.4/20.3	胃腸炎	56/7	Moderate/unlikely	None	Recovered

Abbreviations: M = Male; F = Female; Age in years; BMI: Body mass index (kg/m^2) at baseline;

2.7.4.2.3.4　　臨床薬理試験の結果

健康被験者に対するソマプシタンの単回投与又は反復投与後に重篤な有害事象の報告はなかった（3915 試験、4237 試験及び 4491 試験）。

4297 試験では、腎機能障害を有する被験者において重篤な有害事象は報告されなかった。なお、事後調査から 16 日後に「関節脱臼」を発現した 1 例（血液透析を必要とする被験者）が入院した（重症度は中等度であった）。この重篤な有害事象について、ソマプシタンとの因果関係は「なし」と判定された。当該被験者は、外科手術が施行され、当該事象から回復した。当該事象に関する叙述の一覧を治験総括報告書〔4297 試験（M 5.3.3.3）Sections 14.3.3〕に示す。

4298 試験では、肝機能障害を有する被験者において重篤な有害事象は報告されなかった〔治験総括報告書、4298 試験（M 5.3.3.3）Section 12.2.2〕。

3947 試験では、AGHD 患者を対象として 4 週間までのソマプシタン週 1 回投与後に、4 例 5 件の重篤な有害事象が報告された（表 2.7.4.2-17）。4 例はいずれも回復した。4 件の重篤な有害事象については、治験薬との因果関係は「なし」と判定され、1 件（「国際標準比減少」）は「可能性あり」と判定された。1 件の重篤な有害事象（「胃腸炎」）により治験薬の投与中止に至った（ソマプシタン 0.02 mg/kg）。その他の重篤な有害事象で、治験薬投与の変更に至った事象はなかった。重篤な有害事象 1 件（「敗血症」）は生命を脅かす事象と判断された。重篤な有害事象に関する叙述の一覧を治験総括報告書〔3947 試験（M 5.3.3.2）Section 14.3.3〕に示す。

表 2.7.4.2-17　　AGHD 患者で報告された重篤な有害事象（3947 試験、反復投与）

Treatment somapacitan mg/kg	Sex/Age/ BMI	Preferred term	Onset day/ duration (days)	Severity/ Causality	Action taken	Outcome
0.02 mg/kg	M/34/28.6	胃腸炎	Day 3/5 days	Severe/unlikely	Trial drug withdrawn	Recovered
0.02 mg/kg	M/66/30.4	国際標準比減少	Day 2/10 days	Mild/possibly	No action	Recovered
0.04 mg/kg	M/68/32.2	敗血症	Day 4/16 days	Severe/unlikely	No action	Recovered
		心房細動	Day 6/5 days	Moderate/unlikely	No action	Recovered
0.12 mg/kg	F/64/33.7	腎癌	Day 25/119 days	Severe/unlikely	NA	Recovered

Abbreviations: M = Male; F = Female; Age in years; BMI: Body mass index (kg/m^2) at baseline; Causality as judged by the investigator; INR=International Normalised Ratio. The 'INR decreased' was reported as a suspected unexpected serious adverse reaction (SUSAR); Renal cancer was reported as 'renal cell carcinoma' of the right kidney.

2.7.4.2.4　　その他の重要な有害事象

2.7.4.2.4.1　　試験の中止又は治験薬投与の中止に至った有害事象

試験の中止又は治験薬投与の中止に至った有害事象を試験別に表 2.7.4.2-18 に示す。

AGHD 患者を対象とした第 3 相試験の結果

試験の中止又は治験薬投与の中止に至った有害事象の大部分は 4054 試験で報告された（4054 試験：ソマプシタン群 6 例、ノルディトロピン群 4 例、プラセボ群 1 例、4043 試験：ソマプシタン群 1 例、ノルディトロピン群 1 例、4244 試験：ノルディトロピン群 1 例）。

第 3 相試験において、有害事象のために治験薬の投与を中止した AGHD 患者数はソマプシタン群（7 例）とノルディトロピン群（6 例）で同様であった（表 2.7.4.2-18）。プラセボ群では 1 例が有害事象のために治験薬の投与を中止した。

第 3 相試験において、有害事象のために治験薬の投与を中止したソマプシタン群の 7 例を試験別に表 2.7.4.2-18 に示す。このうち 4 例で認められた有害事象は、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（「グリコヘモグロビン増加」、「脂肪肝」、「下垂体の良性腫瘍」、「疲労」、「無力症」及び「注意力障害」）、3 例で認められた有害事象は治験薬との因果関係が「なし」と判定された〔「下垂体腫瘍」（日本人被験者）、「甲状腺障害」及び「形質細胞性骨髄腫」（日本人被験者）〕。「形質細胞性骨髄腫」は重篤な有害事象であった。「下垂体腫瘍」及び「形質細胞性骨髄腫」の詳細を表 2.7.4.2-38 に示す。

第 3 相試験において、有害事象のために治験薬の投与を中止したノルディトロピン群の 6 例を試験別に表 2.7.4.2-18 に示す。このうち 4 例で認められた有害事象は、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〔「糖尿病」（日本人被験者 2 例）、「血液濃縮」、「無力症」、「傾眠」、「注意力障害」及び「頭痛」〕、2 例で認められた有害事象は治験薬との因果

関係が「なし」と判定された（「胃腸炎」及び「アトピー性皮膚炎」）。重篤な有害事象は 2 件であった（「血液濃縮」及び「アトピー性皮膚炎」）。ノルディトロピン群で報告された 2 件の「糖尿病」の詳細を 2.7.4.3.2.1 に示す。

第 3 相試験で、有害事象のために治験薬の投与中止に至った日本人被験者は 4 例であった〔ソマプシタン群 2 例及びノルディトロピン群 2 例（表 2.7.4.2-18 では該当する被験者に「#」を付している）。

臨床薬理試験の結果

3915 試験では、反復投与パートにおいてソマプシタンの投与を受けた健康被験者 2 例（42 歳及び 26 歳）が心電図の異常及び発熱を伴う上咽頭炎／感冒のために試験を中止した（表 2.7.4.2-18）。いずれもソマプシタン 0.24 mg/kg の投与を受けた被験者であった。治験責任医師は、後に心電図を再評価し、治験薬との因果関係の判定（「可能性あり」）に関し、疑わしいとコメントしている（詳細は表 2.7.4.2-18 の脚注参照）。

3947 試験では、ソマプシタンの投与を受けた AGHD 患者 2 例が最初の 1 週間以内に有害事象のために試験を中止した（表 2.7.4.2-18）。1 件の「胃腸炎」（ソマプシタン 0.02 mg/kg）が重篤な有害事象であったが、治験責任医師により治験薬との因果関係は「なし」と判定された。他の 1 例の中止例は「体重増加」及び「浮腫」（ソマプシタン 0.08 mg/kg、BMI 22.9 kg/m^2、67 歳、男性）によるもので、いずれの事象も非重篤かつ軽度に分類され、治験責任医師により治験薬との因果関係が「あり」と判定された。2 例ともこれらの事象から回復した。

4237 試験、4297 試験、4298 試験及び 4491 試験では有害事象による治験薬投与の中止又は試験の中止は報告されなかった。

治験薬の投与中止に至った有害事象及び試験の中止に至った有害事象に関する叙述を治験総括報告書に示す〔3915 試験（M 5.3.3.1）Section 14.3.3、3947 試験（M 5.3.3.2）Section 14.3.3、4043 試験（M 5.3.5.1）Section 14.3.3、4054 試験（M 5.3.5.1）Section 14.3.3 及び 4244 試験（M 5.3.5.1）Section 14.3.3〕。

表 2.7.4.2-18　試験の中止又は治験薬投与の中止に至った有害事象を発現した被験者

Treatment group	Subject ID	Sex/Age/ BMI	Preferred term	Onset day/ Duration (days)	Severity	SAE	Causality
Phase 3							
Trial 4054 AGHD patients							
Somapacitan	109004[a]	F/29/41.2	グリコヘモグロビン増加* 脂肪肝*	Day 457/ – Day 457/ –	Mild Mild	No No	Possible Possible
Somapacitan	116006[b]	M/73/39.9	下垂体の良性腫瘍	Day 298/64	Moderate	No	Unlikely/ Possible[c]
Somapacitan	204008#	M/52/29.2	下垂体腫瘍*	Day 558/ –	Mild	No	Unlikely
Somapacitan	403001	M/29/34.6	疲労	Day 330/201	Mild	No	Probably
Somapacitan	552001	F/35/29.5	甲状腺障害*	Day 376/ –	Moderate	No	Unlikely
Somapacitan	211004#	M/68/23.3	形質細胞性骨髄腫 [d]*	Day 146/ –	Severe	Yes	Unlikely
Placebo	126005	M/66/28.0	肝酵素上昇*	Day 185/ –	Moderate	No	Unlikely
Norditropin	216003#	M/60/28.0	糖尿病	Day 177/60	Mild	No	Probably
Norditropin	303005	F/39/26.7	胃腸炎	Day 87/17	Moderate	No	Unlikely
Norditropin	455004	M/45/34.2	血液濃縮	Day 236/21	Severe	Yes	Probably
Norditropin	505004	M/49/25.7	アトピー性皮膚炎	Day 10/16	Severe	Yes	Unlikely
Trial 4043 AGHD patients							
somapacitan	303006	M/57/20.7	無力症、注意力障害 [e]*	Day 1/88	Moderate	No	Probably
Norditropin	303004	F/46/22.8	無力症、傾眠、注意力障害、頭痛*	Day 2/ –	Moderate	No	Probably
Trial 4244 AGHD patients (Japanese)							
Norditropin	111006#	F/63/32.8	糖尿病*	236/ –	Mild	No	Possibly
Phase 1 Trial 3915 Healthy subjects							
soma 0.24 mg/kg	201184	M/42/25.5	心電図 2 相性 T 波	Day 8/3	Mild	No	Possibly[f]
soma 0.24 mg/kg	201190	M/26/26.2	上咽頭炎	Day 19/8	Moderate	No	Unlikely
Trial 3947 AGHD patients							
soma 0.02 mg/kg	101002	M/34/28.6	胃腸炎	Day 3/5	Severe	Yes	Unlikely
soma 0.08 mg/kg	102008	M/67/22.9	体重増加	Day 8/8	Mild	No	Probably
			浮腫	Day 8/8	Mild	No	Probably

Abbreviations: M = Male; F = Female; Age in years; BMI: Body mass index (kg/m^2) at baseline; AE causality is based on judgement of investigators. '–' = not available; *Not recovered or recovering at database lock.

Japanese AGHD patient.

[a.] Reason for discontinuation was reported as 'withdrawn by subject' with the comment due to AEs (HbA_{1c} increased and hepatic steatosis).

[b.] Reason for discontinuation was reported as 'other' (pituitary tumour benign).

[c.] Causality in main/extension phase of trial 4054.

[d.] The AE started in the main phase of the trial (while on Norditropin) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial. The condition was considered to be chronic. Outcome was reported as not recovered.

[e.] The reason for withdrawal was reported as 'AE: Dose not efficient' and the actual AEs as the reason for treatment discontinuation. The patient was reported as recovering.

[f.] Later (according to the investigator) the fact that the ECG abnormalities disappeared and reappeared again without dosing made the relationship to trial medication questionable. The subject was a 42-year-old man who experienced mild abnormalities in ECG (ECG T wave biphasic) (8-21 Jan 2013) from 2 days after initiation of trial drug (6-Jan-2013). The subject recovered completely from the events. The subject was withdrawn on 23 Jan 2013. The subject received the planned dose of 0.24 mg/kg on Day 1 and Day 8.

2.7.4.2.4.2　治験薬の投与量減量に至った有害事象

AGHD 患者を対象とした第 3 相試験の結果

4054 試験では、治験薬の投与量減量に至った重篤な有害事象（「血中テストステロン増加」）が 1 件認められた。当該事象は「血液濃縮」を発現したノルディトロピン群の 1 例で報告された（表 2.7.4.2-18）。血中テストステロン濃度が高値であったため、ノルディトロピンの投与量を 0.20 mg/kg/日（一時的に 0.25 mg/kg/日）まで減量し、その後、「血液濃縮」のために治験薬の投与を中止した。

4043 試験では、治験薬の投与量減量に至った有害事象は認められなかった。

4244 試験では、2 例（4.3%）4 件の軽度の有害事象によりソマプシタンの投与量を減量した。

- 被験者 ID：105004「口渇」（ソマプシタンとの因果関係：「なし」、転帰：「回復」）。投与量を 4.10 mg（16 週時点）から記録された最終投与量である 3.8 mg まで減量した。
- 被験者 ID：106002「筋骨格硬直」、「感覚鈍麻」及び「弾発指」（ソマプシタンとの因果関係：「可能性あり」又は「あり」、転帰「軽快」）。投与量を 1.5 mg（8 週時点）から 1.1 mg（12 週時点）、1.0 mg（16 週時点）まで減量した。

臨床薬理試験の結果

3915 試験及び 3947 試験では用量の減量はなかった。3915 試験及び 3947 試験（mg/kg で投与）では予定された用量レベルへの漸増は行われなかった（2.7.4.1.3.3 参照）。

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　完了した第 3 相試験の概要（試験別）

AGHD 患者を対象とした第 3 相試験全体で、特定の有害事象について同様のパターンが認められた。ほとんどの場合、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

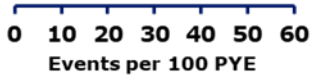
で同様であり、4054 試験ではプラセボ群も大きな違いはみられなかった。投与を受けた AGHD 患者の大部分のデータは 4054 試験から得られており、有害事象の大部分は 4054 試験で認められた。

各試験における特に注目すべき安全性領域及び単位時間あたりの発現件数を器官別又は症候群別に図 2.7.4.2-6 に示す。さらに、特に注目すべき安全性領域を試験別に付録 2.7.4.7.1、Table 145～228 に要約する。

第 3 相試験全体で有害事象のパターンに大きな違いがみられなかったため、特に注目すべき安全性領域も第 3 相試験併合に基づいて評価した。注目すべき安全性領域の詳細を第 3 相試験併合に基づいて、それぞれ 2.7.4.2.5.2～2.7.4.2.5.12 に示す。各項には試験別の結果及び参照先も示す。

■ Somapacitan
● Placebo
▲ Norditropin®

Safety area of special interest	Adverse event rate	Phase 3 pool (N=333/61/166)		Phase 3 pool (N=333/61/166)				Trial 4054 (N=226/61/119)						Trial 4043 (N=61/31)				Trial 4244 (N=46/16)			
		Soma		Placebo		Nordi		Soma		Placebo		Nordi		Soma		Nordi		Soma		Nordi	
		%	R	%	R	%	R	%	R	%	R	%	R	%	R	%	R	%	R	%	R
頭痛		12.9	28.8	16.4	37.7	13.3	52.8	14.2	31.3	16.4	37.7	12.6	55.9	11.5	35.6	19.4	65.5	8.7	8.6	6.3	13.2
アレルギー反応		8.1	8.7	14.8	25.1	15.1	18.6	10.6	10.0	14.8	25.1	15.1	17.6	1.6	3.2	6.5	13.1	4.3	4.3	31.3	33.0
まれな事象		6.3	6.4	8.2	12.6	7.8	11.2	9.3	8.0	8.2	12.6	10.1	12.3			3.2	13.1				
疲労／無力症		9.9	10.3	6.6	10.0	11.4	12.4	8.8	8.0	6.6	10.0	9.2	9.2	19.7	45.3	22.6	45.9	2.2	2.2	6.3	6.6
末梢性浮腫		4.5	7.4	1.6	2.5	4.8	7.5	6.6	9.3	1.6	2.5	6.7	9.2								
関節痛		6.9	6.6	1.6	2.5	10.2	11.2	6.6	5.3	1.6	2.5	11.8	11.5	8.2	16.2	6.5	13.1	6.5	8.6	6.3	6.6
心電図に関連する有害事象		2.7	2.9	3.3	5.0	4.2	6.2	4.0	3.7	3.3	5.0	5.0	6.1			3.2	13.1				
体重増加		2.7	2.6			1.2	1.2	2.7	2.3			0.8	0.8	4.9	9.7	3.2	6.6				
筋肉痛		2.1	2.4	4.9	7.5	4.8	5.0	2.7	2.7	4.9	7.5	5.0	4.6	1.6	3.2	3.2	6.6			6.3	6.6
脂肪肥大症		1.5	1.3					2.2	1.7												
新生物		2.1	1.9			2.4	3.1	2.2	1.7			3.4	3.8					4.3	4.3		
副腎皮質機能不全		2.4	2.1	1.6	2.5	1.2	1.2	2.7	2.0	1.6	2.5	1.7	1.5	3.3	6.5						
注射部位反応		1.5	2.4	4.9	12.6	5.4	5.6	1.8	2.7	4.9	12.6	6.7	6.1					2.2	2.2	6.3	6.6
高血糖		1.2	1.6			0.6	3.1	1.8	2.0			0.8	3.8								
2型糖尿病		1.5	2.1			3.0	5.6	1.8	2.3			3.4	6.1	1.6	3.2					6.3	6.6
錯感覚		1.5	1.6	3.3	5.0	0.6	0.6	1.8	1.7	3.3	5.0	0.8	0.8	1.6	3.2						
代謝系障害（血糖コントロール）		1.5	2.1	1.6	2.5	3.0	5.6	1.8	2.3	1.6	2.5	3.4	6.1	1.6	3.2					6.3	6.6
脂肪組織萎縮症		0.6	1.1			0.6	0.6	0.9	1.3			0.8	0.8								
血中アルカリホスファターゼ増加		0.6	0.5					0.9	0.7												
甲状腺機能低下症		0.6	0.5	1.6	2.5	4.8	5.0	0.4	0.3	1.6	2.5	4.2	3.8	1.6	3.2	9.7	19.7				
手根管症候群		0.6	0.5					0.4	0.3					1.6	3.2						
膵炎				1.6	2.5	0.6	0.6			1.6	2.5	0.8	0.8								



Abbreviations: N = number of patients in somapacitan, placebo and Norditropin groups, respectively; Nordi = Norditropin; % = proportion of patients with event; R = event rate; Soma = somapacitan.

Notes: phase 3 pool includes data from trials 4054, 4244 and 4043.

図 2.7.4.2-6　　特に注目すべき安全性領域（第 3 相試験併合及び試験別）

2.7.4.2.5.2　内分泌障害

甲状腺機能低下症

甲状腺機能低下症の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 145～147 に示す。該当する有害事象は 4054 試験及び 4043 試験で報告された。

甲状腺機能低下症の有害事象を発現した被験者の割合はノルディトロピン群及びプラセボ群と比較してソマプシタン群で低かった（表 2.7.4.2-19）。

表 2.7.4.2-19　AGHD 患者で発現した甲状腺機能低下症の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All hypothyroidism events	1 (1.6)	1	2.5	8 (4.8)	8	5.0	2 (0.6)	2	0.5
内分泌障害	1 (1.6)	1	2.5	8 (4.8)	8	5.0	2 (0.6)	2	0.5
甲状腺機能低下症	1 (1.6)	1	2.5	4 (2.4)	4	2.5	2 (0.6)	2	0.5
続発性甲状腺機能低下症	0			4 (2.4)	4	2.5	0		

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

副腎皮質機能不全

副腎皮質機能不全の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 223～225 に示す。該当する有害事象は 4054 試験及び 4043 試験で報告されたが、4244 試験では報告されなかった。

副腎皮質機能不全の有害事象の発現件数はいずれの投与群でも少なかった（表 2.7.4.2-20）。

副腎皮質機能不全の有害事象の単位時間あたりの発現件数は投与群間で同様であった（ソマプシタン：2.1 件／100 人・年、ノルディトロピン：1.2 件／100 人・年、プラセボ：2.5 件／100 人・年）。これらの事象を発現した被験者数が少なかったことを考慮すると、当該事象を発現した被験者の割合は投与群間で同様であった（ソマプシタン：2.4%、ノルディトロピン：1.2%、プラセボ：1.6%）。

表 2.7.4.2-20　　AGHD 患者で発現した副腎皮質機能不全（二次性）の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All adrenocortical insufficiency (secondary) events	1 (1.6)	1	2.5	2 (1.2)	2	1.2	8 (2.4)	8	2.1
内分泌障害	1 (1.6)	1	2.5	2 (1.2)	2	1.2	8 (2.4)	8	2.1
急性副腎皮質機能不全	1 (1.6)	1	2.5	0			4 (1.2)	4	1.1
副腎機能不全	0			0			4 (1.2)	4	1.1
グルココルチコイド欠乏症	0			1 (0.6)	1	0.6	0		
続発性副腎皮質機能不全	0			1 (0.6)	1	0.6	0		

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

2.7.4.2.5.3　　胃腸障害

膵炎

膵炎の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 148～150 に示す。該当する有害事象は 4054 試験で報告されたが、4043 試験及び 4244 試験では報告されなかった。

ソマプシタン群では膵炎の有害事象の発現はなく、ノルディトロピン群及びプラセボ群ではそれぞれ 1 例で発現した（表 2.7.4.2-21）。

表 2.7.4.2-21　　AGHD 患者で発現した膵炎の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All pancreaitis events	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0		
胃腸障害	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0		
急性膵炎	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0		

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

2.7.4.2.5.4　　一般・全身障害

末梢性浮腫

末梢性浮腫の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 151～153 に示す。該当する有害事象は 4054 試験で報告されたが、4043 試験及び 4244 試験では報告されなかった。

末梢性浮腫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とノルディトロピン群で同様であり、プラセボ群でも 1 件認められた（表 2.7.4.2-22）。

表 2.7.4.2-22　AGHD 患者で発現した末梢性浮腫の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All peripheral oedema events	1 (1.6)	1	2.5	8 (4.8)	12	7.5	15 (4.5)	28	7.4
一般・全身障害および投与部位の状態	1 (1.6)	1	2.5	8 (4.8)	12	7.5	15 (4.5)	28	7.4
末梢性浮腫	0			6 (3.6)	9	5.6	12 (3.6)	24	6.4
末梢腫脹	1 (1.6)	1	2.5	3 (1.8)	3	1.9	4 (1.2)	4	1.1

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

疲労／無力症

疲労／無力症の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 154～156 に示す。該当する有害事象はすべての第 3 相試験で報告された。

疲労／無力症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、ノルディトロピン群及びプラセボ群で同様であったが、疲労／無力症を発現した被験者の割合はソマプシタン群で 9.9%、ノルディトロピン群で 11.4%であったのに対して、プラセボ群では 6.6%であった（表 2.7.4.2-23）。

表 2.7.4.2-23　AGHD 患者で発現した疲労／無力症の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All fatigue/asthenia events	4 (6.6)	4	10.0	19 (11.4)	20	12.4	33 (9.9)	39	10.3
一般・全身障害および投与部位の状態	4 (6.6)	4	10.0	19 (11.4)	20	12.4	33 (9.9)	39	10.3
疲労	2 (3.3)	2	5.0	13 (7.8)	13	8.1	19 (5.7)	23	6.1
無力症	1 (1.6)	1	2.5	4 (2.4)	5	3.1	9 (2.7)	11	2.9
倦怠感	1 (1.6)	1	2.5	2 (1.2)	2	1.2	5 (1.5)	5	1.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

体重増加

体重増加の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 178～180 に示す。該当する有害事象は 4054 試験及び 4043 試験で報告されたが、4244 試験では報告されなかった。

「体重増加」を発現した被験者はソマプシタン群では 9 例（2.7%）及びノルディトロピン群では 2 例（1.2%）であり、プラセボ群での発現はなかった（表 2.7.4.2-24）。6 例で発現した「体重増加」は、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（ソマプシタン群：4 例、ノルディトロピン群：2 例）。

表 2.7.4.2-24　AGHD 患者で発現した体重増加の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All weight increased events	0			2 (1.2)	2	1.2	9 (2.7)	10	2.6
臨床検査	0			2 (1.2)	2	1.2	9 (2.7)	10	2.6
体重増加	0			2 (1.2)	2	1.2	9 (2.7)	10	2.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

2.7.4.2.5.5　免疫系障害

アレルギー反応（非アナフィラキシー反応）

アレルギー反応の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 157～159 に示す。該当する有害事象はすべての第 3 相試験で報告された。

アレルギー反応（非アナフィラキシー反応）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群で 8.7 件／100 人・年であったのに対して、ノルディトロピン群では 18.6 件／100 人・年、プラセボ群では 25.1 件／100 人・年であった（表 2.7.4.2-25）。

表 2.7.4.2-25　AGHD 患者で発現したアレルギー反応（非アナフィラキシー反応）の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All allergic reaction (non-anaphylactic reaction) events	9 (14.8)	10	25.1	25 (15.1)	30	18.6	27 (8.1)	33	8.7
皮膚および皮下組織障害	7 (11.5)	7	17.6	19 (11.4)	23	14.3	20 (6.0)	25	6.6
発疹	2 (3.3)	2	5.0	10 (6.0)	12	7.5	6 (1.8)	6	1.6
蕁麻疹	0			2 (1.2)	2	1.2	5 (1.5)	6	1.6
湿疹	2 (3.3)	2	5.0	2 (1.2)	2	1.2	1 (0.3)	2	0.5
アトピー性皮膚炎	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5
接触皮膚炎	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3
全身性皮疹	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3
皮膚炎	2 (3.3)	2	5.0	0			2 (0.6)	2	0.5
アレルギー性皮膚炎	0			0			1 (0.3)	1	0.3
顔面腫脹	0			0			1 (0.3)	2	0.5
紅斑性皮疹	0			0			1 (0.3)	1	0.3
剥脱性発疹	0			1 (0.6)	1	0.6	0		
斑状丘疹状皮疹	0			1 (0.6)	1	0.6	0		
斑状皮疹	0			1 (0.6)	1	0.6	0		
薬疹	0			0			1 (0.3)	1	0.3
呼吸器、胸郭および縦隔障害	0			3 (1.8)	4	2.5	2 (0.6)	2	0.5
アレルギー性鼻炎	0			3 (1.8)	4	2.5	2 (0.6)	2	0.5
一般・全身障害および投与部位の状態	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	3	0.8
顔面浮腫	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	3	0.8
眼障害	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3
アレルギー性結膜炎	0			0			1 (0.3)	1	0.3
眼部腫脹	0			1 (0.6)	1	0.6	0		
眼瞼浮腫	0			1 (0.6)	1	0.6	0		
胃腸障害	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3
口唇腫脹	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3
免疫系障害	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3
ワクチンアレルギー	1 (1.6)	1	2.5	0			0		
複合アレルギー	0			0			1 (0.3)	1	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

過敏症（アナフィラキシー反応）

過敏症（アナフィラキシー反応）の有害事象の報告はなかった（付録 2.7.4.7.1、Table 49）。

2.7.4.2.5.6　傷害、処置及び投与部位の状態

ソマプシタンの投与を受けた AGHD 患者で臨床的に問題となる局所忍容性の所見は認められなかった。局所注射部位反応は軽度～中等度で、一過性のものであり、（治験薬に対する）アレルギー反応は認められなかった。

注射部位反応

注射部位反応の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 160～162 に示す。該当する有害事象は 4054 試験及び 4244 試験で報告されたが、4043 試験では報告されなかった。

第 3 相試験併合では、注射部位反応の有害事象の発現件数はいずれの投与群でも少なかった（ソマプシタン群：5 例 9 件、ノルディトロピン群：9 例 9 件、プラセボ群：3 例 5 件）（表 2.7.4.2-26）。注射部位反応の単位時間あたりの発現件数は、ソマプシタン群で 2.4 件／100 人・年であったのに対して、ノルディトロピン群では 5.6 件／100 人・年 、プラセボ群では 12.6 件／100 人・年であった。

大部分の事象は治験薬との因果関係が「可能性あり」又は「あり」と判定されたが〔注射部位反応の有害事象 23 件中 20 件（付録 2.7.4.7.1、Table 12）〕、重篤な有害事象となる注射部位反応の有害事象は認められなかった。治験薬投与の中止に至った局所忍容性の問題は認められなかった。

表 2.7.4.2-26　　AGHD 患者で発現した注射部位反応の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N　(%)	E	R	Norditropin N　(%)	E	R	somapacitan N　(%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All injection site reaction events	3 (4.9)	5	12.6	9 (5.4)	9	5.6	5 (1.5)	9	2.4
一般・全身障害および投与部位の状態	3 (4.9)	5	12.6	9 (5.4)	9	5.6	5 (1.5)	9	2.4
注射部位内出血	2 (3.3)	3	7.5	6 (3.6)	6	3.7	1 (0.3)	1	0.3
注射部位疼痛	1 (1.6)	1	2.5	1 (0.6)	1	0.6	2 (0.6)	3	0.8
注射部位反応	0			1 (0.6)	1	0.6	1 (0.3)	3	0.8
注射部位萎縮	0			0			1 (0.3)	1	0.3
注射部位血腫	1 (1.6)	1	2.5	0			0		
注射部位出血	0			1 (0.6)	1	0.6	0		
注射部位肥厚	0			0			1 (0.3)	1	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

脂肪肥大症／リポジストロフィー

脂肪肥大症／リポジストロフィーの有害事象を試験別に要約し、付録 2.7.4.7.1、Table 163～165 に示す。該当する有害事象は 4054 試験で報告されたが、4043 試験及び 4244 試験では報告されなかった。

ソマプシタンの投与後に脂肪肥大症／リポジストロフィーの有害事象を発現した被験者は 5 例であり、そのうち 1 例はリポジストロフィーの既往歴を有していた（表 2.7.4.2-27）。他の 4 例を詳細に評価したところ、3 例は注射による局所炎症が原因と考えられる注射部位の一過性の腫脹であった（大腿部又は腹部でローテーションされず、同じ場所又は狭い範囲内にソマプシタンを注射していた）。画

像診断（MRI、超音波）により脂肪肥大症が確認された被験者は 1 例のみであった。この有害事象は一過性のものであった。重篤な有害事象に分類されたものはなかった。各事象の詳細を表 2.7.4.2-28 に示す。

表 2.7.4.2-27　AGHD 患者で発現した脂肪肥大症／リポジストロフィーの有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All lipohypertrophy events	0			0			5 (1.5)	5	1.3
皮膚および皮下組織障害	0			0			4 (1.2)	4	1.1
後天性リポジストロフィー	0			0			2 (0.6)	2	0.5
脂肪肥大症	0			0			2 (0.6)	2	0.5
一般・全身障害および投与部位の状態	0			0			1 (0.3)	1	0.3
注射部位肥厚	0			0			1 (0.3)	1	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

表 2.7.4.2-28　脂肪肥大症／リポジストロフィーの有害事象別の詳細

Trial/ Trial product	Sex/Age/ BMI	AE Preferred term	Trial day/ Duration (days)	Severity	Causality Main/ Extension	SAE	Dermatology review (yes/no)	Recov (yes/no)	Comment[a]
Trial 4054									
Somapacitan/ somapacitan	M/39/37.0	後天性リポジストロフィー	236/25	Moderate	Possible/ NA	No	No	Yes	Transient ‘contusion’ at the abdominal injection site after multiple injections in the area. The event recovered after 3 weeks.
Somapacitan/ somapacitan	F/35/29.5	脂肪肥大症	193/68	Mild	Possible/ NA	No	No	Yes	Transient ‘swelling’ at the abdominal injection site after cumulated injections in the area. Limited information available.
Somapacitan/ somapacitan	F/45/29.8	脂肪肥大症	225/226	Mild	Possible/ NA	No	Yes	Yes	Transient ‘swelling’ at the abdominal injection site (diameter 8.5 mm) after cumulated injections in the area. MRI and an ultrasound showed ‘increased thickness of s.c. fat in the area of clinical interest’. An independent dermatologic evaluation states ‘Residuum after subcutaneous administration due to very superficial injection technique’
Somapacitan/ somapacitan	F/57/21.0	後天性リポジストロフィー	25/123	Mild	Unlikely/ NA	No	No	Yes	Medical history of lipodystrophy. The patient observed transient worsening of abdominal lipodystrophy.
Norditropin/ somapacitan	F/73/19.6	注射部位肥厚	376/256	Mild	Probable/ Probable	No[b]	No information	No[b]	Transient ‘mild soft tissue expansion’ at the abdominal injections site was reported during the extension phase of the trial (somapacitan)

Abbreviations: M = Male; F = Female; Age in years; BMI: Body mass index (kg/m^2) at baseline; NA = Not applicable; Recov = recovered. In trial 4054 the treatment in the main/extension is indicated by e.g. somapacitan/somapacitan. [a]Based on correspondence with individual sites.

[b] The patient was recovering.

脂肪組織萎縮症

脂肪組織萎縮症の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 166～168 に示す。該当する有害事象は 4054 試験で報告されたが、4043 試験及び 4244 試験では報告されなかった。

ソマプシタン群では 1 例で「脂肪組織減少」が、別の 1 例で「注射部位萎縮」が認められた（表 2.7.4.2-29）。「脂肪組織減少」が認められた 1 例には重度の皮膚疾患（Hand-Schuller-Christian 病）の既往歴を有しており、「注射部位萎縮」が認められた 1 例については十分な背景情報が得られなかった。ノルディトロピン群では 1 例で「脂肪組織減少」が認められた。各事象の詳細を表 2.7.4.2-30 に示す。

表 2.7.4.2-29　AGHD 患者で発現した脂肪組織萎縮症の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All lipoatrophy events	0			1 (0.6)	1	0.6	2 (0.6)	4	1.1
一般・全身障害および投与部位の状態	0			1 (0.6)	1	0.6	2 (0.6)	4	1.1
脂肪組織減少	0			1 (0.6)	1	0.6	1 (0.3)	3	0.8
注射部位萎縮	0			0			1 (0.3)	1	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

表 2.7.4.2-30 脂肪組織萎縮症の有害事象別の詳細

Trial/ Trial product	Sex/Age/BMI	AE Preferred term	Trial day/ phase/ Duration (days)	Severity	Causality Main/ Extension	SAE	Dermatology review (yes/no)	Recov (yes/no)	Comment[a]
Trial 4054									
Placebo/ somapacitan	F/23/22.9	注射部位萎縮	NA/Extension/ 32	Mild	Possible/ Possible	No	No information	Yes	Transient reduction in the subcutaneous fat at the abdominal injection site. Onset date: Jan 2016 (randomisation date: 6-Apr-2015). Limited information available
Norditropin/ somapacitan	F/63/21.2	脂肪組織減少	NA/Main/NA	Mild	Probable/NA	No	No information	No	'Decrements in subcutaneous abdominal fat' at the injection site was reported during the main phase of the trial (Norditropin). Onset date: Jan 2016 (randomisation date: 25-Sep-2015).
Norditropin/ somapacitan	F/66/28.3	脂肪組織減少（右大腿部）	308/extension/ 309	Mild	Unlikely/ Probable	No	No information	Yes	Medical history of Hand–Schüller–Christian disease. 'Successive loss of subcutaneous fat' from injections site areas in the thighs (and abdomen) was reported in the extension part (somapacitan)
		脂肪組織減少（左大腿部）	308/extension/ 309	Mild	Unlikely/ Probable	No	No information	Yes	Medical history of Hand–Schüller–Christian disease. 'Successive loss of subcutaneous fat' from injections site areas in the thighs (and abdomen) was reported in the extension part (somapacitan)
		脂肪組織減少（腹部）	448/extension/ NA	Mild	Possible/ probable	No	No information	No	Medical history of Hand–Schüller–Christian disease. 'Successive loss of subcutaneous fat' from injections site areas in the (thighs and) abdomen was reported in the extension part (somapacitan)

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

[a]Based on correspondence with individual sites.

局所注射部位反応のうち、臨床的に問題となる異常とは判断されず、有害事象として報告されなかった事象については、試験別に治験総括報告書に要約する〔4054 試験（延長試験）（M 5.3.5.1）Section 12.3.5.1、4043 試験（M 5.3.5.1）Section 12.7.5〕。

臨床薬理試験で報告された局所注射部位反応については、試験別に治験総括報告書に要約する〔3915 試験（M 5.3.3.1）Section 12.4.3、4237 試験（M 5.3.3.1）Section 12.5.2、3947 試験（M 5.3.3.2）Section 12.5.3、4297 試験（M 5.3.3.3）Section 12.1.2.5、4298 試験（M 5.3.3.3）Section 12.1.2.1、4491 試験（M 5.3.1.2）Section 12.3.4〕。

2.7.4.2.5.7　臨床検査

血中アルカリホスファターゼ増加

血中アルカリホスファターゼ増加の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 169～171 に示す。当該事象は 4054 試験で報告されたが、4043 試験及び 4244 試験では報告されなかった。

ソマプシタン群では 2 例（0.6%）で 2 件の「血中アルカリホスファターゼ増加」の有害事象が報告されたが、ノルディトロピン群及びプラセボ群での発現はなかった（付録 2.7.4.7.1、Table 32）。

薬物特異性抗体陽性

成人に対するソマプシタンの投与後、薬物特異性抗体陽性に関連する有害事象の報告はなかった（付録 2.7.4.7.1、Table 33 及び 172～174）。免疫原性については 2.7.4.3.1 を参照のこと。

潜在的な催不整脈作用（心電図に関連する有害事象）

QTc 延長の評価に関する FDA の要求に従い、潜在的な催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「心血管系検査（酵素検査を除く）」及び高位グループ語「不整脈」を用いて検索を行った。この検索の結果を試験別に付録 2.7.4.7.1、Table 175～177 に示す。該当する事象は 4054 試験及び 4043 試験で報告されたが、4244 試験では報告されなかった。

4054 試験（投与期間：最長 86 週間）では、潜在的な催不整脈作用を示す有害事象（心電図に関連する有害事象）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及びプラセボ群で同様であった。ソマプシタン群では 9 例（4.0%）11 件、ノルディトロピン群では 6 例（5.0%）8 件、プラセボ群では 2 例（3.3%）2 件の有害事象が発現した（付録 2.7.4.7.1、Table 175）。これらの有害事象にはソマプシタン群で認められた「心室性期外収縮」、「心電図 QT 延長」及び「心室細動」各 1 件が含まれている。これらの事象の詳細を表 2.7.4.2-32 に示す。「心室細動」に関する叙述を 2.7.4.2.2 に示す。4054 試験における心電図に関連する有害事象の詳細を付録 2.7.4.7.1、Listing 68 に示す。

4043 試験（投与期間：最長 26 週間）ではノルディトロピン群の 1 例（3.2%）2 件の「心房粗動」が発現した（付録 2.7.4.7.1、Listing 67 及び Table 176）。

4244 試験（投与期間：最長 52 週間）では潜在的な催不整脈作用を示す有害事象（心電図に関連する有害事象）は認められなかった（付録 2.7.4.7.1、Listing 69 及び Table 177）。

第 3 相試験併合における評価では、これらの高位グループ語に分類される有害事象を発現した被験者の割合は、いずれの投与群でも同様であった（表 2.7.4.2-31）。

心電図の評価の詳細は 2.7.4.4.2.2 を参照のこと。

表 2.7.4.2-31　AGHD 患者で発現した高位グループ語「心血管系検査（酵素検査を除く）」及び高位グループ語「不整脈」に分類される有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All cardiac and vascular investigations and cardiac arrhythmia	2 (3.3)	2	5.0	7 (4.2)	10	6.2	9 (2.7)	11	2.9	18 (4.0)	23	4.0
心臓障害	1 (1.6)	1	2.5	3 (1.8)	4	2.5	6 (1.8)	7	1.9	10 (2.2)	12	2.1
頻脈	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
第一度房室ブロック	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
右脚ブロック	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
徐脈	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
心室細動	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
心室性期外収縮	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
心房粗動	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
洞性不整脈	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
臨床検査	1 (1.6)	1	2.5	4 (2.4)	6	3.7	4 (1.2)	4	1.1	9 (2.0)	11	1.9
血圧上昇	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
血圧低下	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
心雑音	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
心電図ＰＲ延長	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
心電図ＱＴ延長	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
心電図Ｔ波逆転	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
心電図異常	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
心電図異常Ｔ波	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
心拍数増加	0			1 (0.6)	3	1.9	0			1 (0.2)	3	0.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

表 2.7.4.2-32　心電図に関連する有害事象

Trial/ Treatment group	Patient ID	Sex/Age/ BMI	AE/ SAE	Trial day/ phase/ duration (days)	Preferred term	Severity	Causality main/ extension	Action taken	Recovered/r ecovering	Comment
Trial 4054										
Somapacitan/ somapacitan	106003	M/50/26.0	SAE	331/ext/12	心室性期外収縮	Moderate	Unlikely/ unlikely	NA	Yes	Dose not changed. Trial period: extension (somapacitan).
Somapacitan/ somapacitan	209001#	F/35/20.8	AE	615/ext/7	心電図 QT 延長	Mild	Possible/ Possible	NA	Yes	Abnormal CS by the investigator and central assessment. Trial period: extension (somapacitan).
Placebo/ somapacitan	601003	M/66/32.4	SAE	363/ext/12	心室細動	Severe	Unlikely/ unlikely	Drug interrupted	No	Trial period: extension (somapacitan).

Abbreviations: M = Male; F = Female; Age in years; BMI = Body mass index (kg/m^2) at baseline; AE = adverse event; SAE = serious adverse event; CS = Clinically significant; NA = not applicable; ECG = Electrocardiogram; ext = extension; In trial 4054, the treatment in the main/extension is indicated by e.g. somapacitan/somapacitan.

Japanese

2.7.4.2.5.8　　代謝系障害

高血糖

高血糖の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 181～183 に示す。該当する有害事象は 4054 試験で報告されたが、4043 試験及び 4244 試験では報告されなかった。

糖代謝に関連する有害事象は実薬投与群のみで報告された。

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（1.6 件／100 人・年）、ノルディトロピン群（3.1 件／100 人・年）のいずれも少なかった（表 2.7.4.2-33）。プラセボ群では高血糖の有害事象の発現はなかった。ソマプシタン群で新たに糖尿病と診断された被験者はいなかったが、ノルディトロピン群では 3 例が新たに糖尿病と診断された。ベースラインで糖尿病を有する被験者については、2.7.4.3.2.1 を参照のこと。

表 2.7.4.2-33　　AGHD 患者で発現した高血糖の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All hyperglycemia events	0			1 (0.6)	5	3.1	4 (1.2)	6	1.6
臨床検査	0			1 (0.6)	5	3.1	3 (0.9)	5	1.3
グリコヘモグロビン増加	0			1 (0.6)	2	1.2	3 (0.9)	4	1.1
血中ブドウ糖増加	0			1 (0.6)	3	1.9	1 (0.3)	1	0.3
代謝および栄養障害	0			0			1 (0.3)	1	0.3
高血糖	0			0			1 (0.3)	1	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

2 型糖尿病の徴候

2 型糖尿病の徴候の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 184～186 に示す。該当する事象はすべての第 3 相試験で報告された。

2 型糖尿病に関連する事象の単位時間あたりの発現件数はソマプシタン群（2.1 件／100 人・年）、ノルディトロピン群（5.6 件／100 人・年）のいずれでも少なかった（表 2.7.4.2-34）。ソマプシタン群で新たに糖尿病と診断された被験者はいなかったが、ノルディトロピン群では 3 例が新たに糖尿病と診断された（4054 試験で 2 例、4244 試験で 1 例）。プラセボ群で 2 型糖尿病に関連する事象の発現はなかった。ベースラインで糖尿病を有する被験者については、2.7.4.3.2.1 を参照のこと。

表 2.7.4.2-34　　AGHD 患者で発現した 2 型糖尿病の徴候の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N　(%)	E	R	Norditropin N　(%)	E	R	somapacitan N　(%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All type 2 diabetes events	0			5 (3.0)	9	5.6	5 (1.5)	8	2.1
臨床検査	0			2 (1.2)	6	3.7	4 (1.2)	7	1.9
グリコヘモグロビン増加	0			1 (0.6)	2	1.2	3 (0.9)	4	1.1
血中インスリン増加	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5
血中ブドウ糖増加	0			1 (0.6)	3	1.9	1 (0.3)	1	0.3
代謝および栄養障害	0			3 (1.8)	3	1.9	1 (0.3)	1	0.3
糖尿病	0			3 (1.8)	3	1.9	0		
高血糖	0			0			1 (0.3)	1	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

2.7.4.2.5.9　　筋骨格系障害

関節痛

関節痛の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 187～189 に示す。当該事象はすべての第 3 相試験で報告された。

関節痛は GH 治療の有害事象としてよく知られているものである[8,16]。「関節痛」の単位時間あたりの発現件数はソマプシタン群で 6.6 件／100 人・年、ノルディトロピン群で 11.2 件／100 人・年であったが、プラセボ群で 2.5 件／100 人・年であった（表 2.7.4.2-35）。

表 2.7.4.2-35　　AGHD 患者で発現した関節痛の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N　(%)	E	R	Norditropin N　(%)	E	R	somapacitan N　(%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All athralgia events	1 (1.6)	1	2.5	17 (10.2)	18	11.2	23 (6.9)	25	6.6
筋骨格系および結合組織障害	1 (1.6)	1	2.5	17 (10.2)	18	11.2	23 (6.9)	25	6.6
関節痛	1 (1.6)	1	2.5	17 (10.2)	18	11.2	23 (6.9)	25	6.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

筋肉痛

筋肉痛の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 190～192 に示す。当該事象はすべての第 3 相試験で報告された。

筋肉痛は GH 治療の有害事象としてよく知られているものである。「筋肉痛」の単位時間あたりの発現件数は、ノルディトロピン群で 5.0 件／100 人・年及びプラセボ群で 7.5 件／100 人・年と比較しソマプシタン群で 2.4 件／100 人・年であった（表 2.7.4.2-36）。

表 2.7.4.2-36　　AGHD 患者で発現した筋肉痛の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All myalgia events	3 (4.9)	3	7.5	8 (4.8)	8	5.0	7 (2.1)	9	2.4
筋骨格系および結合組織障害	3 (4.9)	3	7.5	8 (4.8)	8	5.0	7 (2.1)	9	2.4
筋肉痛	3 (4.9)	3	7.5	8 (4.8)	8	5.0	7 (2.1)	9	2.4

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

側弯症

側弯症の有害事象の報告はなかった（付録 2.7.4.7.1、Table 40）。

2.7.4.2.5.10　新生物

良性、悪性及び詳細不明の新生物

新生物の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 196～198 に示す。該当する事象は 4054 試験及び 4244 試験で報告されたが、4043 試験では報告されなかった。

良性、悪性及び詳細不明の新生物の有害事象は 12 件発現し、これらの事象を発現した被験者の割合はソマプシタン群（2.1%、7 件）とノルディトロピン群（2.4%、5 件）で同様であった（表 2.7.4.2-37）。プラセボ群での発現はなかった。3 件の下垂体腫瘍に関連する事象が発現した。新生物に関する詳細を表 2.7.4.2-38 に示す。

発現した新生物の有害事象のうち、3 件は悪性であった〔ソマプシタン群で発現した「基底細胞癌」及び「膀胱移行上皮癌」（重篤な有害事象）、ノルディトロピン群で発現した「形質細胞性骨髄腫」〕。「基底細胞癌」及び「膀胱移行上皮癌」は、治験責任医師により治験薬との因果関係が「可

能性あり」と判定された（被験者は、4054 試験の主要試験期間にはノルディトロピンの投与を受け、延長期間にはソマプシタンの投与を受けていた。これらの有害事象は延長期間に報告された）。「形質細胞性骨髄腫」は、治験薬との因果関係が「なし」と判定された。「膀胱移行上皮癌」と診断された被験者には 30 年にわたる喫煙歴があった。各事象の詳細を表 2.7.4.2-38 に示し、「膀胱移行上皮癌」に関する叙述を治験総括報告書〔4054 試験（延長期間）（M 5.3.5.1）Section 12.2.2.1〕に示す。

さらに 1 件の新生物「下垂体の良性腫瘍」が、治験薬との因果関係が「可能性あり」と判定された（被験者は、4054 試験の主要試験期間にはノルディトロピンの投与を受け、延長期間にはソマプシタンの投与を受けていた。当該有害事象は延長期間に報告された）。「下垂体の良性腫瘍」と診断された被験者には下垂体腺腫の既往歴があり、残存腺腫が試験期間中に増大した。詳細を表 2.7.4.2-38 に示す。

表 2.7.4.2-37　AGHD 患者で発現した良性、悪性及び詳細不明の新生物の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All benign, malignant and unspecified neoplasm events	0			4 (2.4)	5	3.1	7 (2.1)	7	1.9
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0			4 (2.4)	5	3.1	7 (2.1)	7	1.9
下垂体の良性腫瘍	0			0			2 (0.6)	2	0.5
脂肪腫	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3
メラノサイト性母斑	0			1 (0.6)	1	0.6	0		
下垂体腫瘍	0			0			1 (0.3)	1	0.3
基底細胞癌	0			0			1 (0.3)	1	0.3
形質細胞性骨髄腫	0			1 (0.6)	1	0.6	0		
血管筋脂肪腫	0			1 (0.6)	1	0.6	0		
軟部組織新生物	0			1 (0.6)	1	0.6	0		
膀胱移行上皮癌	0			0			1 (0.3)	1	0.3
膵管内乳頭粘液性腫瘍	0			0			1 (0.3)	1	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

表 2.7.4.2-38 良性、悪性及び詳細不明の新生物の有害事象別の詳細

Trial product	Subject ID	Sex/Age/ BMI	AE preferred term	Trial day/ Phase/ Duration (days)	Severity	Causality * Main/ extension	SAE	Recov (Yes/No)	Action taken	Comment
Trial 4054										
Placebo/ somapacitan	204008#	M/52/29.2	下垂体腫瘍	558/ Extension/ NA	Mild	Unlikely/ Unlikely	No	No	Drug withdrawn	1 year after start of somapacitan the patient experienced an 'enlargement of residual pituitary tumour'. Trial product was discontinued on study day 558. Limited information available.
Placebo/ somapacitan	251002	M/29/17.9	脂肪腫	334/ Extension/ NA	Mild	Unlikely/ Unlikely	No	No	None	
Norditropin/ Norditropin	101002	F/62/27.8	メラノサイト性母斑	109/ main/ 1	Mild	Unlikely/ NA	No	Yes	None	No information
Norditropin/ Norditropin	128001	F/46/36.4	脂肪腫	300/ Extension/ NA	Mild	Unlikely/ Unlikely	No	No	None	
			軟部組織新生物	451/ Extension/ NA	Mild	Unlikely/ Unlikely	No	No	None	
Norditropin/ Norditropin	605009	F/76/30.8	血管筋脂肪腫	197/ Main/ NA	Mild	Unlikely/ NA	No	No	None	
Norditropin/ somapacitan	116006	M/73/39.9	下垂体の良性腫瘍	298/ Extension/ 64	Moderate	Unlikely/ Possible	No	Yes	Drug withdrawn	10 months after start of Norditropin the patient experienced 'Interval increase 78% in size of residual pituitary adenoma' on MRI. Trial product was discontinued. The patient was treated with Norditropin in the main phase and with somapacitan in the extension phase. The AEs were reported during the extension phase.

Trial product	Subject ID	Sex/Age/ BMI	AE preferred term	Trial day/ Phase/ Duration (days)	Severity	Causality * Main/ extension	SAE	Recov (Yes/No)	Action taken	Comment
										2 months after a control MRI showed decrease in the size of the tumour. According to conventional tumour response criteria (WHO criteria) an increase must be confirmed which was not the case. Therefore, no progression of tumour was observed
Norditropin/ Somapacitan	211004#	M/68/23.3	形質細胞性骨髄腫	146/ main/ NA	Severe	Unlikely/ Unlikely	Yes	No	Drug withdrawn in extension	5 months after start of Norditropin, the patient experienced 'plasma cell myeloma'. Exposed 34 weeks in main (Norditropin) and 7 weeks in extension (somapacitan).
Norditropin/ Somapacitan	603005	M/72/27.8	膀胱移行上皮癌	564/ Extension/ NA	Severe	Possible/ Possible	Yes	No	None	20 months after starting trial products (Norditropin; somapacitan) the patient experienced bladder carcinoma. The patient was treated with Norditropin in the main phase and with somapacitan in the extension phase. The AEs were reported during the extension phase. A medical history of 30 years of smoking is an alternative explanation for the event.
Norditropin/ Somapacitan	853002	F/66/28.3	基底細胞癌	405/ Extension/ 212	Moderate	Possible/ Possible	No	No[a]	None	The patient was treated with Norditropin in the main phase and with somapacitan in the extension phase. The AEs were reported during the extension phase. No other information
Onset prior to exposure in trial 4054										
Somapacitan/ somapacitan	350004	F/32/23.0	メラノサイト性母斑	NA/NA/ NA	Moderate	NA/NA	No	Yes	NA	The onset of the event was prior to commencing the first dose in trial 4054
Non-randomised patients	601006	M/34/48.2	頭蓋咽頭腫	NA/NA/ 53	Severe	NA/NA	Yes	Yes	NA	The patient was a screening failure (trial 4054) and the event was the recurrence of previously diagnosed craniopharyngioma
Trial 4244										

Trial product	Subject ID	Sex/Age/ BMI	AE preferred term	Trial day/ Phase/ Duration (days)	Severity	Causality * Main/ extension	SAE	Recov (Yes/No)	Action taken	Comment
somapacitan	101001#	M/67.4/23.6	下垂体の良性腫瘍	195/NA/ NA	Moderate	Unlikely	No	No		7 months after start of somapacitan treatment the patient developed 'regrowth of pituitary adenoma' by MRI. There was no information about the size of the suspected tumour relapse and no information if a confirmatory MRI scan had been performed.
somapacitan	106004#	F/62.4/21.3	膵管内乳頭粘液性腫瘍	362/NA/ NA	Mild	Unlikely	No	No		12 months after start of somapacitan, the patient was diagnosed with a benign breast neoplasm. Limited information.

Abbreviations: M = Male, F = Female; Age in years; BMI: Body mass index (kg/m^2) at baseline; *AE causality is based on judgement of investigators. NA: Not applicable/Not available. Recov = recovered. # Japanese.

[a] The patient was recovering.

MedDRA version 21.0

2.7.4.2.5.11　神経系障害

頭痛

頭痛の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 199～201 に示す。該当する事象はすべての第 3 相試験で報告された。

頭痛は高頻度で報告された有害事象のひとつであり、GH 治療の有害事象としてよく知られている（図 2.7.4.2-5）。頭痛の有害事象を発現した被験者の割合は投与群を通じて同様であったが（ソマプシタン群：12.9%、ノルディトロピン群：13.3%、プラセボ群：16.4%）、単位時間あたりの発現件数には違いがみられた（ソマプシタン群：28.8 件／100 人・年、ノルディトロピン群：52.8 件／100 人・年、プラセボ群：37.7 件／100 人・年）（表 2.7.4.2-39）。

表 2.7.4.2-39　AGHD 患者で発現した頭痛の有害事象（第 3 相試験併合）

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R
Subjects Exposed	61			166			333		
Total patient years	39.8			161.0			377.8		
All headache events	10 (16.4)	15	37.7	22 (13.3)	85	52.8	43 (12.9)	109	28.8
神経系障害	10 (16.4)	15	37.7	22 (13.3)	85	52.8	43 (12.9)	109	28.8
頭痛	10 (16.4)	15	37.7	22 (13.3)	85	52.8	43 (12.9)	109	28.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

錯感覚

錯感覚の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 202～204 に示す。該当する事象は 4054 試験及び 4043 試験で報告されが、4244 試験では報告されなかった。

「錯感覚」は、ノルディトロピン群で 1 例（0.6%）及びプラセボ群で 2 例（3.3%）発現したが、ソマプシタン群では 5 例（1.5%）で発現した（付録 2.7.4.7.1、Table 43）。

脳卒中

脳卒中の有害事象の報告はなかった（付録 2.7.4.7.1、Table 44）。

良性頭蓋内圧亢進

良性頭蓋内圧亢進の有害事象の報告はなかった（付録 2.7.4.7.1、Table 46）。

手根管症候群

手根管症候群の有害事象を試験別に要約し、付録 2.7.4.7.1、Table 208～210 に示す。4054 試験及び 4043 試験でそれぞれ 1 件報告されたが、4244 試験では報告されなかった。

「手根管症候群」はソマプシタン群の 2 例（0.6%）で発現し（いずれも非重篤）、ノルディトロピン群及びプラセボ群での発現はなかった（付録 2.7.4.7.1、Table 45）。

2.7.4.2.5.12　その他の事象

まれな事象

まれな事象を試験別に要約し、付録 2.7.4.7.1、Table 214～216 に示す。まれな事象は 4054 試験及び 4043 試験で報告され、4244 試験では報告されなかった。

発現頻度の高くない事象を特定するため、追加でまれな事象を検索した。検討した有害事象に関していずれの投与群でも特定の傾向は認められなかった（付録 2.7.4.7.1、Table 47）。まれな事象の検索により、5 件の心電図に関連する有害事象が特定された（2.7.4.2.5.7 参照）。

2.7.4.2.5.13　ノルディトロピン/ソマプシタン併合での結果

ノルディトロピン/ソマプシタン併合を用いた安全性データ（一部の有害事象）ついて、CMH の調整を行う場合と行わない場合とで、臨床的に関連する違いは認められなかった。SMQ 検索に基づく有害事象について、この併合解析に基づく要約表を付録 2.7.4.7.1、Table 110 に示す。

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に基づいて行った。ソマプシタンと有害事象との因果関係について合理的な可能性がある adverse drug reaction を特定するため、綿密な医学的評価を実施した。

CCDS に提示する、AGHD 患者において特定されたソマプシタンの adverse drug reaction を表 2.7.4.2-40 に示す。AGHD 患者を対象とする 3 つの完了した第 3 相試験で収集された安全性データを併合し、adverse drug reaction の発現頻度を算出した。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。

概して、Adverse drug reaction は非重篤であり、軽度又は中等度であった。

表 2.7.4.2-40　　ソマプシタンの adverse drug reaction（AGHD 患者）

System organ class	Very common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)
Endocrine disorders		Adrenocortical insufficiency	
General disorders and administration site conditions	Fatigue/Asthenia	Peripheral oedema Injection site reactions	
Metabolism and nutrition disorders		Hyperglycaemia	
Muscolo-skeletal and connective tissue disorders		Arthralgia	
Nervous system disorders	Headache	Paraesthesia	Carpal tunnel syndrome
Skin and subcutaneous tissue disorders			Lipohypertrophy

2.7.4.2.7　　有害事象の要約

完了した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は既存の 1 日 1 回投与の GH 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る。AGHD 患者に対する単回投与及び反復投与後（86 週間まで）のソマプシタンの臨床安全性データからは臨床的に重要な安全性の問題又は重大な局所忍容性の問題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 GH 製剤の臨床試験で認められた有害事象と同様であり、AGHD 患者における GH 治療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、関節痛、疲労、末梢性浮腫等）。AGHD 患者に対するソマプシタンの投与後に新たな安全性の問題は認められなかった。

成人に対するソマプシタンの投与後、薬物特異性抗体の報告はなかった。

これまでに実施した AGHD 患者を対象とするソマプシタンの臨床試験では、ソマプシタンの投与により新生物の発現頻度が上昇することを裏付けるデータは得られなかった。GH 治療により新生物又は二次腫瘍の発現頻度が上昇することを示すエビデンスはない[3,18,19]。

ノルディトロピンと比較してソマプシタンで糖代謝障害のリスクが高くなることは示されなかった。高血糖の単位時間あたりの発現件数はソマプシタン群（1.6 件／100 人・年）、ノルディトロピン群（3.1 件／100 人・年）のいずれにおいても少なかった。ソマプシタン群では新たに糖尿病と診断された被験者はいなかったが、ノルディトロピン群では 3 例が新たに糖尿病と診断された。糖代謝障害はすべての GH 製剤に伴うリスクである。

2.7.4.3 臨床検査値の評価

2.7.4.3.1 免疫原性

AGHD 患者において、抗ソマプシタン／抗 GH 抗体産生又はソマプシタンに対するアレルギー／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。

7 つの完了した臨床試験（4237 試験及び 4491 試験では評価せず）では、健康成人被験者又は AGHD 患者で、ソマプシタンの投与後に抗ソマプシタン抗体は検出されなかった。

4 つの完了した AGHD 患者を対象とした臨床試験では、4054 試験（主要試験期間）で、ノルディトロピンの投与後 4 週（用量調整期間）で 1 回（一過性）抗 GH 抗体が陽性となり、その後陰性となった 1 例を除き、AGHD 患者でノルディトロピンの投与後に抗 GH 抗体は検出されなかった。

4244 試験では、1 例で投与前（無作為割り付け来院時）に抗ソマプシタン抗体が陽性となった。投与後に抗ソマプシタン抗体が陽性を示した被験者はいなかった。

免疫原性の詳細については、Module 2.7.1.1.3 及び Integrated summary of immunogenicity（M 5.3.5.3）を参照のこと。

2.7.4.3.2 血糖コントロール

空腹時血糖値、空腹時インスリン及び HbA1c については、試験により評価時期が異なっていたため、試験別に示す（2.7.4.2.5.8 に示す糖代謝に関連する有害事象を除く）。4054 試験については、主要試験期間及び延長期間をあわせた試験期間（86 週間の投与期間）の結果を示す。主要試験期間中の血糖コントロールの評価については、4054 試験（M 5.3.5.1）の治験総括報告書を参照のこと。

2.7.4.3.2.1 AGHD 患者を対象とした第 3 相試験の結果

4054 試験

空腹時血糖値の平均は基準範囲内であった。86 週間のソマプシタン投与において、空腹時血糖値及び HbA1c の平均にベースラインからの臨床的に意味のあ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）。プラセボ及びノルディトロピン投与後も変化はみられなかった。

ベースライン及び投与後 86 週の空腹時血糖値の平均は、いずれの投与群においても 4.9～5.2 mmol/L の範囲であった〔治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）EOT Table 14.3.5.6〕。ベースライン及び投与後 86 週の HbA1c の平均は、いずれの投与群においても 5.4～5.5%の範囲であった〔治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）EOT Table 14.3.5.21〕。

空腹時インスリンの平均は、投与期間を通じて基準範囲内であった〔図 2.7.4.3-3 及び治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）EOT Table 14.3.5.16～19〕。空腹時インスリンにみられた変化は、GH 製剤を投与した時に予想される範囲内であった。

各パラメータの測定値には外れ値（以下の図においては、ベースラインにおいて糖尿病を有していない被験者の場合は○、糖尿病を有している被験者の場合は×で示した。）が認められた。

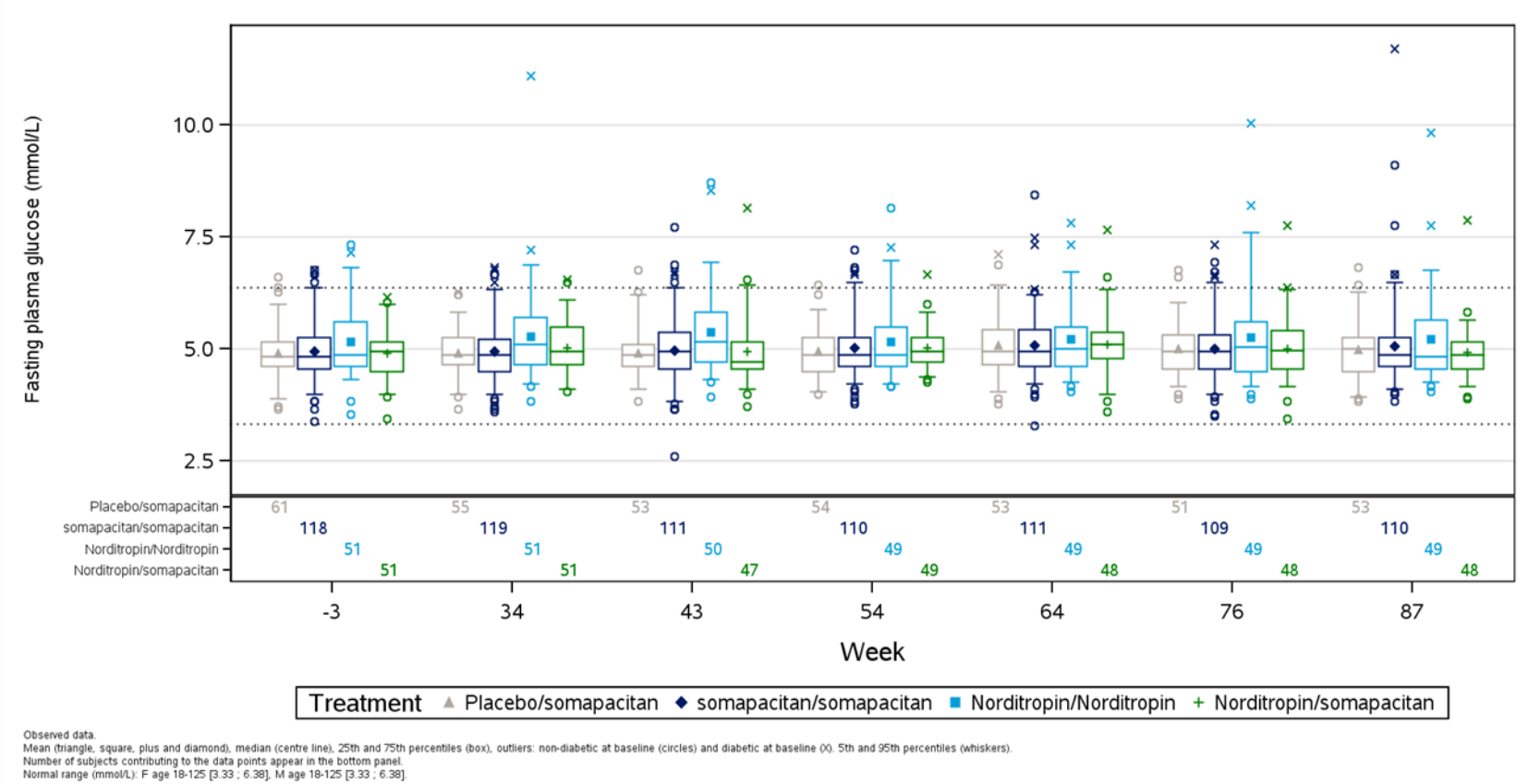
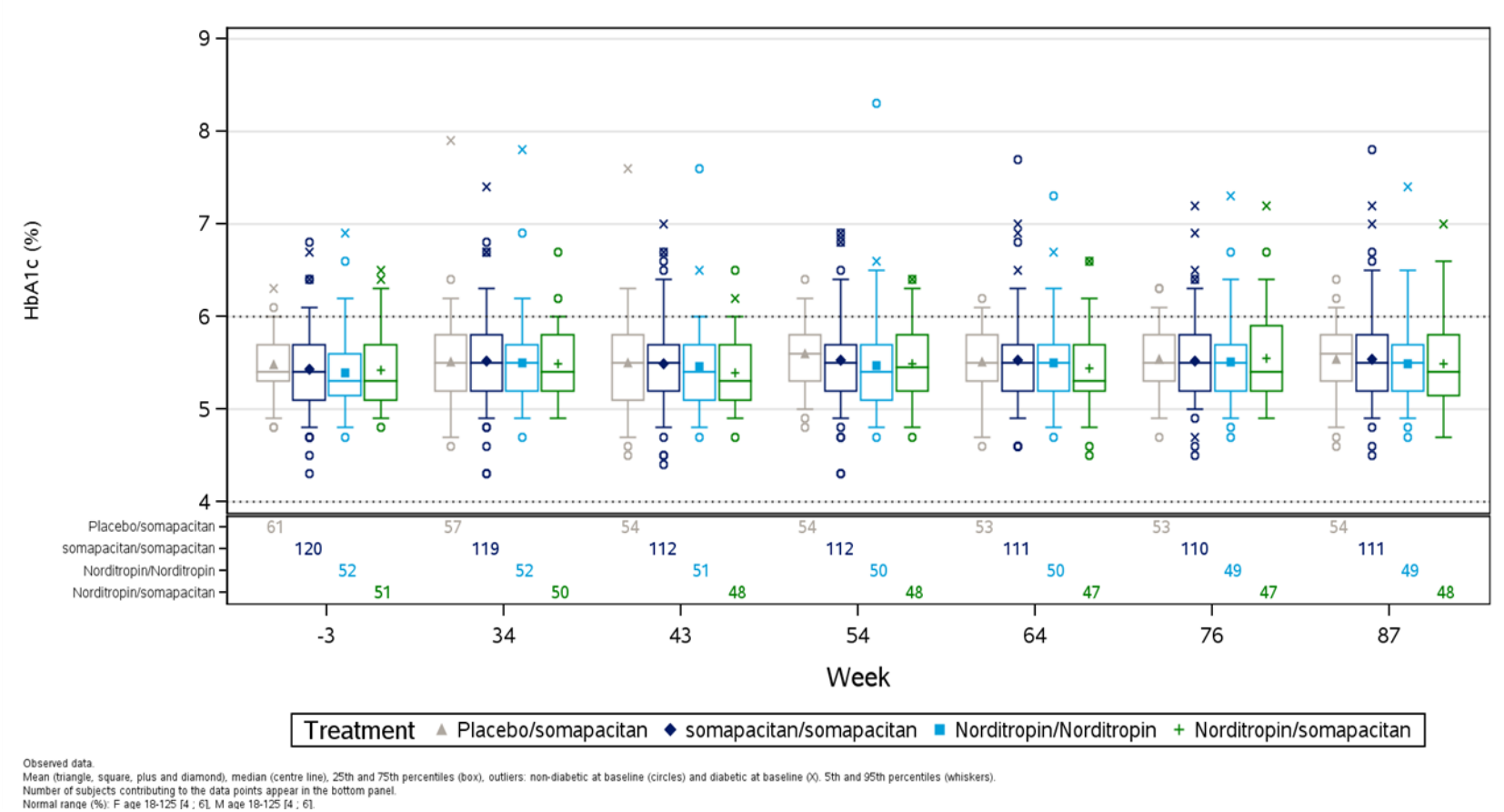


図 2.7.4.3-1　　AGHD 患者における空腹時血糖値（mmol/L）の箱ひげ図（4054 試験）



Observed data.
Mean (triangle, square, plus and diamond), median (centre line), 25th and 75th percentiles (box), outliers: non-diabetic at baseline (circles) and diabetic at baseline (X). 5th and 95th percentiles (whiskers).
Number of subjects contributing to the data points appear in the bottom panel.
Normal range (%): F age 18-125 [4 ; 6], M age 18-125 [4 ; 6].

図 2.7.4.3-2 AGHD 患者における HbA1c（%）の箱ひげ図（4054 試験）

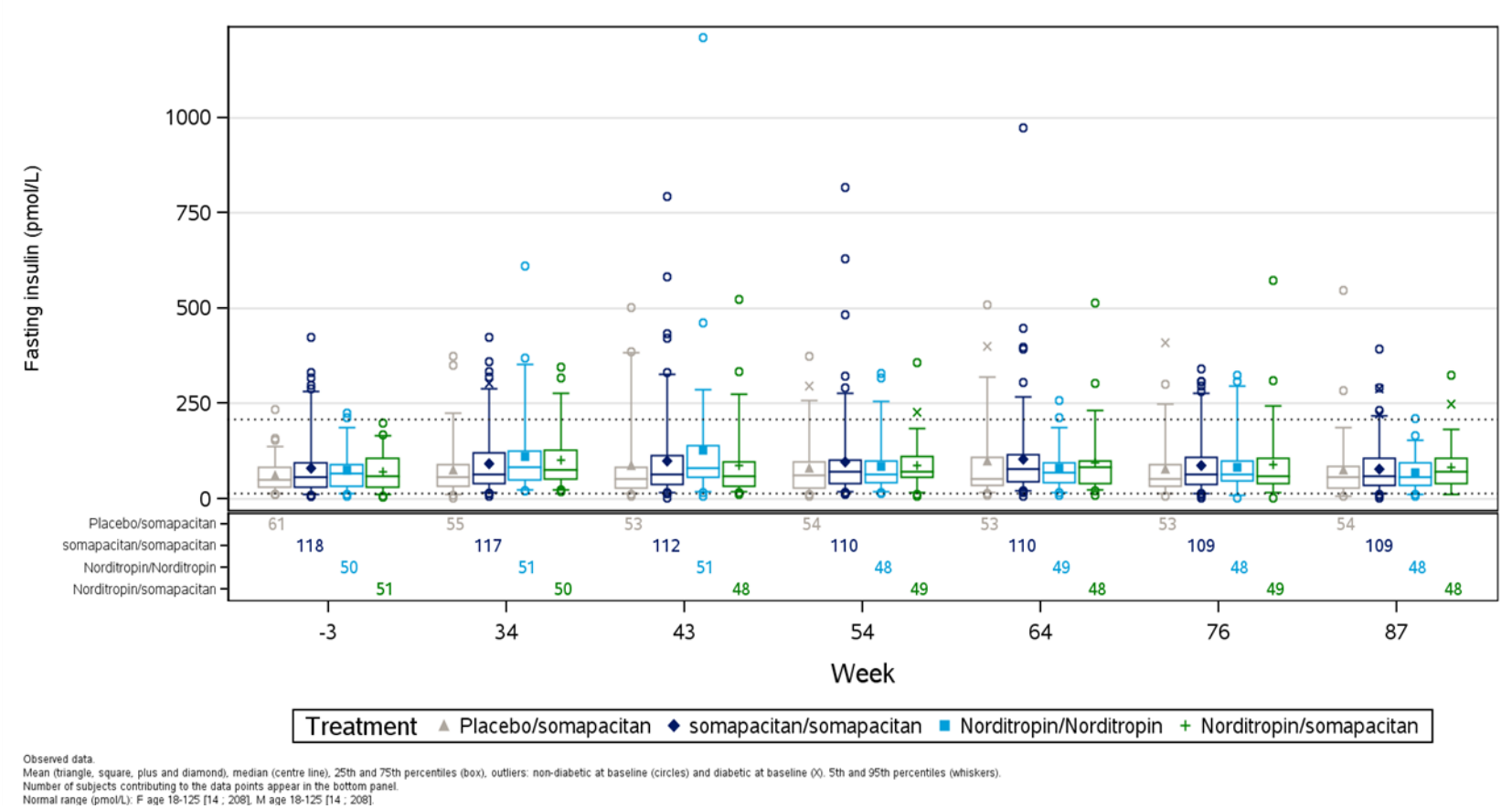


図 2.7.4.3-3　　AGHD 患者における空腹時インスリン（pmol/L）の箱ひげ図（4054 試験）

ベースラインで糖尿病を合併していた被験者又は試験期間中に糖尿病と診断された被験者

4054 試験への組み入れ前に糖尿病と診断されていた被験者（糖尿病を合併していた被験者）は 16 例（5.3%）であった（表 2.7.4.3-1、日本では、糖尿病を合併する被験者は除外された）。当該 16 例で、試験期間中に糖尿病に関連する治療の大きな変更を行った被験者はいなかった〔治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）EOT Table 14.3.7.6〕。

表 2.7.4.3-1　　ベースライン時の糖尿病の有無（4054 試験）

	Placebo	Norditropin	Somapacitan	Total
Diabetes Mellitus, N (%)	61 (100.0)	119 (100.0)	120 (100.0)	300 (100.0)
Diabetic	3 (4.9)	6 (5.0)	7 (5.8)	16 (5.3)
Non-Diabetic	58 (95.1)	113 (95.0)	113 (94.2)	284 (94.7)

N: Number of subjects, %: Percentage of subjects, SD: Standard deviation

ベースラインで糖尿病を合併していた 16 例において、血糖コントロールについてソマプシタンとノルディトロピン間で臨床的に問題となる違いはみられなかった〔治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）Appendix 16.2.8、Listing 16.2.8.5〕。糖代謝に関連する有害事象により治験薬の投与を中止した被験者はいなかった〔治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1〕。ベースラインで糖尿病を合併していた被験者 16 例中 15 例では、糖代謝に関連する有害事象の報告はなかった（付録 2.7.4.7.1、Listing 71）。ベースラインで糖尿病を合併していたノルディトロピン群の 1 例（被験者 ID：101002）で、「血中ブドウ糖増加」（3 件）及び「グリコヘモグロビン増加」（2 件）が報告され、ノルディトロピンとの因果関係が「可能性あり」と判定された（付録 2.7.4.7.1、Listing 71）。これら 5 件の事象はすべて非重篤であり、軽度又は中等度であった。当該被験者は「血中ブドウ糖増加」のためノルディトロピン投与を中断した（付録 2.7.4.7.1、Listing 71）。ベースラインで糖尿病を合併していたノルディトロピン群の他の 1 例（被験者 ID：902003）でも、空腹時血糖値の顕著な上昇（来院 27 における空腹時血糖値：10.05 mmol/L）がみられた（付録 2.7.4.7.1、Figure 79）。当該被験者の空腹時血糖値は低下したが、試験終了時でも 7.0 mmo/L を超えていた（来院 28 における空腹時血糖値：7.77 mmol/L）。

ソマプシタン投与後に新たに糖尿病と診断された被験者はいなかった〔治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）EOT Listing 14.3.7.6〕。4054 試験では、試験中にノルディトロピン群の 2 例が糖尿病と診断され、このうち、日本人被験者の 1 例は試験を中止し、もう 1 例は試験を完了した〔治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）〕。これら 2 例についての詳細を以下に示す（両被験者とも非重篤であった）。

- 60 歳の日本人男性患者（被験者 ID：216003）（BMI：28.0 kg/m^2）は、4054 試験の主要試験期間を完了した後に糖尿病と診断されたため試験を中止した。投与後 177 日に「糖尿病」と診断され、軽度で非重篤な有害事象（因果関係「あり」）と報告された。当該被験者は 8.6 週後に回復した（持続期間：60 日）。空腹時血糖値（ベースライン：5.9 mmol/L、来院 13：7.3 mmol/L、来院 14：5.9 mmol/L）及び空腹時インスリン（ベースライン：226 pmol/L、来院 13：560 pmol/L、来院 14：119 pmol/L）は一過性に上昇した。主要試験期間中に HbA1c の変化はみられなかった（ベースライン：6.1%、来院 13：6.5%、来院 14：6.2%）。当該被験者は、その後インフルエンザに罹患し、死亡した。
- 65 歳の男性患者（被験者 ID：410002、英国）（BMI：38.7 kg/m^2）は、4054 試験を完了した。「糖尿病」は、軽度、非重篤、治験薬との因果関係が「なし」と報告された。当該事象による治験薬の投与量の変更はなかった。診断時（投与後 74 日、主要試験期間）の空腹時血糖値は 6.5 mmol/L、空腹時インスリンは 156 pmol/L、HbA1c は 7.2%であった。試験終了時の空腹時血糖値は 5.8 mmol/L、空腹時インスリンは 183 pmol/L、HbA1c は 6.5%であった。

ベースライン又は投与後に ADA の診断基準以上の値を少なくとも 1 回以上有する被験者

ベースライン又は投与後に 1 回以上の来院で ADA（Diabetes Care vol.39, suppl.1, Jan 2016）の診断基準以上の値（空腹時血糖値が 7.0 mmol/L 以上又は HbA1c が 6.5%以上）を有する被験者は 26 例であった（付録 2.7.4.7.1、Listing 75）。26 例中 12 例（ソマプシタン/ソマプシタン群：5 例、ノルディトロピン/ノルディトロピン群：3 例、ノルディトロピン/ソマプシタン群：2 例、プラセボ/ソマプシタン群：2 例）が、ベースラインで糖尿病を合併しており（付録 2.7.4.7.1、Listing 75）、12 例中 10 例が、糖尿病に関連する治療を受けていた〔治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）EOT Listing 14.3.7.6〕。

26 例中 21 例が、投与後に 1 回以上の来院で ADA の診断基準以上の値を有していた（付録 2.7.4.7.1、Listing 75）。この 21 例中 9 例がベースラインで糖尿病を合併しており、糖尿病に関連する治療を実施していた（付録 2.7.4.7.1、Listing 75）。これら 9 例で、糖尿病に関連する治療の大きな変更を行った被験者はいなかった。この 21 例中の残りの 12 例は、ベースラインで糖尿病を合併しておらず（付録 2.7.4.7.1、Listing 75）、12 例中 1 例（被験者 ID：308001、ソマプシタン/ソマプシタン群）が予防のために糖尿病に関連する治療を受けていた〔治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）EOT Listing 14.3.7.6 及び Appendix 16.2.7、Listing 16.2.7.1〕。

ADA の診断基準以上の値（空腹時血糖値が 7.0 mmol/L 以上又は HbA1c が 6.5%以上）を有する被験者 26 例について、各被験者の空腹時血糖値及び HbA1c の推移を試験別及び投与群別に示す（付録 2.7.4.7.1、それぞれ Figure 78～82 及び 87～91）。多くの場合で、各投与群の 1～2 例でカットオフ値を超える数値が 1～2 回みられ、その一部はベースライン値であった。

4054 試験で、ソマプシタン/ソマプシタン群で空腹時血糖値が 7.0 mmol/L 以上の値を有する被験者を図 2.7.4.3-4 に、HbA1c が 6.5%以上の値を有する被験者を図 2.7.4.3-5 に示す。

空腹時血糖値が 7.0 mmol/L 以上の値を有する被験者は、プラセボ/ソマプシタン群の 2 例に対して、ソマプシタン/ソマプシタン群では 9 例、ノルディトロピン/ノルディトロピン（ノルディトロピン/ー群も含む）群では 6 例であった（付録 2.7.4.7.1、Figure 78～82、複数の治療を受けたノルディトロピン/ソマプシタン群を除く）。空腹時血糖値が上昇した被験者の大部分では、空腹時インスリン又は HbA1c、あるいは空腹時インスリン及び HbA1c いずれも上昇していた。

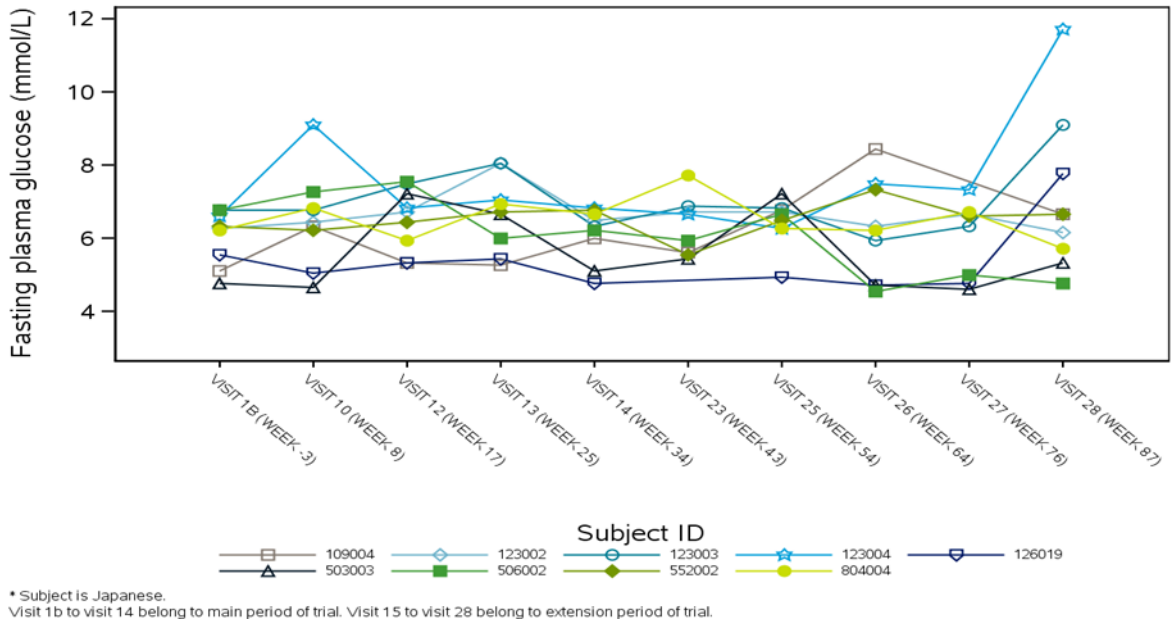


図 2.7.4.3-4　　ソマプシタン/ソマプシタン群で空腹時血糖値が 7.0 mmol/L 以上の値を有する被験者（4054 試験）

試験中にベースラインを含む 1 回以上の来院で HbA1c が 6.5%以上の値を有する被験者は、プラセボ/ソマプシタン群の 1 例に対して、ソマプシタン/ソマプシタン群では 9 例、ノルディトロピン/ノルディトロピン群では 5 例であった（付録 2.7.4.7.1、Figure 87～91、複数の治療を受けたノルディトロピン/ソマプシタン群を除く）。

空腹時血糖値が 7.0 mmol/L 以上又は HbA1c が 6.5%以上の値を有する被験者において、糖代謝に関連する有害事象の発現はわずかであった〔治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）Listing 16.2.7.1〕。糖代謝に関連する有害事象を投与群別に要約し、治験総括報告書〔4054 試験（延長期間）（M 5.3.5.1）EOT Table 14.3.1.9〕に示す。

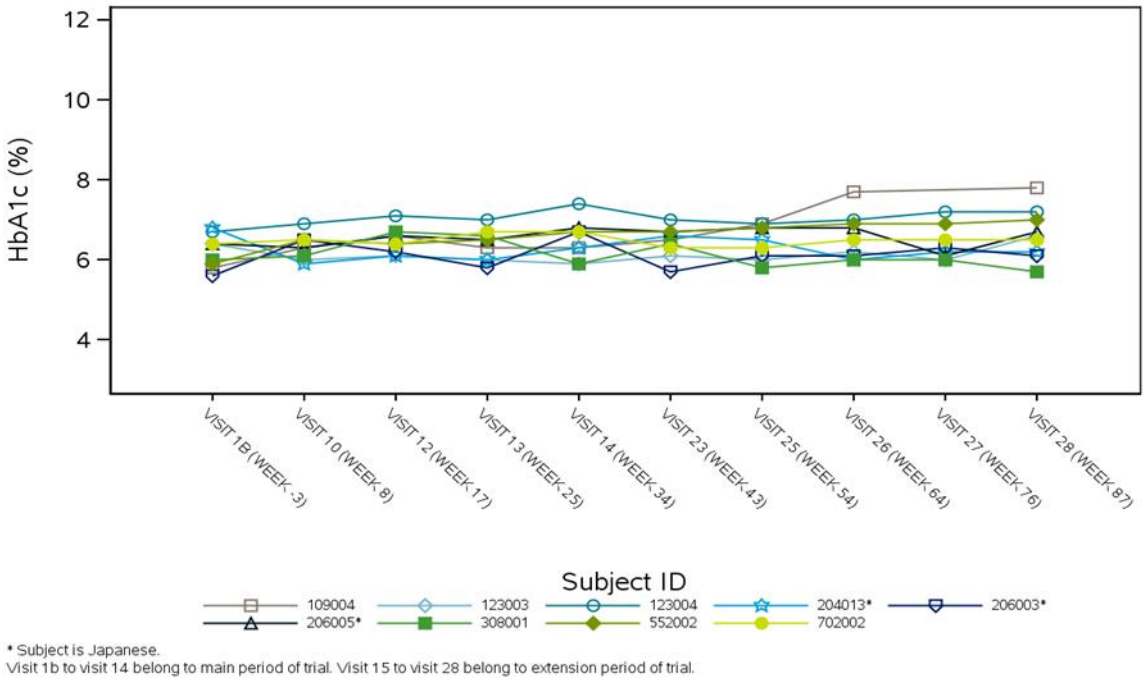


図 2.7.4.3-5　　ソマプシタン/ソマプシタン群で HbA1c が 6.5%以上の値を有する被験者（4054 試験）

ベースラインで糖尿病と診断されていなかった 2 例が、糖代謝に関連する有害事象により投与を中止した（表 2.7.4.2-18）。

- 被験者 ID：216003「糖尿病」（主要試験期間：ノルディトロピンを投与）
- 被験者 ID：109004「グリコヘモグロビン増加」（延長期間：ソマプシタンを投与）

4043 試験

ソマプシタン群とノルディトロピン群ともに空腹時血糖値、空腹時インスリン及び HbA1c にベースラインからの変化はみられず、投与群間で同様であった。

ベースラインで糖尿病を合併していた被験者又は試験期間中に糖尿病と診断された被験者

ベースラインで糖尿病を合併していた被験者は 1 例（被験者 ID：608001）であった。糖代謝に関連する有害事象の報告はなかった（付録 2.7.4.7.1、Listing 70）。また、実施されていた糖尿病に関連する治療（メトホルミン）について、試験期間中に大きな変更はなかった〔治験総括報告書、4043 試験（M 5.3.5.1）EOT Listing 14.3.7.5〕。試験中に新たに糖尿病と診断された被験者はいなかった〔治験総括報告書、4043 試験（M 5.3.5.1）Section 12.6.1.2〕。

ベースライン又は投与後に ADA の診断基準以上の値を少なくとも 1 回以上有する被験者

ベースライン又は投与後に 1 回以上の来院で ADA（Diabetes Care vol.39, suppl.1, Jan 2016）の診断基準以上の値（空腹時血糖値が 7.0 mmol/L 以上又は HbA1c が 6.5%以上）を有する被験者は 8 例であった（付録 2.7.4.7.1、Listing 75）。8 例中 1 例（被験者 ID：608001）が、ベースラインで糖尿病を合併していた。8 例中 4 例が、投与後に 1 回以上の来院で ADA の診断基準以上の値を有していたが（付録 2.7.4.7.1、Listing 75）、これら 4 例で糖尿病に関連する治療を受けた被験者はいなかった〔治験総括報告書、4043 試験（M 5.3.5.1）EOT Listing 14.3.7.5〕。

試験中にベースライン時を含む 1 回以上の来院で空腹時血糖値が 7.0 mmol/L 以上となった被験者は、ソマプシタン群で 3 例及びノルディトロピン群で 2 例であった（付録 2.7.4.7.1、Figure 76 及び 77）。また、試験中に 1 回以上の来院で HbA1c が 6.5%以上となった被験者は、ソマプシタン群で 2 例及びノルディトロピン群で 2 例であったが、ベースラインからの変化はわずかであった（付録 2.7.4.7.1、Figure 85 及び 86）。

4244 試験

ソマプシタン群とノルディトロピン群ともに空腹時血糖値、空腹時インスリン及び HbA1c にベースラインからの臨床的に問題となる変化はみられず、投与群間で同様であった。（図 2.7.4.3-6 及び図 2.7.4.3-7）。

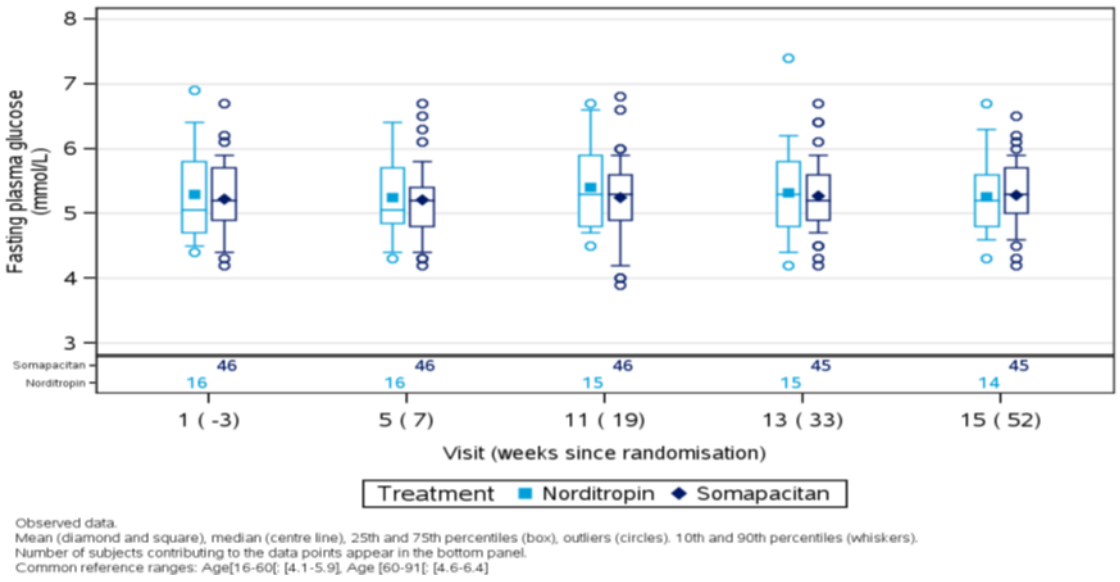


図 2.7.4.3-6　　空腹時血糖値（mmol/L）の箱ひげ図（来院ごと）（4244 試験）

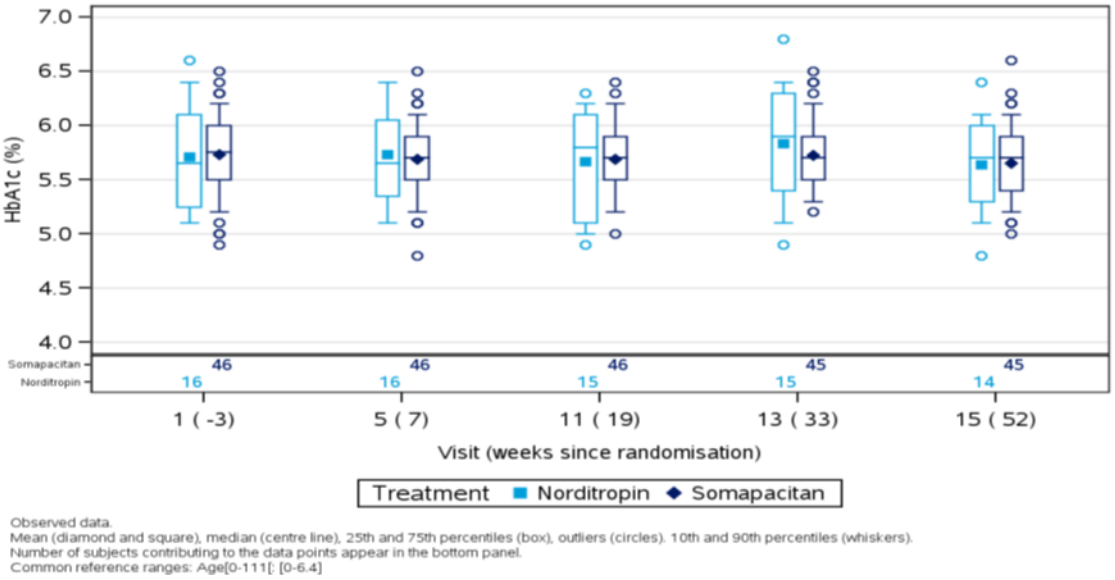


図 2.7.4.3-7　　HbA1c（%）の箱ひげ図（来院ごと）（4244 試験）

<u>試験期間中に糖尿病と診断された被験者</u>

ソマプシタン投与後に糖尿病と診断された被験者はいなかった。ノルディトロピン群で糖尿病と診断された被験者が 1 例報告された〔治験総括報告書、4244 試験（M 5.3.5.1）Section 12.4.1 及び付録 2.7.4.7.1、Listing 75〕。当該被験者について以下に示す。

63 歳の日本人女性患者（被験者 ID：111006）（BMI 32.8 kg/m^2）は、「糖尿病」により治験薬の投与を中止したが〔日本では、糖尿病は治験薬（ノルディトロピン）の禁忌であり、治験実施計画書にも中止基準として規定されていたため、当該被験者は治験薬の投与を中止した〕試験は完了した。当該被験者は、投与後 236 日（来院 13）に糖尿病と診断され、軽度で非重篤な有害事象（因果関係：「可能性あり」）として報告された。空腹時血糖値は診断時（来院 13）で 7.4 mmol/L、来院 15 で 8.0 mmol/L であった〔治験総括報告書、4244 試験（M 5.3.5.1）Listing 16.2.8.5 及び付録 2.7.4.7.1、Figure 83〕。HbA1c は診断時で 6.8%、52 週で 7.1%であった〔治験総括報告書、4244 試験（M 5.3.5.1）Listing 16.2.8.5 及び付録 2.7.4.7.1、Figure 92〕。

<u>ベースライン又は投与後に ADA の診断基準以上の値を少なくとも 1 回以上有する被験者</u>

ベースライン又は投与後に 1 回以上の来院で ADA（Diabetes Care vol.39, suppl.1, Jan 2016）の診断基準以上の値（空腹時血糖値が 7.0 mmol/L 以上又は HbA1c が 6.5%以上）を有する被験者は 4 例であった（付録 2.7.4.7.1、Listing 75）。4 例中 2 例が、投与後に 1 回以上の来院で ADA の診断基準以上の値を

有していたが（付録 2.7.4.7.1、Listing 75）、いずれの被験者においても糖尿病に関連する治療を受けていなかった〔治験総括報告書、4244 試験（M 5.3.5.1）、Appendix 16.2.4、Listing 16.2.4.6〕。

ソマプシタン群では、空腹時血糖値が 7.0 mmol/L 以上の値を有する被験者はいなかった（付録 2.7.4.7.1、Figure 84）。ソマプシタン群の 2 例で HbA1c が 6.5%以上の値を有していた（付録 2.7.4.7.1、Figure 93）。ノルディトロピン群では、試験中の 1 回以上の来院で HbA1c が 6.5%以上となった被験者は、上述の糖尿病を発症した 1 例を含めて 2 例であった（付録 2.7.4.7.1、Figure 92）。

2.7.4.3.2.2　臨床薬理試験の結果

3915 試験（健康被験者）では、空腹時血糖値の平均は基準範囲内であり、試験期間中に臨床的に問題となる変化はみられなかった。数例で空腹時インスリンに一過性の変化がみられたが、GH 製剤を投与した時に予想される範囲内であった。プラセボ群及びソマプシタン群いずれにおいても、インスリンの高値がみられた。詳細は、治験総括報告書〔3915 試験（M 5.3.3.1）Section 12.5.1.2 及び 12.5.1.3〕を参照のこと。

4237 試験及び 4491 試験（健康被験者）では、糖代謝について臨床的に問題となる変化はみられなかった。詳細は、治験総括報告書〔4237 試験（M 5.3.3.1）Section 12.6 及び 4491 試験（M 5.3.1.2）Section 12.4.3〕を参照のこと。

3947 試験（AGHD 患者）では、空腹時血糖値の平均は、ソマプシタン 0.08 mg/kg までの投与群では基準範囲内であり、ソマプシタン 0.12 mg/kg 群及びノルディトロピン群では基準範囲の上限又はこれをわずかに超える値となった。空腹時血糖値の平均は、ソマプシタン群とノルディトロピン群を通じて 5.2～5.5 mmol/L の範囲であった。ソマプシタン群及びノルディトロピン群の両群で空腹時インスリンの平均に高値が認められ、ソマプシタン 0.12 mg/kg 群で最も頻度が高かった。HbA1c の平均はソマプシタン群及びノルディトロピン群の両群で低下する傾向がみられ、平均で 0.3%低下した（範囲：0.2～0.5%）。ソマプシタン群とノルディトロピン群間に明らかな違いはみられなかった。新たに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〔3947 試験（M 5.3.3.2）Section 12.6.1.2〕を参照のこと。

4297 試験（腎機能障害を有する被験者）では、様々な程度の腎機能を有する被験者の一部で、空腹時血糖値及び空腹時インスリンに変動がみられた。これらの被験者は、1 型又は 2 型糖尿病を有していたか、ある程度のインスリン抵抗性が予想される BMI 及び年齢であった。詳細は、治験総括報告書〔4297 試験（M 5.3.3.3）Section 12.4.1〕を参照のこと。

4298 試験（肝機能障害を有する被験者）では、被験者の血糖値及びインスリンに関するパラメータに変化がみられたが、組み入れ前より耐糖能障害又は 2 型糖尿病の状態であったためと考えられた。詳細については、治験総括報告書〔4298 試験（M 5.3.3.3）Section 12.4.1〕を参照のこと。

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

AGHD 患者及び健康被験者（日本人健康被験者を含む）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、いずれの試験及び投与群でも、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〔3915 試験及び 4237 試験（M 5.3.3.1）、3947 試験（M 5.3.3.2）、4297 試験及び 4298 試験（M 5.3.3.3）、4491 試験（M 5.3.1.2）、4054 試験、4043 試験及び 4244 試験（M 5.3.5.1）〕を参照のこと。

臨床検査項目について、臨床的に問題のある変化はすべて有害事象として報告され、付録 2.7.4.7.1、Table 7（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。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　AGHD 患者を対象とした第 3 相試験の結果

IGF-I 濃度が長期間にわたり生理的濃度の上限を超えると、安全性の懸念が生じる可能性があるため、標準的な診療として IGF-I 濃度を測定する必要がある。AGHD 患者を対象とした第 3 相試験（4054 試験、4043 試験及び 4244 試験）では、IGF-I 濃度が基準範囲内（AGHD に対する現在の診療基準）に維持されるよう、各被験者の用量を IGF-I SD スコアに基づいて調整した。用量調整の詳細については、Module 2.7.3.1.3.6 を参照のこと。

IGF-I 濃度及び IGF-I SD スコアは、試験により投与群及び来院時期が異なることから、試験別に示す。4054 試験については、全試験期間（86 週間の投与期間、主要試験期間及び延長期間）の結果を示す。

4054 試験

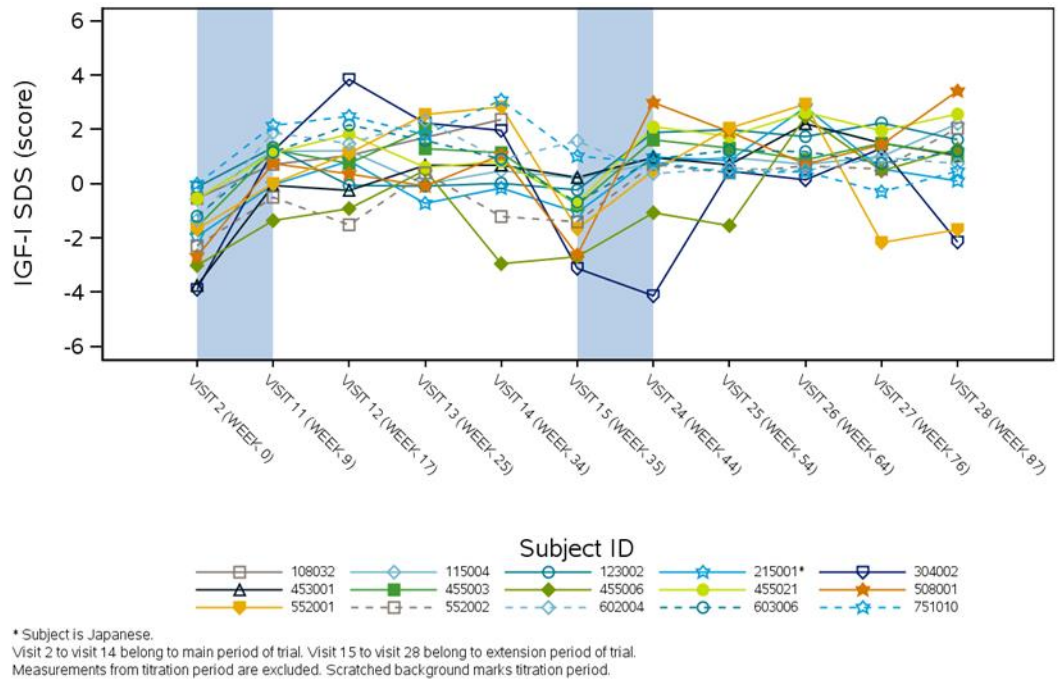
IGF-I SD スコアの平均は、86 週間の投与期間を通して基準範囲内であり、IGF-I SD スコアはソマプシタン群とノルディトロピン群で同様であった〔治験総括報告書、4054 試験（延長期間）（M 5.3.5.1）EOT Figure 14.2.65〕。

用量維持期間中に 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 スコアの推移を投与群別に示す（付録 2.7.4.7.1、Figure 96～100）。ほとんどの場合、IGF-I SD スコアの最高値は、基準範囲の上限である+2 をわずかに上回る値であった。

主要試験期間及び延長期間を通してソマプシタンの投与を受けた被験者のうち、用量維持期間（4054 試験の主要試験期間及び延長期間）中に IGF-I SD スコアが+2 を超えた被験者は 15 例であった（図 2.7.4.3-8）。これら 15 例のうち 5 例（被験者 ID：552001、455021、304002、508001、751010）は、86 週間中の用量維持期間中に 2 回以上、IGF-I SD スコアが+2 を超えた。1 例（被験者 ID：

304002）は治験薬を減量したが、特定の有害事象は報告されなかった（来院 10 で 4.5 mg であった投与量を来院 15 で 1.5 mg に減量した後、来院 17、19 及び 21 でそれぞれ 3 mg、4 mg、4.5 mg に増量）。

すべての投与群の IGF-I SD スコアの推移図を付録 2.7.4.7.1、Figure 96～100 に示す。



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

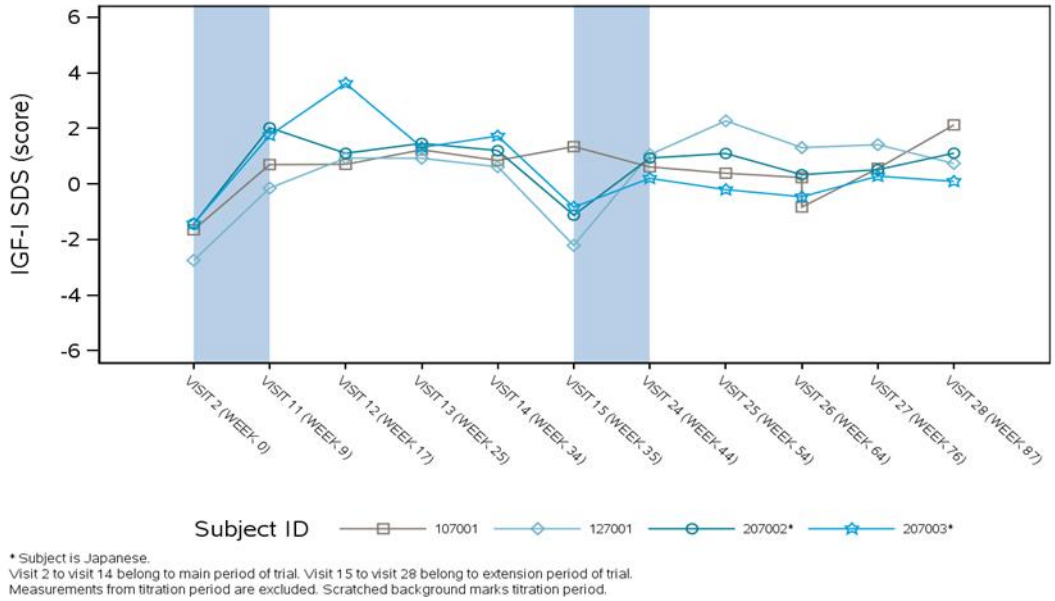
図 2.7.4.3-8　　ソマプシタン/ソマプシタン群で用量維持期間中に IGF-I SD スコアが+2 を超えた被験者（4054 試験）

一時的に生理的範囲を超えた最高 IGF-I 濃度が安全性への懸念に関連しないことを確認するため、86 週間の用量維持期間中に 2 回以上 IGF-I SD スコアが+2 超となったソマプシタン/ソマプシタン群の 5 例の有害事象を評価した。

- 3 例では、報告された有害事象は、非重篤で、治験薬との因果関係は「なし」と判定された（被験者 ID：304002「血中クレアチンホスホキナーゼ増加」2 件、被験者 ID：508001「尿路感染」、被験者 ID：751010「背部痛」及び「足骨折」）。
- 1 例（被験者 ID：455021）で、「頭痛」が複数回報告され、治験薬との因果関係は「可能性あり」と判定されたが、投与量の変更はなかった。重篤な有害事象として報告された事象はなかった。
- 1 例（被験者 ID：552001）で、「高血圧」（重篤な有害事象、因果関係：「なし」）、「関節痛」（因果関係：「あり」）を含む複数の有害事象が報告され、「脂肪肥大症」（因果関係：「可能性あり」）も報告された。

有害事象の詳細については、被験者別に一覧を治験総括報告書〔4054 試験（延長期間）（M 5.3.5.1）Listing 16.2.7.1〕に示す。

主要試験期間及び延長期間を通してノルディトロピン投与を受けた被験者では、用量維持期間中に 3 例で IGF-I SD スコアが基準範囲の上限の+2 となり、1 例で最高 IGF-I SD スコアが+2 を超えた（図 2.7.4.3-9）。最高 IGF-I SD スコアが+2 を超えた 1 例（被験者 ID：207003）は、投与後 170 日に「背部痛」及び「四肢痛」（重症度：軽度、因果関係：「可能性あり」）を発現したため、治験薬を減量した。



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

図 2.7.4.3-9　　ノルディトロピン/ノルディトロピン群で用量維持期間中に IGF-I SD スコアが+2 を超えた被験者（4054 試験）

4043 試験

IGF-I SD スコアの平均は+2 を超えなかった。IGF-I SD スコアの平均の詳細については、Module 2.7.3.3.2.2.2、表 2.7.3.3-16 を参照のこと。用量維持期間中に IGF-I SD スコアが+2 を超えた被験者はいなかった（付録 2.7.4.7.1、Figure 94 及び 95）。

4244 試験

IGF-I SD スコアの平均は+2 を超えなかった。IGF-I SD スコアの平均の詳細については、Module 2.7.3.3.2.2.2、表 2.7.3.3-16 を参照のこと。

当該試験の用量維持期間中にソマプシタン群の 2 例でそれぞれ 1 回、IGF-I SD スコアが+2 を超えた（付録 2.7.4.7.1、Figure 102）。これらの 2 例で重度又は重症と考えられる有害事象は報告されなかった〔被験者 ID：110003「歯周炎」、「低カリウム血症」、「関節痛」、被験者 ID：111005「上咽頭炎」、「小腸炎」（治験総括報告書、4244 試験（M 5.3.5.1）Listing 16.2.7.1）〕。

ノルディトロピン群では、当該試験の用量維持期間中に IGF-I SD スコアが+2 を超えた被験者はいなかった（付録 2.7.4.7.1、Figure 101）。1 例では、用量調整来院終了時にのみ IGF-I SD スコアがわずかに+2 を超えた。

2.7.4.3.3.2.2　臨床薬理試験の結果

成人被験者を対象としたすべての完了した臨床薬理試験（3915 試験及び 3947 試験）で、用量依存的な IGF-I 反応が誘導された。詳細については、Module 2.7.2.3.2.7 を参照のこと。

150 例の健康被験者（3915 試験、4237 試験、4297 試験、4298 試験及び 4491 試験）、腎機能障害を有する被験者 29 例（4297 試験）、肝機能障害を有する被験者 18 例（4298 試験）及び AGHD 患者 26 例（3947 試験）で、ソマプシタンの投与後に新たな安全性の問題は認められなかった（表 2.7.4.1-13）。3915 試験及び 3947 試験では用量レベルの変更を行った。2.7.4.1.3.3 を参照のこと。

各試験の詳細は治験総括報告書の以下の項を参照のこと。

3915 試験（M 5.3.3.1）、Section 11.2.6、Figure 11-11

3947 試験（M 5.3.3.2）、Section 11.3.1、EOT Figure 14.2.49

4237 試験（M 5.3.3.1）、Section 11.3.1、Figure 11-15

4297 試験（M 5.3.3.3）、Section 11.5.1、Figure 11-9

4298 試験（M 5.3.3.3）、Section 11.4、EOT Figure 14.2.21

4491 試験（M 5.3.1.2）、Section 11.3.2、Figure 11-3

2.7.4.3.4　臨床検査値の評価の要約

AGHD 患者において、抗ソマプシタン／抗 GH 抗体産生又はソマプシタンに対するアレルギー／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。7 つの完了した臨床試験（4237 試験及び 4491 試験では評価せず）では、健康成人被験者又は AGHD 患者で、ソマプシタンの投与後に抗ソマプシタン抗体は検出されなかった。

AGHD 患者及び健康被験者（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投与群間の差はみられなかった。AGHD 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、臨床的に問題のあ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）。

3 つの第 3 相試験を通じ、血糖コントロールについてソマプシタンとノルディトロピン間で臨床的に問題となる違いはみられず、ソマプシタンで耐糖能障害のリスクが高くなることは示唆されなかった。健康被験者及び AGHD 患者を対象として完了した臨床試験では、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 相試験のデータによる）。

AGHD 患者を対象とした第 3 相試験において、最高 IGF-I 濃度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 バイタルサイン及び体重

2.7.4.4.1.1 AGHD 患者を対象とした第 3 相試験の結果

試験ごとに投与群及び来院時期が異なることから、結果を試験別に示す。

バイタルサイン

いずれの第 3 相試験（4054 試験、4043 試験及び 4244 試験）においても、AGHD 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。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、血圧に軽微な変化のみが認められた。収縮期／拡張期血圧のベースラインからの変化量の平均（標準偏差）を試験別に表 2.7.4.4-1 に要約する。なお、標準偏差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。

表 2.7.4.4-1 収縮期／拡張期血圧（mmHg）のベースラインからの変化量（4054 試験、4043 試験及び 4244 試験）

Trial ID	**Trial duration**	**somapacitan**		**Norditropin**	
	Weeks	Change in systolic	Change in diastolic	Change in systolic	Change in diastolic
		Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Trial 4054[a]	86	0.45 (13.01)	-0.85 (9.21)	-1.35 (13.07)	-0.61 (8.71)
Trial 4043	26	-1.70 (13.69)	0.08 (9.84)	0.79 (13.77)	2.21 (8.99)
Trial 4244	52	-3.3 (11.7)	0.9 (8.7)	-3.1 (14.8)	1.1 (9.7)

[a] Means (SD) are for the somapacitan/somapacitan and the Norditropin/Norditropin groups.

4054 試験における、投与群を通じたベースラインから試験終了（88 週）までの変化量の平均は、拡張期血圧で-2.48～-0.61 mmHg、収縮期血圧で-1.83～+0.45 mmHg の範囲であった。

4043 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（表 2.7.4.4-1）。

4244 試験では、日本人 AGHD 患者において、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（表 2.7.4.4-1）。

バイタルサインの詳細は、各試験の治験総括報告書〔4054 試験（M 5.3.5.1）Section 12.5.1、4043 試験（M 5.3.5.1）Section 12.7.1 及び 4244 試験（M 5.3.5.1）Section 12.5.3〕を参照のこと。

体重

体重は、有効性のセカンダリーエンドポイントとして設定していた。体重の結果を Module 2.7.3.3.2.1 に示す。

いずれの第 3 相試験（4054 試験、4043 試験及び 4244 試験）においても、AGHD 患者へのソマプシタン反復投与後の体重の平均に、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（表 2.7.4.4-2）。体重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。

表 2.7.4.4-2　　体重（kg）のベースラインからの変化量（4054 試験、4043 試験及び 4244 試験）

Trial ID	Trial duration	somapacitan	Norditropin
	Weeks	Mean (SD)	Mean (SD)
Trial 4054	88	1.5 (4.8)	0.0 (5.2)
Trial 4043	26	0.38 (3.14)	-0.62 (2.17)
Trial 4244	52	-0.29 (3.49)	0.66 (2.50)

[a] Means (SD) are for the somapacitan/somapacitan and the Norditropin/Norditropin groups.

4244 試験では、試験終了時にソマプシタン群の 3 例で、体重がそれぞれ 9.4 kg、5.8 kg、10.4 kg 減少していた。これら 3 例の個々のデータを検討したが、体重減少の明らかな原因は特定できなかった。

体重増加に関連する有害事象の発現については、2.7.4.2.5.4 を参照のこと。

体重の詳細は、各試験の治験総括報告書〔4054 試験（M 5.3.5.1）Section 12.5.2、4043 試験（M 5.3.5.1）Section 12.7.1 及び 4244 試験（M 5.3.5.1）Section 12.5.3〕を参照のこと。

2.7.4.4.1.2　　臨床薬理試験の結果

健康被験者（3915 試験、4237 試験、4297 試験、4298 試験及び 4491 試験）、特別な患者集団（4297 試験及び 4298 試験）及び AGHD 患者（3947 試験）において、somapacitan の単回投与及び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）及び体重に臨床的に問題となるスクリーニングからの変化はみられなかった。

各試験の詳細は治験総括報告書の以下の項を参照のこと。

3915 試験（M 5.3.3.1）、Section 12.6.1

4237 試験（M 5.3.3.1）、Section 12.7.1

4297 試験（M 5.3.3.3）、Section 12.5.1

4298 試験（M 5.3.3.3）、Section 12.5.1

4491 試験（M 5.3.1.2）、Section 12.5.1 及び 12.5.3
3947 試験（M 5.3.3.2）、Section 12.7.1 及び 12.7.2

2.7.4.4.2　心電図

2.7.4.4.2.1　概要

実施した臨床試験において、健康被験者及び AGHD 患者へのソマプシタン投与後に心電図に臨床的に問題となる変化はみられなかった。

2.7.4.4.2.2　AGHD 患者を対象とした第 3 相試験の結果

試験ごとに投与群及び来院時期が異なることから、結果を試験別に示す。

4054 試験

4054 試験では、心電図に臨床的に問題となる変化はみられず、ソマプシタン、ノルディトロピン及びプラセボで心電図の結果に臨床的に問題となる違いはみられなかった〔4054 試験（延長期間）（M 5.3.5.1） Section 12.5.4〕。

心電図の評価の大部分は、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。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」）別の要約を表 2.7.4.4-3 に示す。

9 例の心電図が、投与開始後に 1 つ以上の時点で治験責任医師により「異常／臨床的に問題あり」と判定された〔ソマプシタン/ソマプシタン群：4 例、プラセボ/ソマプシタン群：2 例（1 例はプラセボ投与中、1 例はソマプシタン投与中）、ノルディトロピン/ソマプシタン群：1 例（ソマプシタン投与中）、ノルディトロピン/ノルディトロピン群：2 例〕（表 2.7.4.4-4）。潜在的な催不整脈作用に関連する有害事象を 2.7.4.2.5.7 に示す。

また、ベースラインにおいて、5 例の心電図が治験責任医師により「異常／臨床的に問題あり」と判定された〔ソマプシタン群：3 例（2.5%）、プラセボ群：2 例（3.3%）〕。これらのうち、2 例では、試験中にも心電図が異常と判定された〔ソマプシタン/ソマプシタン群の被験者（被験者 ID：554001）では 25 週及び 35 週、プラセボ/ソマプシタン群の被験者（被験者 ID：251008）ではすべての週〕。

表 2.7.4.4-3　心電図の判定（治験責任医師の判定に基づく）結果の要約（来院別）（4054 試験）

Main/ extension	Placebo/ somapacitan	somapacitan/ somapacitan	Norditropin/ Norditropin	Norditropin/ somapacitan	Norditropin/ -
Safety analysis set, N	61	120	52	51	16
Visit 1B (Week -3)					
N	61 (100.0)	120 (100.0)	52 (100.0)	51 (100.0)	16 (100.0)
Normal	30 (49.2)	77 (64.2)	26 (50.0)	34 (66.7)	7 (43.8)
Abnormal, NCS	29 (47.5)	40 (33.3)	26 (50.0)	17 (33.3)	9 (56.3)
Abnormal, CS	2 (3.3)	3 (2.5)	0	0	0
Missing	0	0	0	0	0
Visit 13 (Week 25)					
N	55 (100.0)	114 (100.0)	52 (100.0)	51 (100.0)	8 (100.0)
Normal	29 (52.7)	78 (68.4)	34 (65.4)	33 (64.7)	4 (50.0)
Abnormal, NCS	22 (40.0)	31 (27.2)	18 (34.6)	16 (31.4)	3 (37.5)
Abnormal, CS	2 (3.6)	1 (0.9)	0	0	0
Missing	2 (3.6)	4 (3.5)	0	2 (3.9)	1 (12.5)
Visit 15 (Week 35)					
N	57 (100.0)	119 (100.0)	52 (100.0)	51 (100.0)	8 (100.0)
Normal	29 (50.9)	77 (64.7)	29 (55.8)	33 (64.7)	3 (37.5)
Abnormal, NCS	26 (45.6)	34 (28.6)	23 (44.2)	17 (33.3)	2 (25.0)
Abnormal, CS	1 (1.8)	2 (1.7)	0	0	0
Missing	1 (1.8)	6 (5.0)	0	1 (2.0)	3 (37.5)
Visit 26 (Week 64)					
N	53 (100.0)	112 (100.0)	50 (100.0)	50 (100.0)	2 (100.0)
Normal	29 (54.7)	77 (68.8)	32 (64.0)	30 (60.0)	1 (50.0)
Abnormal, NCS	23 (43.4)	34 (30.4)	18 (36.0)	19 (38.0)	1 (50.0)
Abnormal, CS	1 (1.9)	1 (0.9)	0	0	0
Missing	0	0	0	1 (2.0)	0

N: Number of subjects, CS: Clinically significant, NCS: Not clinically significant, %: Percentage of subjects, ECG: Electrocardiogram

Summary of ECG (evaluated by investigator) by visit - safety analysis set

Main/ extension	Placebo/ somapacitan	somapacitan/ somapacitan	Norditropin/ Norditropin	Norditropin/ somapacitan	Norditropin/ -
Visit 29 (Week 88)					
N	54 (100.0)	109 (100.0)	49 (100.0)	49 (100.0)	1 (100.0)
Normal	34 (63.0)	74 (67.9)	29 (59.2)	35 (71.4)	0
Abnormal, NCS	18 (33.3)	34 (31.2)	18 (36.7)	12 (24.5)	0
Abnormal, CS	1 (1.9)	1 (0.9)	2 (4.1)	1 (2.0)	0
Missing	1 (1.9)	0	0	1 (2.0)	1 (100.0)

N: Number of subjects, CS: Clinically significant, NCS: Not clinically significant, %: Percentage of subjects, ECG: Electrocardiogram.

表 2.7.4.4-4 治験責任医師により「異常／臨床的に問題あり」と判定（治験責任医師の判定に基づく）された心電図の一覧（4054 試験）

Treatment	Subject ID	Visit (Week)	Treatment	Subject ID	Visit (Week)	Treatment	Subject ID	Visit (Week)
Placebo/ somapacitan	204008	Visit 13 (Week 25)	somapacitan/ somapacitan	106003	Visit 26 (Week 64)	Norditropin/ Norditropin	303002	Visit 29 (Week 88)
	251008	Visit 1b (Week -3)		112001	Visit 15 (Week 35)		303007	Visit 29 (Week 88)
		Visit 13 (Week 25)		209001	Visit 29 (Week 88)	Norditropin/ somapacitan	354001	Visit 29 (Week 88)
		Visit 15 (Week 35)		554001	Visit 1b (Week -3)			
		Visit 26 (Week 64)			Visit 13 (Week 25)			
		Visit 29 (Week 88)			Visit 15 (Week 35)			
	252003	Visit 1b (Week -3)		605006	Visit 1b (Week -3)			
				605007	Visit 1b (Week -3)			

CS: Clinically significant.

心電図の大部分は、ソマプシタン濃度が C_{max} に到達すると予測される時点で測定され（C_{max} への到達は、投与後 16～32 時間と定義）、中央検査機関で判定された（2.7.4.1.2.2）。ソマプシタン投与後の QTc と C_{max} の評価についての詳細は、Module 2.7.2.4.2 に示す。

4054 試験の試験期間中、治験薬の初回投与後の来院で QTc（QTcF、Fridericia の補正式で補正）間隔が 450 msec 超となった被験者は 21 例であり、このうち 1 例（プラセボ群）は QTcF 間隔が 480 msec 超となった（以下に詳細を示す）。C_{max} 付近の来院で測定した心電図で、QTcF 間隔が 500 msec 超となった被験者はいなかった。

QTcF 間隔が 480 msec 超となった被験者（プラセボ群）の来院 15（C_{max} 付近ではない来院）で測定された心電図の QTcF 間隔が 485 msec であった。QTcF 間隔は、ベースラインから 26 msec 延長した。当該被験者は、活動電位持続時間を延長させることが知られている抗不整脈薬のアミオダロンを併用投与しており、このことが 480 msec を超える QTcF 間隔に寄与した可能性が考えられた（治験責任医師のコメントに基づく）。当該被験者で心電図に関連する有害事象の報告はなかった。

心電図の評価に関する詳細は、治験総括報告書〔4054 試験（延長期間）（M 5.3.5.1）Section 12.5.4.2〕を参照のこと。

4043 試験

試験期間中（最長 26 週）、心電図に変化はみられなかった。心電図について投与群間で臨床的に問題となる違いは認められなかった。

1 例（ソマプシタン群、被験者 ID：201005、男性、27 歳、BMI 25.8 kg/m^2）で、投与終了時に心電図の「異常／臨床的に問題あり」が報告された。当該被験者で報告された、その他のすべての心電図は正常であった。心電図の「異常／臨床的に問題あり」の評価は、治験実施計画書の規定に従い、有害事象として報告された。当該被験者に、この他に心電図に関連する特定の有害事象は報告されなかった（「急性副腎皮質機能不全」が 170 日目に報告されたが、非重篤の有害事象と判定され、37 日間持続した。因果関係は「なし」で、完全に回復した。）。

他の 1 例（ノルディトロピン群、被験者 ID：103007）で、「心房粗動」が 2 件報告された（最長 26 週投与）。潜在的な催不整脈作用に関連する有害事象を 2.7.4.2.5.7 に示す。

詳細は、治験総括報告書〔4043 試験（M 5.3.5.1）Section 12.7.3〕を参照のこと。

4244 試験

日本人 AGHD 患者では、試験中又は投与群間で心電図に臨床的に意味のある違いはみられなかった。4244 試験（52 週間）では、心電図に関連する特定の有害事象は報告されなかった。詳細については、治験総括報告書〔4244 試験（M 5.3.5.1）Section 12.5.4〕を参照のこと。

2.7.4.4.2.3　　臨床薬理試験の結果

3915 試験、4237 試験、4297 試験、4298 試験及び 4491 試験の健康被験者 150 例、4297 試験及び 4298 試験の腎機能障害を有する被験者 29 例及び肝機能障害を有する被験者 18 例、3947 試験の AGHD 患者 26 例で、ソマプシタンの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。

健康被験者 1 例（3915 試験、ソマプシタン 0.24 mg/kg）は、心電図に関連する有害事象（軽度の心電図の異常「心電図 2 相性 T 波」）のため試験を中止した。当初、この有害事象は治験薬との因果関係は「可能性あり」と判定された。治験責任医師は、後に当該事象を再評価し、治験薬との因果関係の判定（「可能性あり」）に関し、疑わしいとコメントしている。表 2.7.4.2-18 を脚注も含めて参照のこと。

心電図に異常が認められた記録があったが、いずれも臨床的に問題とはならないと判定された。健康被験者（3915 試験）及び AGHD 患者（3947 試験）では、プラセボ群及びソマプシタン群の数例の被験者で、心電図 QTc 延長の事象として報告された記録がみられた。各試験における詳細は、治験総括報告書〔3915 試験（M 5.3.3.1）Section 12.6.3 及び 3947 試験（M 5.3.3.2）Section 12.7.3〕を参照のこと。心電図 QTc 延長の事象はほとんどが単発であり、QTc の通常の変動と解釈された。治験実施計画書の規定に従い、QTc 間隔が 450 msec 超となった場合を有害事象とした。

2.7.4.4.3　　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

実施された臨床試験において、AGHD 患者へのソマプシタンの反復投与後に、バイタルサイン（収縮期／拡張期血圧及び脈拍数の平均）及び体重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。

実施された臨床試験において、健康被験者及び AGHD 患者へのソマプシタン投与後に、心電図に臨床的に問題とな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 性別（第 3 相試験併合）

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）。性別の部分集団では、第 3 相試験併合での結果と大きな違いはみられなかった。第 3 相試験併合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。有害事象を発現した被験者の割合は、男性より女性の方が高い傾向がみられた。男女別の有害事象の概要及び有害事象の要約を付録 2.7.4.7.1、Table 52～55 に示す。

2.7.4.5.1.2 年齢グループ（第 3 相試験併合）

ソマプシタンの安全性は、いずれの年齢グループにおいても一貫していると考えられた。年齢グループの部分集団では、第 3 相試験併合での結果と大きな違いはみられなかった。第 3 相試験併合に基づく年齢グループ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。年齢グループ別（65 歳未満及び 65 歳以上）の有害事象の概要及び有害事象の要約を付録 2.7.4.7.1、Table 60～63 に示す。

AGHD 患者では、すべての投与群で 65 歳未満の被験者と比較して 65 歳以上の被験者で有害事象の単位時間あたりの発現件数が多かった。しかし、治験薬との因果関係が「可能性あり」と判定された有害事象を発現した被験者の割合は 2 つの年齢グループで同様であった。また、ソマプシタン群では、治験薬との因果関係が「あり」と判定された有害事象を発現した被験者の割合は、65 歳以上の被験者と 65 歳未満の被験者で同様であった（表 2.7.4.5-2）。ノルディトロピン群の結果はこれとは異なり、治験薬との因果関係が「あり」と判定された有害事象を発現した被験者の割合は、65 歳未満の被験者と比較して 65 歳以上の被験者で高かった。

2.7.4.5.1.3 GHD 発症型（第 3 相試験併合）

ソマプシタンの安全性は、GHD 発症型に関わらず一貫していると考えられた。GHD 発症型の部分集団では、第 3 相試験併合での結果と大きな違いはみられなかった。第 3 相試験併合に基づく GHD 発症型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。GHD 発症型別の有害事象の概要及び有害事象の要約を付録 2.7.4.7.1、Table 56～59 に示す。

すべての投与群を通じて、有害事象を発現した被験者の割合は、小児期発症の被験者と比較して成人期発症の被験者で高かった（表 2.7.4.5-3）。しかし、ソマプシタン群における重篤な有害事象及び治験薬との因果関係が「あり」と判定された有害事象を発現した被験者の割合は、成人期発症の被験者と小児期発症の被験者で同様であった。

表 2.7.4.5-1 男女別の有害事象の概要（第 3 相試験併合）

	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Men												
Subjects exposed	29			84			164			228		
Total patient years	18.5			79.6			181.0			279.1		
All adverse events	18 (62.1)	56	302.4	61 (72.6)	371	466.0	125 (76.2)	508	280.6	178 (78.1)	935	334.9
Serious adverse events	2 (6.9)	2	10.8	11 (13.1)	16	20.1	17 (10.4)	30	16.6	29 (12.7)	48	17.2
Causality												
Possible	1 (3.4)	1	5.4	21 (25.0)	39	49.0	28 (17.1)	71	39.2	49 (21.5)	111	39.8
Probable	2 (6.9)	2	10.8	10 (11.9)	21	26.4	17 (10.4)	31	17.1	29 (12.7)	54	19.3
Treatment discont. due to AEs*	1 (3.4)	1	5.4	4 (4.8)	4	5.0	4 (2.4)	5	2.8	9 (3.9)	10	3.6
Women												
Subjects exposed	32			82			169			226		
Total patient years	21.3			81.4			196.8			299.6		
All adverse events	28 (87.5)	126	590.9	69 (84.1)	368	451.9	150 (88.8)	915	464.9	204 (90.3)	1409	470.4
Serious adverse events	3 (9.4)	5	23.4	5 (6.1)	6	7.4	12 (7.1)	20	10.2	18 (8.0)	31	10.3
Causality												
Possible	8 (25.0)	12	56.3	13 (15.9)	29	35.6	37 (21.9)	109	55.4	52 (23.0)	150	50.1
Probable	2 (6.3)	4	18.8	10 (12.2)	21	25.8	20 (11.8)	36	18.3	28 (12.4)	61	20.4
Treatment discont. due to AEs	0			3 (3.7)	6	7.4	2 (1.2)	3	1.5	5 (2.2)	9	3.0

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years. Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054. AE causality is based on judgement of investigators. MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

表 2.7.4.5-2 年齢グループ別の有害事象の概要（第 3 相試験併合）

	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Age <65 years												
Subjects Exposed	51			138			281			380		
Total patient years	33.3			137.2			323.9			494.5		
All adverse events	37 (72.5)	139	417.3	110 (79.7)	589	429.2	229 (81.5)	1212	374.2	320 (84.2)	1940	392.3
Serious adverse events	4 (7.8)	6	18.0	10 (7.2)	13	9.5	24 (8.5)	40	12.3	35 (9.2)	59	11.9
Causality												
Possible	8 (15.7)	12	36.0	28 (20.3)	58	42.3	55 (19.6)	164	50.6	86 (22.6)	234	47.3
Probable	3 (5.9)	5	15.0	13 (9.4)	21	15.3	33 (11.7)	58	17.9	47 (12.4)	84	17.0
Treatment discontinuations due to adverse events	0			6 (4.3)	9	6.6	5 (1.8)	7	2.2	11 (2.9)	16	3.2
Age ≥65 years												
Subjects Exposed	10			28			52			74		
Total patient years	6.5			23.8			53.9			84.2		
All adverse events	9 (90.0)	43	658.5	20 (71.4)	150	630.2	46 (88.5)	211	391.5	62 (83.8)	404	479.6
Serious adverse events	1 (10.0)	1	15.3	6 (21.4)	9	37.8	5 (9.6)	10	18.6	12 (16.2)	20	23.7
Causality												
Possible	1 (10.0)	1	15.3	6 (21.4)	10	42.0	10 (19.2)	16	29.7	15 (20.3)	27	32.1
Probable	1 (10.0)	1	15.3	7 (25.0)	21	88.2	4 (7.7)	9	16.7	10 (13.5)	31	36.8
Treatment discontinuations due to adverse events	1 (10.0)	1	15.3	1 (3.6)	1	4.2	1 (1.9)	1	1.9	3 (4.1)	3	3.6

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years. Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054. AE causality is based on judgement of investigators. MedDRA version 21.0.

表 2.7.4.5-3 GHD 発症型別の有害事象の概要（第 3 相試験併合）

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Childhood onset												
Subjects Exposed	20			45			103			136		
Total patient years	12.5			43.6			116.1			172.2		
All adverse events	11 (55.0)	31	247.6	32 (71.1)	189	433.5	79 (76.7)	377	324.6	105 (77.2)	597	346.6
Serious adverse events	0			2 (4.4)	2	4.6	9 (8.7)	11	9.5	10 (7.4)	13	7.5
Causality												
Possible	2 (10.0)	2	16.0	6 (13.3)	16	36.7	24 (23.3)	45	38.8	31 (22.8)	63	36.6
Probable	1 (5.0)	1	8.0	3 (6.7)	5	11.5	11 (10.7)	19	16.4	14 (10.3)	25	14.5
Treatment discontinuations due to adverse events	0			1 (2.2)	1	2.3	1 (1.0)	2	1.7	2 (1.5)	3	1.7
Adulthood onset												
Subjects Exposed	41			121			230			318		
Total patient years	27.3			117.4			261.7			406.5		
All adverse events	35 (85.4)	151	552.7	98 (81.0)	550	468.3	196 (85.2)	1046	399.7	277 (87.1)	1747	429.8
Serious adverse events	5 (12.2)	7	25.6	14 (11.6)	20	17.0	20 (8.7)	39	14.9	37 (11.6)	66	16.2
Causality												
Possible	7 (17.1)	11	40.3	28 (23.1)	52	44.3	41 (17.8)	135	51.6	70 (22.0)	198	48.7
Probable	3 (7.3)	5	18.3	17 (14.0)	37	31.5	26 (11.3)	48	18.3	43 (13.5)	90	22.1
Treatment discontinuations due to adverse events	1 (2.4)	1	3.7	6 (5.0)	9	7.7	5 (2.2)	6	2.3	12 (3.8)	16	3.9

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years. Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054. AE causality is based on judgement of investigators. MedDRA version 21.0.

2.7.4.5.1.4　　腎機能障害を有する患者の安全性

腎機能障害（軽度、中等度及び重度、ならびに血液透析を必要とする腎機能障害）を有する被験者及び正常な腎機能を有する被験者において、ソマプシタンの週 1 回皮下投与を 3 回実施後の忍容性は良好であった。詳細は、治験総括報告書〔4297 試験（M 5.3.3.3）Section 13.2〕を参照のこと。

2.7.4.5.1.5　　肝機能障害を有する患者の安全性

肝機能障害（軽度又は中等度の肝機能障害）を有する被験者及び正常な肝機能を有する被験者において、ソマプシタンの週 1 回皮下投与を 3 回実施後の忍容性は良好であった。詳細は、治験総括報告書〔4298 試験（M 5.3.3.3）Section 13.2〕を参照のこと。

2.7.4.5.1.6　　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

4054 試験及び 4043 試験では、全集団と日本人集団の間の人口統計学的特性及びベースライン特性の一貫性について、内因性民族的要因（年齢、性別及び GHD 発症型）の一貫性を検討することで評価した。4054 試験の年齢及び GHD 発症型ならびに 4043 試験の性別について、日本人集団と全集団間でわずかな違いがみられた（Module 2.7.3、付録 2.7.3.6.2、Table 5 及び 6）。

4054 試験の年齢及び GHD 発症型ならびに 4043 試験の性別が安全性（有害事象及び重篤な有害事象）に及ぼす影響を検討した。日本人集団と全集団の間でこれらの要因にわずかな違いがみられたが、日本人集団と全集団のいずれにおいても、4054 試験では年齢及び GHD 発症型、4043 試験では性別が安全性に対して明らかな影響を与えることはなかった。なお、日本人集団の各部分集団におけるそれぞれの投与群の被験者数は非常に少なかったことに留意する必要がある。

4054 試験及び 4043 試験における全集団及び日本人集団の年齢、性別及び GHD 発症型別の有害事象の概要及び有害事象の要約を付録 2.7.4.7.2、Table 45～52（4054 試験、年齢別）、Table 29～36（4043 試験、男女別）及び Table 37～44（4054 試験、GHD 発症型別）に示す。

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については、特定の統計解析は行わなかった。

GH 製剤の 1 日 1 回投与から切り替える患者

ノルディトロピンの 1 日 1 回投与からソマプシタンの週 1 回投与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、4054 試験におけるノルディトロピン/ソマプシタン群の被験者の安全性のデータに基づいて行われた。

ノルディトロピンの 1 日 1 回投与からソマプシタンの週 1 回投与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。4054 試験の投与群別の有害事象の概要を治験総括報告書〔4054 試験（延長期間）（M 5.3.5.1）Table 12-1 及び Figure 12-1〔有害事象を発現した被験者の割合が 5%以上であった有害事象（基本語別）〕〕に示す。

さらに、ノルディトロピンの 1 日 1 回投与からソマプシタンの週 1 回投与に切り替えた被験者の安全性は、組み入れ前に GH 製剤の 1 日 1 回投与で治療中の被験者を対象とした 4043 試験及び 4244 試験におけるソマプシタン群の安全性のデータからも支持された（2.7.4.2.1～2.7.4.2.4）。

2.7.4.5.3 薬物相互作用

臨床的に問題となる可能性があるソマプシタンの薬物相互作用の一覧を表 2.7.4.5-4 に示す。また、糖質コルチコイドと GH 製剤との相互作用は、表 2.7.4.5-5 に示す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 GH 製剤の相互作用としてよく知られているものである。

表 2.7.4.5-4 CCDS に提示した薬物相互作用

Topic	**Descriptive text**
Cytocrome P450 metabolized 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.
Oral estrogens	In women on oral estrogen replacement, a higher dose of GH may be required to achieve the treatment goal.
Insulin	In insulin treated patients adjustment of insulin dose may be needed after initiation of GH treatment.
Other	The metabolic effects of GH can also be influenced by additional therapy with other hormones, e.g. thyroid hormones.

表 2.7.4.5-5 CCDS に提示したソマプシタンの警告及び使用上の注意

Topic by SOC and PT	**Proposed text**
Endocrine disorders	
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 therapy, patients should have their thyroid function tested regularly, and should receive replacement therapy with thyroid hormone when indicated.
Adrenocortical insufficiency	Patients receiving GH therapy 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.
Metabolism disorders	
Hyperglycaemia	Treatment with GH may decrease insulin sensitivity, particularly at higher doses in susceptible patients. Consequently, hyperglycaemia may occur in subjects 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 therapy. The doses of antihyperglycemic drugs (i.e. insulin or oral agents) may require adjustment when GH therapy is instituted in these patients.
Neoplasms benign, malignant & unspecified	
Neoplasms	There is no evidence for increased risk of new primary cancers in adults, treated with GH. In patients in complete remission from tumours or malignant disease, GH therapy has not been associated with an increased relapse rate. An overall slight increase in second neoplasms has been observed in childhood cancer survivors treated with GH, with the most frequent being intracranial tumours. The dominant risk factor for second neoplasms seems to be prior exposure to radiation. Patients who have achieved complete remission of malignant disease should be followed closely for relapse after commencement of GH therapy. GH treatment should be interrupted in case of any development or reoccurrence of malignant disease.
Nervous system disorders	
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.

2.7.4.5.4　　妊娠及び授乳時の使用

受胎能

ソマプシタンの受胎能に関する臨床経験はなく、その使用が受胎能に与える潜在的な影響は、臨床において検討していない。

想定される最大臨床曝露量（8 mg/週）の 29 倍以上の曝露量となる用量のソマプシタンをラットに投与したが、雌雄の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。

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。

想定される最大臨床曝露量（8 mg/週）を大きく上回る曝露量（18 倍以上）となる用量のソマプシタンを妊娠中（器官形成期）のラット及びウサギに皮下投与したが、胎児に有害な影響を示すエビデンスは認められなかった。

想定される最大臨床曝露量（8 mg/週）の 250 倍以上の曝露量となる高用量のソマプシタンを投与した雌ラットの胎児に、長骨の短小、彎曲及び肥厚が認められた。ラットにおけるこれらの所見は、出生後に消失することが示されており、不可逆的な異常ではなく軽微な奇形と考えられる。

妊娠ウサギに想定される最大臨床曝露量（8 mg/週）の 130 倍以上の曝露量となる用量のソマプシタンを皮下投与した結果、胎児の発育抑制が認められた。

想定される最大臨床曝露量（8 mg/週）の 600 倍以上の曝露量となる用量でソマプシタンをラットに皮下投与したが、出生前及び出生後の発生に有害な影響はみられなかった。

授乳

ソマプシタン投与の授乳に関する臨床経験はなく、ソマプシタンの使用が授乳に与える潜在的な影響は、臨床において検討していない。

授乳中のラットでは、ソマプシタンに関連する物質が母乳中に分泌されたが、血漿中濃度より低濃度であった（最大で 50%）。

ソマプシタンがヒト母乳中に移行するか否かは不明である。多くの薬剤がヒト母乳中に移行するため、授乳中の女性にソマプシタンを投与する場合は注意が必要である。

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ない。

2.7.4.5.6　薬物乱用及び依存

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、離脱症状及び反跳効作用の可能性はないと考えられる。他の GH 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　最高投与量のソマプシタンを投与した被験者の安全性

すべての第 3 相試験（4054 試験、4043 試験及び 4244 試験）では、ソマプシタンの用量は最大 8 mg/週まで調整可能であった（Module 2.7.3.4.2.1）。各試験での最高投与量は、4054 試験及び 4043 試験 4244 試験では 8.0 mg/週、4244 試験では 4.8 mg/週であった。

本項では、第 3 相試験でソマプシタンを最高投与量まで投与した被験者の安全性データを要約する。また、臨床薬理試験の 3947 試験及び 3915 試験で、8 mg/週を超える用量でソマプシタンを投与した被験者（AGHD 患者及び日本人を含む健康被験者）の安全性データも要約する。

第 3 相試験で最高投与量まで用量調整された被験者及び臨床薬理試験で 8 mg/週を超える用量が投与された被験者で、特段の安全性上の懸念は認められなかった。

2.7.4.5.9.1　AGHD 患者を対象とした第 3 相試験

4054 試験

主要試験期間中に、1 例（被験者 ID：502002）が、ソマプシタンの最大用量である 8.0 mg まで用量調整された〔治験総括報告書、4054 試験（M 5.3.5.1）Appendix 16.2.5、Listing 16.2.5.1〕。当該被験者では、特別な安全性の懸念はみられず、有害事象の報告はなかった〔治験総括報告書、4054 試験（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1〕。

4043 試験

1 例（被験者 ID：303001）が、ソマプシタンの最大用量である 8.0 mg まで用量調整された〔治験総括報告書、4043 試験（M 5.3.5.1）Appendix 16.2.5、Listing 16.2.5.1〕。当該被験者では、1 件の重篤な有害事象「乳房形成」が報告された。本事象は、重度であり、ソマプシタンとの因果関係は「なし」と判定された〔治験総括報告書、4043 試験（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1〕。

当該被験者は、その他に 12 件の有害事象を発現したが、いずれも臨床的に重大な懸念はないと考えられた〔治験総括報告書、4043 試験（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.2〕。これらの 12 件の有害事象のうち、複数回発現した事象は「無力症」（2 件）であった。3 件の有害事象（「無力症」、「悪心」及び「嘔吐」）が重度に分類されたことを除き、いずれの事象も重症度は軽度又は中等度であった。ソマプシタンとの因果関係が「可能性あり」と判定された事象は 2 件（「無力症」及び「体重増加」）であり、その他の事象では因果関係は「なし」と判定された。「無力症」（2 件目の事象）、「疼痛」、「睡眠障害」及び「脱毛症」以外の有害事象の転帰は「回復」であった。

4244 試験

4244 試験では、ソマプシタンの最大用量である 8.0 mg まで用量調整された被験者はいなかった。本試験での最高投与量は 4.8 mg/週であった〔治験総括報告書、4244 試験（M 5.3.5.1）Appendix 16.2.5、

Listing 16.2.5.1〕。当該被験者（被験者 ID：106003）は、2 件の有害事象（「胃腸炎」及び「耳鳴」）を発現したが、いずれの事象も重症度は軽度であり、ソマプシタンとの因果関係は「なし」と判定された〔治験総括報告書、4244 試験（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.1〕。当該被験者は、有害事象から回復した。

2.7.4.5.9.2　臨床薬理試験

健康被験者を対象としたヒトへの初回投与試験（3915 試験、体重当たりの用量（mg/kg）で投与）

3915 試験の反復投与パートでは、0.16 mg/kg/週又は 0.24 mg/kg/週を投与した日本人健康被験者が、8 mg/週を超える用量（18.1 mg/週までの用量）でソマプシタンの投与を受けた〔表 2.7.4.5-6、治験総括報告書、3915 試験（M 5.3.5.1）Appendix 16.2.5、Listing 16.2.5.2〕。有害事象はいずれも軽度又は中等度に分類され、非重篤であった。すべての被験者は、有害事象から回復した〔治験総括報告書、3915 試験（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.5〕。「下痢」1 件及び「錯感覚」1 件を除くすべての有害事象は、ソマプシタンとの因果関係は「なし」と判定された。これらの事象は、同一被験者で報告された〔被験者 ID：201193、0.24 mg/kg/週（16.8 mg/週）、治験総括報告書、3915 試験（M 5.3.5.1）Appendix 16.2.5、Listing 16.2.5.2〕。ソマプシタンとの因果関係は、「下痢」が「可能性あり」、「錯感覚」が「あり」と判定された。本試験におけるソマプシタンの最高用量（18.1mg/週）を投与した 1 例（被験者番号：201194、0.24mg/kg/週）では、軽度の有害事象「便秘」を発現したが、ソマプシタンとの因果関係は「なし」と判定された。

0.16 mg/kg/週又は 0.24 mg/kg/週を投与した非アジア人健康被験者が、8 mg/週を超える用量（22.1 mg/週までの用量）でソマプシタンの投与を受けた〔表 2.7.4.5-6、治験総括報告書、3915 試験（M 5.3.5.1）Appendix 16.2.5、Listing 16.2.5.3〕。有害事象はいずれも軽度又は中等度に分類され、非重篤であった。すべての被験者は、有害事象から回復した〔治験総括報告書、3915 試験（M 5.3.5.1）Appendix 16.2.7、Listing 16.2.7.6〕。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、0.16 mg/kg/週及び 0.24 mg/kg/週を投与した被験者で、それぞれ 20 件及び 17 件であった。これらの被験者で、高頻度で報告され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は、「末梢性浮腫」、「関節痛」、「筋肉痛」及び「錯感覚」であった〔治験総括報告書、3915 試験（M 5.3.5.1）Table 12-10〕。

報告された有害事象はいずれも臨床的に重大な懸念はないと考えられ、多くの有害事象が GH 投与に関連する既知の事象であった [8,16]。

表 2.7.4.5-6　8 mg/週を超える用量でソマプシタンを投与した日本人及び非アジア人健康被験者の投与量及び有害事象（3915 試験、反復投与パート）

	Japanese				Non-Asian			
Weekly dose (mg/kg)	0.16		0.24		0.16		0.24	
Subjects exposed	6		6		6		7	
Weekly dose (mg/week) (range)	9.94 (8.71; 11.39)		15.63 (13.40; 18.09)		13.07 (10.72; 15.41)		19.24 (15.41; 22.11)	
	N (%)	E	N (%)	E	N (%)	E	N (%)	E
Adverse events	1 (17)	2	2 (33)	4	6 (100)	23	7 (100)	22
Serious	0	0	0	0	0	0	0	0
Severity								
Mild	1 (17)	2	2 (33)	3	6 (100)	16	7 (100)	18
Moderate	0	0	1 (17)	1	1 (17)	7	3 (43)	4
Causality								
Possible	0	0	1 (17)	1	5 (83)	10	5 (71)	9
Probable	0	0	1 (17)	1	4 (67)	10	4 (57)	8
Unlikely	1 (17)	2	1 (17)	2	3 (50)	3	3 (43)	5

N is defined as the number of subjects having the given event, or an event in the given system organ class at least once. E is defined as the number of adverse events (AEs) reported. % is the percentage of exposed subjects having the event.
AE causality is based on judgement of investigators.

AGHD 患者を対象とした第 1 相、安全性、用量探索〔体重当たりの用量（mg/kg）〕試験（3947 試験）

0.08 mg/kg/週のソマプシタンを投与した AGHD 患者 6 例のうち、1 例（被験者 ID：102005）の投与量が 9.65 mg/週であった。当該被験者では有害事象の発現はなかった〔治験総括報告書、3947 試験（M.5.3.3.2）Appendix 16.2.5、Listing 16.2.5.1 ならびに Appendix 16.2.7、Listing 16.2.7.1 及び 16.2.7.5〕。

0.12mg/kg/週のソマプシタンを投与した AGHD 患者 6 例で、計 40 件の有害事象が報告された〔治験総括報告書、3947 試験（M.5.3.3.2）Table 12-2〕。大部分の有害事象は、重症度が軽度（32 件）又は中等度（6 件）に分類され、ソマプシタンとの因果関係は「なし」（24 件）と判定された。因果関係が「可能性あり」又は「あり」と判定された有害事象 16 件のうち、高頻度で報告された有害事象は、「体重増加」及び「血中ブドウ糖増加」であった〔治験総括報告書、3947 試験（M.5.3.3.2）Table 12-5〕。0.12mg/kg/週のソマプシタンを投与した AGHD 患者で報告された有害事象はいずれも臨床的に重大な懸念はないと考えられ、本用量までの忍容性は良好であり、安全性及び局所忍容性に懸念は認められなかった。

0.12 mg/kg/週のソマプシタン（11.59 mg/週）を投与された 1 例（被験者 ID：103010）では、1 件の重度で重篤な有害事象「腎癌」が報告された。当該事象は、ソマプシタンとの因果関係は「なし」と判定された〔表 2.7.4.2-17、ならびに治験総括報告書、3947 試験（M.5.3.3.2）Appendix 16.2.5、Listing 16.2.5.1 及び Appendix 16.2.7、Listing 16.2.7.1〕。0.12 mg/kg/週のソマプシタンを投与された別の 1 例（被験者 ID：103011、8.31 mg/週を投与）では、ソマプシタンとの因果関係が「可能性あり」と判定された、重度の「酵素異常」が 1 件認められた。いずれの被験者も有害事象から回復した。

2.7.4.5.10　特別な患者集団及び状況下における安全性の要約

部分集団（年齢、性別及び GHD 発症型）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懸念はなかった。各部分集団では、第 3 相試験併合での結果と大きな違いはみられなかった。

ノルディトロピンの 1 日 1 回投与からソマプシタンの週 1 回投与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（軽度、中等度及び重度、ならびに血液透析を必要とする腎機能障害）を有する被験者及び肝機能障害（軽度又は中等度肝機能障害）を有する被験者で、ソマプシタンの忍容性は良好であった。

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 GH 製剤の相互作用としてよく知られているものである。

ソマプシタン投与の受胎能、妊娠及び授乳に関する臨床経験はなく、ソマプシタンの使用がそれらに与える潜在的な影響は、臨床において検討していない。

特別な状況（過量投与又は薬物乱用及び依存）でのソマプシタンの臨床経験はない。

4054 試験及び 4043 試験で最大用量の 8.0 mg/週を投与した被験者及び 4244 試験で最高投与量の 4.8 mg/週を投与した被験者で、特段の安全性上の懸念は認められなかった。

臨床薬理試験の 3947 試験では、0.12 mg/kg/週（約 11.6 mg/週）までのソマプシタンの投与は、良好な忍容性を示し、安全性の懸念は認められなかった。さらに、8.0 mg/週を超える用量での安全性は、3915 試験（日本人及び非日本人健康被験者における最高投与量：18.1 mg/週及び 22.1 mg/週）の結果からも支持された。

2.7.4.6 市販後データ

ソマプシタンは市販されていないため、市販後データはない。

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ソマプシタン（遺伝子組換え）

2.7.4.7 付録

1. 第 3 相試験結果に基づく解析帳票（試験別及び併合）

ノボ ノルディスク ファーマ株式会社

Table of contents

Page

1 Summary of adherence (%) - full analysis set 10
2 Summary of baseline characteristics - full analysis set 11
3 Summary of exposure - safety analysis set 13
4 Subject exposure by 3 month periods - summary - full analysis set 14
5 Adverse Events - safety analysis set 15
6 Serious adverse events - safety analysis set 17
7 Adverse events by system organ class and preferred term - safety analysis set 19
8 Serious adverse events by system organ class, preferred term, and treatment group - safety analysis set 39
9 Severe adverse events by system organ class and preferred term - safety analysis set 43
10 Moderate adverse events by system organ class and preferred term - safety analysis set 47
11 Mild adverse events by system organ class and preferred term - safety analysis set 56
12 Possibly or probably related adverse events by system organ class and preferred term - safety analysis set 72
13 Possibly or probably related serious adverse events by system organ class and preferred term - safety analysis set 78
14 Possibly or probably related severe adverse events by system organ class and preferred term - safety analysis set 79
15 Possibly related adverse events by system organ class and preferred term - safety analysis set 80
16 Possibly related serious adverse events by system organ class and preferred term - safety analysis set 85
17 Possibly related severe adverse events by system organ class and preferred term - safety analysis set 86
18 Probably related adverse events by system organ class and preferred term - safety analysis set 87
19 Probably related serious adverse events by system organ class and preferred term - safety analysis set 90
20 Probably related severe adverse events by system organ class and preferred term - safety analysis set 91
21 Most frequent adverse events (>=5%) by system organ class and preferred term - safety analysis 92
22 Most frequent adverse events by preferred term (>=5%) - safety analysis set 93
23 Serious adverse events onset by 3 month periods - summary - safety analysis set 94
24 Adverse events by system organ class and preferred term - Hypothyroidism - safety analysis set 95
25 Adverse events by system organ class and preferred term - Pancreaitis - safety analysis set 96
26 Adverse events by system organ class and preferred term - Peripheral oedema - safety analysis set 97
27 Adverse events by system organ class and preferred term - Fatigue/Asthenia - safety analysis set 98
28 Adverse events by system organ class and preferred term - Allergic reactions (non-anaphylactic reactions) - safety analysis set 99
29 Adverse events by system organ class and preferred term - Injection site reactions - safety analysis set 101

30 Adverse events by system organ class and preferred term - Lipohypertrophy - safety analysis set 102
31 Adverse events by system organ class and preferred term - Lipoatrophy - safety analysis set 103
32 Adverse events by system organ class and preferred term - Blood alkaline phosphatase increased (bone) - safety analysis set 104
33 Adverse events by system organ class and preferred term - Drug specific antibodies present - safety analysis set.....104
34 Adverse events by system organ class and preferred term - High level group terms Cardiac and vascular investigations incl. arrhythmia - safety analysis set 105
35 Adverse events by system organ class and preferred term - Weight increased - safety analysis set 106
36 Adverse events by system organ class and preferred term - Hyperglycaemia - safety analysis set.....107
37 Adverse events by system organ class and preferred term - Type 2 diabetes - safety analysis set.....108
38 Adverse events by system organ class and preferred term - Arthralgia - safety analysis set 109
39 Adverse events by system organ class and preferred term - Myalgia - safety analysis set 110
40 Adverse events by system organ class and preferred term - Scoliosis - safety analysis set 110
41 Adverse events by system organ class and preferred term - All benign, malignant and unspecified neoplasms - safety analysis set 111
42 Adverse events by system organ class and preferred term - Headache - safety analysis set 112
43 Adverse events by system organ class and preferred term - Paraesthesia - safety analysis set 113
44 Adverse events by system organ class and preferred term - Stroke - safety analysis set 113
45 Adverse events by system organ class and preferred term - Carpal tunnel syndrome - safety analysis set.....114
46 Adverse events by system organ class and preferred term - Benign intracranial hypertension - safety analysis set.....114
47 Adverse events by system organ class and preferred term - Rare events - safety analysis set 115
48 Adverse events by system organ class and preferred term - Fatal outcome - safety analysis set 117
49 Adverse events by system organ class and preferred term - Hypersensitivity (Anaphylactic reactions) - safety analysis set 118
50 Adverse events by system organ class and preferred term - Adrenocortical insufficiency (secondary) - safety analysis set 118
51 Adverse events by system organ class and preferred term - metabolism disorders - glycaemic control - safety analysis set 119
52 Adverse Events - Male - safety analysis set 120
53 Adverse events by system organ class and preferred term - Male - safety analysis set 122
54 Adverse Events - Female - safety analysis set.....135
55 Adverse events by system organ class and preferred term - Female - safety analysis set.....137
56 Adverse Events - Childhood onset - safety analysis set 152
57 Adverse events by system organ class and preferred term - Childhood onset - safety analysis set.....154
58 Adverse Events - Adulthood onset - safety analysis set.....163
59 Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set.....165
60 Adverse Events - age <65 - safety analysis set 183

61 Adverse events by system organ class and preferred term - age <65 - safety analysis set 185
62 Adverse Events - age >=65 - safety analysis set 203
63 Adverse events by system organ class and preferred term - age >=65 - safety analysis set 205
64 Adverse events - Neoplasms benign, malignant and unspecified (including cysts and polyps) - 4043 - listing - safety analysis set 213
65 Adverse events - Neoplasms benign, malignant and unspecified (including cysts and polyps) - 4054 - listing - safety analysis set 214
66 Adverse events - Neoplasms benign, malignant and unspecified (including cysts and polyps) - 4244 - listing - safety analysis set 217
67 Adverse events - Cardiac and vascular investigations incl. arrhythmia - 4043 - listing - safety analysis set 218
68 Adverse events - Cardiac and vascular investigations incl. arrhythmia - 4054 - listing - safety analysis set 219
69 Adverse events - Cardiac and vascular investigations incl. arrhythmia - 4244 - listing - safety analysis set 222
70 Adverse events for patients with diabetes (diagnosis present at baseline) - 4043 - listing - safety analysis set 223
71 Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set 224
72 Box plot for fasting subjects of fasting plasma glucose (mmol/L) by visit - 4054 extension – safety analysis set 241
73 Box plot for fasting subjects of fasting insulin (pmol/L) by visit - 4054 extension – safety analysis set 242
74 Box plot of HbA1c (%) by visit - 4054 extension – safety analysis set 243
75 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 244
76 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4043 - Norditropin - safety analysis set 264
77 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4043 - somapacitan - safety analysis set 265
78 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4054 - Norditropin/no treatment - safety analysis set 266
79 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4054 - Norditropin/Norditropin - safety analysis set 267
80 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4054 - Norditropin/somapacitan - safety analysis set 268
81 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4054 - placebo/somapacitan - safety analysis set 269
82 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4054 - somapacitan/somapacitan - safety analysis set 270
83 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4244 - Norditropin - safety analysis set 271

84 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4244 - somapacitan - safety analysis set 272
85 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4043 - Norditropin - safety analysis set 273
86 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4043 - somapacitan - safety analysis set 274
87 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4054 - Norditropin/no treatment - safety analysis set 275
88 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4054 - Norditropin/Norditropin - safety analysis set 276
89 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4054 - Norditropin/somapacitan - safety analysis set 277
90 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4054 - placebo/somapacitan - safety analysis set 278
91 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4054 - somapacitan/somapacitan - safety analysis set 279
92 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4244 - Norditropin - safety analysis set 280
93 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4244 - somapacitan - safety analysis set 281
94 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4043 - Norditropin - safety analysis set 282
95 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4043 - somapacitan - safety analysis set 283
96 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4054 - Norditropin/no treatment - safety analysis set 284
97 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4054 - Norditropin/Norditropin - safety analysis set 285
98 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4054 - Norditropin/somapacitan - safety analysis set 286
99 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4054 - placebo/somapacitan - safety analysis set 287
100 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4054 - somapacitan/somapacitan - safety analysis set 288
101 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4244 - Norditropin - safety analysis set 289
102 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4244 - somapacitan - safety analysis set 290
103 Summary of exposure - Norditropin/somapacitan pool - safety analysis set 291
104 Summary of baseline characteristics - Norditropin/somapacitan pool - full analysis set 292
105 Adverse events - Cochran-Mantel-Haenszel adjusted vs Naïve - Norditropin/somapacitan pool - safety analysis set 294

106 Serious adverse events - Cochran-Mantel-Haenszel adjusted vs Naïve - Norditropin/somapacitan pool - safety analysis set 295
107 Most frequent adverse events (>=5%) by system organ class and preferred term - naive - Norditropin/somapacitan pool - safety analysis set 296
108 Most frequent adverse events (>=5%) by system organ class and preferred term - Cochran-Mantel-Haenszel adjusted - Norditropin/somapacitan po ol - safety analysis set....297
109 Most frequent adverse events (>=5%) by system organ class and preferred term -Cochran-Mantel-Haenszel adjusted - Norditropin/somapacitan poo l - safety analysis set....298
110 Adverse events - SMQ - Cochran-Mantel-Haenszel adjusted vs. Naïve - Norditropin/somapacitan pool - safety analysis set 299
111 Listing of preferred terms used for SMQ 20000160 - Hypothyroidism....303
112 Listing of preferred terms used for SMQ 20000022 - Pancreatitis 304
113 Listing of preferred terms used for SMQ 20000214 - Allergic reactions (non-anaphylactic reactions) 305
114 Listing of preferred terms used for SMQ 20000060 - Stroke....310
115 Listing of preferred terms used for SMQ 20000021 - Hypersensitivity (Anaphylactic reactions) 313
116 Listing of preferred terms used for NNMQ - Peripheral oedema 313
117 Listing of preferred terms used for NNMQ - Fatique/Asthenia....313
118 Listing of preferred terms used for NNMQ - Weight increased 314
119 Listing of preferred terms used for NNMQ - Injection site reaction....315
120 Listing of preferred terms used for NNMQ - Lipohypertrophy....316
121 Listing of preferred terms used for NNMQ - Lipoatrophy....316
122 Listing of preferred terms used for NNMQ - Blood alkaline phosphatase increased (bone)....317
123 Listing of preferred terms used for NNMQ - Drug specific antibodies present 318
124 Listing of preferred terms used for NNMQ - Cardiac and vascular investigations incl. arrhythmia 319
125 Listing of preferred terms used for NNMQ - Hyperglycaemia....327
126 Listing of preferred terms used for NNMQ - Type 2 diabetes....328
127 Listing of preferred terms used for NNMQ - Athralgia 329
128 Listing of preferred terms used for NNMQ - Myalgia 329
129 Listing of preferred terms used for NNMQ - Scoliosis 329
130 Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms 330
131 Listing of preferred terms used for NNMQ - Headache....366
132 Listing of preferred terms used for NNMQ - Paraesthesia....367
133 Listing of preferred terms used for NNMQ - Carpal tunnel syndrome....367
134 Listing of preferred terms used for NNMQ - Benign intracranial hypertension....367
135 Listing of preferred terms used for NNMQ - Rare events....368
136 Listing of preferred terms used for NNMQ - Adrenocortical insufficiency (secondary)....398
137 Summary of baseline characteristics by treatment - 4054 - full analysis set 399
138 Summary of exposure by treatment - 4054 entire trial - safety analysis set 401
139 Adverse Events - 4054 entire trial - safety analysis set....402

140 Serious adverse events - 4054 entire trial - safety analysis set 404
141 Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set....406
142 Serious adverse events by system organ class, preferred term, and treatment group - 4054 entire trial - safety analysis set 425
143 Most frequent adverse events (>=5%) by system organ class and preferred term - 4054 entire trial - safety analysis....429
144 Most frequent adverse events by preferred term (>=5%) - 4054 entire trial - safety analysis set....431
145 Adverse events by system organ class and preferred term - Hypothyroidism - 4054 - safety analysis set....432
146 Adverse events by system organ class and preferred term - Hypothyroidism - 4043 - safety analysis set....433
147 Adverse events by system organ class and preferred term - Hypothyroidism - 4244 - safety analysis set....433
148 Adverse events by system organ class and preferred term - Pancreaitis - 4054 - safety analysis set....434
149 Adverse events by system organ class and preferred term - Pancreaitis - 4043 - safety analysis set....434
150 Adverse events by system organ class and preferred term - Pancreaitis - 4244 - safety analysis set....434
151 Adverse events by system organ class and preferred term - Peripheral oedema - 4054 - safety analysis set....435
152 Adverse events by system organ class and preferred term - Peripheral oedema - 4043 - safety analysis set....435
153 Adverse events by system organ class and preferred term - Peripheral oedema - 4244 - safety analysis set....436
154 Adverse events by system organ class and preferred term - Fatigue/Asthenia - 4054 - safety analysis set....436
155 Adverse events by system organ class and preferred term - Fatigue/Asthenia - 4043 - safety analysis set....437
156 Adverse events by system organ class and preferred term - Fatigue/Asthenia - 4244 - safety analysis set....438
157 Adverse events by system organ class and preferred term - Allergic reactions (non-anaphylactic reactions) - 4054 - safety analysis set 439
158 Adverse events by system organ class and preferred term - Allergic reactions (non-anaphylactic reactions) - 4043 - safety analysis set 441
159 Adverse events by system organ class and preferred term - Allergic reactions (non-anaphylactic reactions) - 4244 - safety analysis set 442
160 Adverse events by system organ class and preferred term - Injection site reactions - 4054 - safety analysis set....443
161 Adverse events by system organ class and preferred term - Injection site reactions - 4043 - safety analysis set....443
162 Adverse events by system organ class and preferred term - Injection site reactions - 4244 - safety analysis set....444
163 Adverse events by system organ class and preferred term - Lipohypertrophy - 4054 - safety analysis set....445

164 Adverse events by system organ class and preferred term - Lipohypertrophy - 4043 - safety analysis set....445
165 Adverse events by system organ class and preferred term - Lipohypertrophy - 4244 - safety analysis set....446
166 Adverse events by system organ class and preferred term - Lipoatrophy - 4054 - safety analysis set ...446
167 Adverse events by system organ class and preferred term - Lipoatrophy - 4043 - safety analysis set ...447
168 Adverse events by system organ class and preferred term - Lipoatrophy - 4244 - safety analysis set ...447
169 Adverse events by system organ class and preferred term - Blood alkaline phosphatase increased (bone) - 4054 - safety analysis set....448
170 Adverse events by system organ class and preferred term - Blood alkaline phosphatase increased (bone) - 4043 - safety analysis set....448
171 Adverse events by system organ class and preferred term - Blood alkaline phosphatase increased (bone) - 4244 - safety analysis set....449
172 Adverse events by system organ class and preferred term - Drug specific antibodies present - 4054 - safety analysis set....449
173 Adverse events by system organ class and preferred term - Drug specific antibodies present - 4043 - safety analysis set....449
174 Adverse events by system organ class and preferred term - Drug specific antibodies present - 4244 - safety analysis set....449
175 Adverse events by system organ class and preferred term - High level group terms Cardiac and vascular investigations incl. arrhythmia - 4054 - safety analysis set....450
176 Adverse events by system organ class and preferred term - High level group terms Cardiac and vascular investigations incl. arrhythmia - 4043 - safety analysis set....451
177 Adverse events by system organ class and preferred term - High level group terms Cardiac and vascular investigations incl. arrhythmia - 4244 - safety analysis set....451
178 Adverse events by system organ class and preferred term - Weight increased - 4054 - safety analysis set....452
179 Adverse events by system organ class and preferred term - Weight increased - 4043 - safety analysis set....453
180 Adverse events by system organ class and preferred term - Weight increased - 4244 - safety analysis set....453
181 Adverse events by system organ class and preferred term - Hyperglycaemia - 4054 - safety analysis set....454
182 Adverse events by system organ class and preferred term - Hyperglycaemia - 4043 - safety analysis set....454
183 Adverse events by system organ class and preferred term - Hyperglycaemia - 4244 - safety analysis set....455
184 Adverse events by system organ class and preferred term - Type 2 diabetes - 4054 - safety analysis set....455
185 Adverse events by system organ class and preferred term - Type 2 diabetes - 4043 - safety analysis set....456

186 Adverse events by system organ class and preferred term - Type 2 diabetes - 4244 - safety analysis set....457
187 Adverse events by system organ class and preferred term - Arthralgia - 4054 - safety analysis set....458
188 Adverse events by system organ class and preferred term - Arthralgia - 4043 - safety analysis set....459
189 Adverse events by system organ class and preferred term - Arthralgia - 4244 - safety analysis set....460
190 Adverse events by system organ class and preferred term - Myalgia - 4054 - safety analysis set....461
191 Adverse events by system organ class and preferred term - Myalgia - 4043 - safety analysis set....462
192 Adverse events by system organ class and preferred term - Myalgia - 4244 - safety analysis set....463
193 Adverse events by system organ class and preferred term - Scoliosis - 4054 - safety analysis set....463
194 Adverse events by system organ class and preferred term - Scoliosis - 4043 - safety analysis set....463
195 Adverse events by system organ class and preferred term - Scoliosis - 4244 - safety analysis set....464
196 Adverse events by system organ class and preferred term - All benign, malignant and unspecified neoplasms - 4054 - safety analysis set....464
197 Adverse events by system organ class and preferred term - All benign, malignant and unspecified neoplasms - 4043 - safety analysis set....465
198 Adverse events by system organ class and preferred term - All benign, malignant and unspecified neoplasms - 4244 - safety analysis set....465
199 Adverse events by system organ class and preferred term - Headache - 4054 - safety analysis set....466
200 Adverse events by system organ class and preferred term - Headache - 4043 - safety analysis set....467
201 Adverse events by system organ class and preferred term - Headache - 4244 - safety analysis set....468
202 Adverse events by system organ class and preferred term - Paraesthesia - 4054 - safety analysis set....469
203 Adverse events by system organ class and preferred term - Paraesthesia - 4043 - safety analysis set....470
204 Adverse events by system organ class and preferred term - Paraesthesia - 4244 - safety analysis set....470
205 Adverse events by system organ class and preferred term - Stroke - 4054 - safety analysis set....470
206 Adverse events by system organ class and preferred term - Stroke - 4043 - safety analysis set....471
207 Adverse events by system organ class and preferred term - Stroke - 4244 - safety analysis set....471
208 Adverse events by system organ class and preferred term - Carpal tunnel syndrome - 4054 - safety analysis set....471
209 Adverse events by system organ class and preferred term - Carpal tunnel syndrome - 4043 - safety analysis set....472
210 Adverse events by system organ class and preferred term - Carpal tunnel syndrome - 4244 - safety analysis set....472
211 Adverse events by system organ class and preferred term - Benign intracranial hypertension - 4054 - safety analysis set....472
212 Adverse events by system organ class and preferred term - Benign intracranial hypertension - 4043 - safety analysis set....473
213 Adverse events by system organ class and preferred term - Benign intracranial hypertension - 4244 - safety analysis set....473
214 Adverse events by system organ class and preferred term - Rare events - 4054 - safety analysis set....474
215 Adverse events by system organ class and preferred term - Rare events - 4043 - safety analysis set....476
216 Adverse events by system organ class and preferred term - Rare events - 4244 - safety analysis set....476

217 Adverse events by system organ class and preferred term - Fatal outcome - 4054 - safety analysis set....477
218 Adverse events by system organ class and preferred term - Fatal outcome - 4043 - safety analysis set....478
219 Adverse events by system organ class and preferred term - Fatal outcome - 4244 - safety analysis set....478
220 Adverse events by system organ class and preferred term - Hypersensitivity (Anaphylactic reactions) - 4054 - safety analysis set....478
221 Adverse events by system organ class and preferred term - Hypersensitivity (Anaphylactic reactions) - 4043 - safety analysis set....478
222 Adverse events by system organ class and preferred term - Hypersensitivity (Anaphylactic reactions) - 4244 - safety analysis set....479
223 Adverse events by system organ class and preferred term - Adrenocortical insufficiency (secondary) - 4054 - safety analysis set....479
224 Adverse events by system organ class and preferred term - Adrenocortical insufficiency (secondary) - 4043 - safety analysis set....480
225 Adverse events by system organ class and preferred term - Adrenocortical insufficiency (secondary) - 4244 - safety analysis set....480
226 Adverse events by system organ class and preferred term - metabolism disorders - glycaemic control - 4054 - safety analysis set....481
227 Adverse events by system organ class and preferred term - metabolism disorders - glycaemic control - 4043 - safety analysis set....482
228 Adverse events by system organ class and preferred term - metabolism disorders - glycaemic control - 4244 - safety analysis set....483

1 Summary of adherence (%) - full analysis set

	placebo	Norditropin	somapacitan
Number of exposed subjects	61	166	333
Number of reported dosings	1954	53644	18708
Adherence according to diary*			
Mean (SD)	93.8 (16.6)	89.6 (23.3)	94.6 (17.2)
Median	100.0	99.2	100.0
Min; Max	11.8; 100.0	0.4; 100.0	2.9; 100.0
Adherence according to diary* for subjects completing treatment period			
Mean (SD)	98.2 (7.8)	96.8 (8.5)	98.2 (8.0)
Median	100.0	99.5	100.0
Min; Max	42.9; 100.0	22.2; 100.0	11.1; 100.0

* Number of reported dosings from diary and observed dosing visits divided by number of planned dosings multiplied by 100.

2 Summary of baseline characteristics - full analysis set

	placebo	Norditropin	somapacitan	total
Number of Subjects	61	166	333	454
Age (years), N	61	166	333	454
Mean (SD)	45.0 (15.7)	47.2 (15.5)	46.5 (15.1)	47.0 (15.2)
Median	46.0	47.0	46.0	47.0
Min ; Max	23.0 ; 76.0	20.0 ; 77.0	19.0 ; 77.0	19.0 ; 77.0
Agegroup, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
18 - 64 years	51 (83.6)	138 (83.1)	281 (84.4)	380 (83.7)
>= 65 years	10 (16.4)	28 (16.9)	52 (15.6)	74 (16.3)
Sex, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
Female	32 (52.5)	82 (49.4)	169 (50.8)	226 (49.8)
Male	29 (47.5)	84 (50.6)	164 (49.2)	228 (50.2)
Ethnicity, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
Hispanic Or Latino	4 (6.6)	8 (4.8)	15 (4.5)	18 (4.0)
Not Hispanic Or Latino	57 (93.4)	149 (89.8)	303 (91.0)	414 (91.2)
NA	0	9 (5.4)	15 (4.5)	22 (4.8)
Race, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
Asian	16 (26.2)	58 (34.9)	122 (36.6)	166 (36.6)
White	42 (68.9)	94 (56.6)	188 (56.5)	254 (55.9)
Black Or African American	2 (3.3)	3 (1.8)	4 (1.2)	7 (1.5)
Native Hawaiian Or Other Pacific Islander	0	0	1 (0.3)	1 (0.2)
Other	1 (1.6)	2 (1.2)	3 (0.9)	4 (0.9)
NA	0	9 (5.4)	15 (4.5)	22 (4.8)
Country, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
Australia	7 (11.5)	10 (6.0)	26 (7.8)	30 (6.6)
Denmark	0	6 (3.6)	16 (4.8)	22 (4.8)
France	0	7 (4.2)	13 (3.9)	20 (4.4)
Germany	2 (3.3)	8 (4.8)	13 (3.9)	21 (4.6)
India	6 (9.8)	11 (6.6)	19 (5.7)	28 (6.2)
Japan	10 (16.4)	40 (24.1)	93 (27.9)	125 (27.5)
Latvia	2 (3.3)	1 (0.6)	2 (0.6)	3 (0.7)
Lithuania	4 (6.6)	3 (1.8)	7 (2.1)	8 (1.8)
Malaysia	0	3 (1.8)	5 (1.5)	7 (1.5)
Poland	1 (1.6)	2 (1.2)	8 (2.4)	11 (2.4)
Romania	2 (3.3)	14 (8.4)	21 (6.3)	28 (6.2)
Russian Federation	5 (8.2)	6 (3.6)	15 (4.5)	18 (4.0)
South Africa	1 (1.6)	4 (2.4)	7 (2.1)	9 (2.0)
Sweden	0	6 (3.6)	6 (1.8)	10 (2.2)
Turkey	3 (4.9)	1 (0.6)	7 (2.1)	8 (1.8)
Ukraine	4 (6.6)	1 (0.6)	6 (1.8)	8 (1.8)
United Kingdom	0	9 (5.4)	13 (3.9)	19 (4.2)
United States	14 (23.0)	34 (20.5)	56 (16.8)	79 (17.4)
Height (m), N	61	166	333	454
Mean (SD)	1.63 (0.10)	1.65 (0.13)	1.65 (0.11)	1.65 (0.12)
Median	1.64	1.65	1.65	1.65
Min ; Max	1.39 ; 1.83	1.07 ; 1.93	1.30 ; 1.94	1.07 ; 1.94
Body Weight (kg), N	61	166	333	454
Mean (SD)	69.8 (19.7)	76.2 (21.9)	75.0 (21.4)	75.4 (21.2)
Median	69.0	74.3	72.0	73.5
Min ; Max	38.0 ; 115	22.5 ; 151	34.5 ; 151	22.5 ; 151

N: Number of subjects, %: Percentage of subjects, SD: Standard deviation
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.

Summary of baseline characteristics - full analysis set

	placebo	Norditropin	somapacitan	total
BMI (kg/m^2), N	61	166	333	454
Mean (SD)	26.1 (6.4)	27.6 (5.9)	27.4 (6.2)	27.5 (6.1)
Median	25.4	26.8	26.6	26.7
Min ; Max	13.3 ; 44.3	17.0 ; 45.0	13.3 ; 51.9	13.3 ; 51.9
Waist circumference (cm), N	61	119	226	300
Mean (SD)	88.2 (14.5)	94.3 (16.6)	92.2 (15.5)	92.9 (15.7)
Median	87.7	94.6	90.8	92.8
Min ; Max	60.0 ; 123	45.3 ; 153	60.0 ; 153	45.3 ; 153
GHD Onset, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
Childhood-Idiopathic	13 (21.3)	25 (15.1)	53 (15.9)	69 (15.2)
Childhood-Organic	7 (11.5)	20 (12.0)	50 (15.0)	67 (14.8)
Adulthood	41 (67.2)	121 (72.9)	230 (69.1)	318 (70.0)
Diabetes Mellitus, N (%)	61 (100.0)	166 (100.0)	333 (100.0)	454 (100.0)
Diabetic	3 (4.9)	7 (4.2)	11 (3.3)	17 (3.7)
Non-Diabetic	58 (95.1)	159 (95.8)	322 (96.7)	437 (96.3)

N: Number of subjects, %: Percentage of subjects, SD: Standard deviation
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.

3 Summary of exposure - safety analysis set

	placebo	Norditropin	somapacitan
	once weekly	once daily	once weekly
Number of exposed subjects	61	166	333
Days of exposure*			
Mean (SD)	228 (36.1)	336 (184.3)	399 (165.2)
Median	238	238	364
Min; Max	28; 252	1; 619	7; 623
Treatment dose** (mg)			
Mean (SD)	2.20 (0.74)	0.29 (0.19)	2.38 (1.46)
Median	2.00	0.25	2.00
Min; Max	1.00; 3.50	0.05; 1.10	0.10; 8.00
Treatment dose** (mg/kg)			
Mean (SD)	0.034 (0.016)	0.005 (0.004)	0.036 (0.027)
Median	0.032	0.003	0.027
Min; Max	0.014; 0.080	0.001; 0.044	0.001; 0.171
Total Exposure*** (years)	38.2	152.6	363.7

SD: Standard deviation
* Exposure days are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan.
** Stable dose at last titration visit. For subjects in 4054 receiving same treatment in main and extension period, only first titration period is included.
*** Including titration period.

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

	placebo N (%)	Norditropin N (%)	somapacitan N (%)
Number of subjects	61	166	333
Exposure period			
>0 months	61 (100.0)	166 (100.0)	333 (100.0)
>3 months	60 (98.4)	158 (95.2)	326 (97.9)
>6 months	55 (90.2)	151 (91.0)	319 (95.8)
>9 months	0	67 (40.4)	257 (77.2)
>12 months	0	66 (39.8)	253 (76.0)
>15 months	0	50 (30.1)	110 (33.0)
>18 months	0	47 (28.3)	109 (32.7)

N: Number of subjects, %: Percentage of subjects
Subjects from 4054 switching treatment after main trial period are included for each treatment.
Exposure to placebo was only done in 4054 and for no more than 35 weeks.
Month = 30 days.

5 Adverse Events - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All adverse events	46 (75.4)	182	456.8	130 (78.3)	739	458.9	275 (82.6)	1423	376.6	382 (84.1)	2344	405.0
Serious adverse events	5 (8.2)	7	17.6	16 (9.6)	22	13.7	29 (8.7)	50	13.2	47 (10.4)	79	13.7
Medical events of special interest	0			0			0			0		
Severity												
Mild	41 (67.2)	144	361.5	115 (69.3)	499	309.9	250 (75.1)	1081	286.1	347 (76.4)	1724	297.9
Moderate	17 (27.9)	32	80.3	63 (38.0)	221	137.2	99 (29.7)	295	78.1	161 (35.5)	548	94.7
Severe	4 (6.6)	6	15.1	12 (7.2)	19	11.8	26 (7.8)	47	12.4	41 (9.0)	72	12.4
Causality												
Unlikely	45 (73.8)	163	409.2	125 (75.3)	629	390.6	257 (77.2)	1176	311.3	362 (79.7)	1968	340.1
Possible	9 (14.8)	13	32.6	34 (20.5)	68	42.2	65 (19.5)	180	47.6	101 (22.2)	261	45.1
Probable	4 (6.6)	6	15.1	20 (12.0)	42	26.1	37 (11.1)	67	17.7	57 (12.6)	115	19.9
Outcome												
Recovered/Resolved	43 (70.5)	160	401.6	121 (72.9)	594	368.9	254 (76.3)	1169	309.4	359 (79.1)	1923	332.3
Recovering/Resolving	1 (1.6)	2	5.0	13 (7.8)	19	11.8	25 (7.5)	34	9.0	39 (8.6)	55	9.5
Recovered/Resolved With Sequelae	1 (1.6)	1	2.5	4 (2.4)	5	3.1	3 (0.9)	3	0.8	7 (1.5)	9	1.6
Not Recovered/Not Resolved	13 (21.3)	18	45.2	58 (34.9)	116	72.0	108 (32.4)	212	56.1	165 (36.3)	346	59.8
Fatal	1 (1.6)	1	2.5	2 (1.2)	2	1.2	2 (0.6)	4	1.1	5 (1.1)	7	1.2

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Adverse Events - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Unknown	0			1	(0.6)	3 1.9	1	(0.3)	1 0.3	2	(0.4)	4 0.7
Action												
Drug Interrupted	3	(4.9)	5 12.6	6	(3.6)	10 6.2	3	(0.9)	6 1.6	12	(2.6)	21 3.6
Drug Withdrawn	1	(1.6)	1 2.5	6	(3.6)	9 5.6	6	(1.8)	8 2.1	13	(2.9)	18 3.1
Dose Reduced	0			5	(3.0)	7 4.3	10	(3.0)	14 3.7	15	(3.3)	21 3.6
Dose Not Changed	45	(73.8)	170 426.7	126	(75.9)	689 427.9	273	(82.0)	1327 351.2	376	(82.8)	2186 377.7
Not Applicable	3	(4.9)	6 15.1	15	(9.0)	24 14.9	38	(11.4)	68 18.0	56	(12.3)	98 16.9
Treatment discontinuations due to adverse events*	1	(1.6)	1 2.5	7	(4.2)	10 6.2	6	(1.8)	8 2.1	14	(3.1)	19 3.3

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

6 Serious adverse events - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All serious adverse events	5	(8.2)	7 17.6	16	(9.6)	22 13.7	29	(8.7)	50 13.2	47	(10.4)	79 13.7
Medical events of special interest	0			0			0			0		
Severity												
Mild	1	(1.6)	1 2.5	1	(0.6)	1 0.6	6	(1.8)	6 1.6	7	(1.5)	8 1.4
Moderate	1	(1.6)	1 2.5	7	(4.2)	7 4.3	11	(3.3)	15 4.0	18	(4.0)	23 4.0
Severe	3	(4.9)	5 12.6	10	(6.0)	14 8.7	15	(4.5)	29 7.7	27	(5.9)	48 8.3
Causality												
Unlikely	5	(8.2)	7 17.6	16	(9.6)	21 13.0	28	(8.4)	49 13.0	46	(10.1)	77 13.3
Possible	0			0			1	(0.3)	1 0.3	1	(0.2)	1 0.2
Probable	0			1	(0.6)	1 0.6	0			1	(0.2)	1 0.2
Outcome												
Recovered/Resolved	3	(4.9)	5 12.6	13	(7.8)	18 11.2	22	(6.6)	41 10.9	36	(7.9)	64 11.1
Recovering/Resolving	0			0			1	(0.3)	1 0.3	1	(0.2)	1 0.2
Recovered/Resolved With Sequelae	1	(1.6)	1 2.5	1	(0.6)	1 0.6	0			2	(0.4)	2 0.3
Not Recovered/Not Resolved	0			1	(0.6)	1 0.6	3	(0.9)	3 0.8	4	(0.9)	4 0.7
Fatal	1	(1.6)	1 2.5	2	(1.2)	2 1.2	2	(0.6)	4 1.1	5	(1.1)	7 1.2
Unknown	0			0			1	(0.3)	1 0.3	1	(0.2)	1 0.2
Action												

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Serious adverse events - safety analysis set

	placebo				Norditropin				somapacitan				total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Drug Interrupted	1	(1.6)	1	2.5	4	(2.4)	6	3.7	1	(0.3)	3	0.8	6	(1.3)	10	1.7
Drug Withdrawn	0				2	(1.2)	2	1.2	0				2	(0.4)	2	0.3
Dose Reduced	0				1	(0.6)	1	0.6	0				1	(0.2)	1	0.2
Dose Not Changed	3	(4.9)	5	12.6	9	(5.4)	11	6.8	25	(7.5)	39	10.3	35	(7.7)	55	9.5
Not Applicable	1	(1.6)	1	2.5	2	(1.2)	2	1.2	4	(1.2)	8	2.1	7	(1.5)	11	1.9
Treatment discontinuations due to adverse events*	0				3	(1.8)	3	1.9	0				3	(0.7)	3	0.5

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
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AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

7 Adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All adverse events	46 (75.4)	182	456.8	130 (78.3)	739	458.9	275 (82.6)	1423	376.6	382 (84.1)	2344	405.0
Infections and infestations	36 (59.0)	50	125.5	83 (50.0)	158	98.1	171 (51.4)	353	93.4	254 (55.9)	561	96.9
Nasopharyngitis	9 (14.8)	12	30.1	38 (22.9)	53	32.9	84 (25.2)	129	34.1	121 (26.7)	194	33.5
Upper respiratory tract infection	7 (11.5)	7	17.6	13 (7.8)	19	11.8	22 (6.6)	25	6.6	37 (8.1)	51	8.8
Gastroenteritis	2 (3.3)	2	5.0	3 (1.8)	4	2.5	17 (5.1)	21	5.6	22 (4.8)	27	4.7
Influenza	2 (3.3)	3	7.5	3 (1.8)	4	2.5	18 (5.4)	21	5.6	22 (4.8)	28	4.8
Urinary tract infection	1 (1.6)	1	2.5	3 (1.8)	4	2.5	14 (4.2)	20	5.3	17 (3.7)	25	4.3
Sinusitis	3 (4.9)	6	15.1	4 (2.4)	4	2.5	9 (2.7)	11	2.9	15 (3.3)	21	3.6
Bronchitis	3 (4.9)	3	7.5	4 (2.4)	4	2.5	8 (2.4)	8	2.1	14 (3.1)	15	2.6
Tonsillitis	1 (1.6)	1	2.5	4 (2.4)	5	3.1	8 (2.4)	8	2.1	13 (2.9)	14	2.4
Pharyngitis	1 (1.6)	1	2.5	4 (2.4)	6	3.7	3 (0.9)	3	0.8	8 (1.8)	10	1.7
Respiratory tract infection	2 (3.3)	2	5.0	3 (1.8)	4	2.5	3 (0.9)	4	1.1	8 (1.8)	10	1.7
Ear infection	1 (1.6)	1	2.5	2 (1.2)	2	1.2	4 (1.2)	7	1.9	7 (1.5)	10	1.7
Herpes zoster	1 (1.6)	1	2.5	2 (1.2)	2	1.2	4 (1.2)	9	2.4	7 (1.5)	12	2.1
Viral infection	0			1 (0.6)	1	0.6	6 (1.8)	6	1.6	7 (1.5)	7	1.2
Gastroenteritis viral	2 (3.3)	2	5.0	2 (1.2)	2	1.2	2 (0.6)	2	0.5	6 (1.3)	6	1.0
Lower respiratory tract infection	0			1 (0.6)	2	1.2	5 (1.5)	5	1.3	6 (1.3)	7	1.2
Respiratory tract infection viral	0			3 (1.8)	3	1.9	3 (0.9)	3	0.8	6 (1.3)	6	1.0
Rhinitis	0			2 (1.2)	2	1.2	4 (1.2)	4	1.1	6 (1.3)	6	1.0
Tooth abscess	0			3 (1.8)	3	1.9	3 (0.9)	3	0.8	6 (1.3)	6	1.0
Cystitis	2 (3.3)	2	5.0	0			3 (0.9)	4	1.1	5 (1.1)	6	1.0
Fungal infection	0			2 (1.2)	2	1.2	3 (0.9)	3	0.8	5 (1.1)	5	0.9
Viral upper respiratory tract infection	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	3	0.8	5 (1.1)	5	0.9
Gingivitis	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Oral herpes	0			1 (0.6)	1	0.6	3 (0.9)	4	1.1	4 (0.9)	5	0.9
Pharyngitis streptococcal	0			0			4 (1.2)	5	1.3	4 (0.9)	5	0.9

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Cellulitis	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Hordeolum	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Otitis media	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Periodontitis	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Pulpitis dental	0			3 (1.8)	3	1.9	0			3 (0.7)	3	0.5
Tooth infection	0			2 (1.2)	3	1.9	1 (0.3)	2	0.5	3 (0.7)	5	0.9
Appendicitis	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Bronchitis viral	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Clostridium difficile infection	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Conjunctivitis	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Laryngitis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Parotitis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Pneumonia	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Tinea infection	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Abscess	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Acarodermatitis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Candida infection	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Device related sepsis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Diverticulitis	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Escherichia infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eye infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Folliculitis	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Gastrointestinal infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Helicobacter infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Herpes simplex	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Herpes virus infection	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Lung infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Meningitis viral	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Molluscum contagiosum	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Onychomycosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ophthalmic herpes zoster	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Oral candidiasis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Otitis externa	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Paronychia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Periporitis staphylogenes	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pilonidal cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pneumonia bacterial	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Pneumonia viral	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Post procedural infection	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pulmonary tuberculosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pyoderma	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Rotavirus infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sepsis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tinea capitis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tinea cruris	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tinea pedis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Upper respiratory tract infection bacterial	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Urosepsis	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Vaginal infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vulvovaginal candidiasis	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Vulvovaginal mycotic infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Wound infection	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Gastrointestinal disorders	13 (21.3)	24	60.2	38 (22.9)	67	41.6	90 (27.0)	171	45.3	133 (29.3)	262	45.3
Diarrhoea	5 (8.2)	8	20.1	8 (4.8)	8	5.0	21 (6.3)	31	8.2	33 (7.3)	47	8.1
Vomiting	1 (1.6)	2	5.0	6 (3.6)	8	5.0	15 (4.5)	18	4.8	22 (4.8)	28	4.8
Nausea	1 (1.6)	1	2.5	6 (3.6)	8	5.0	9 (2.7)	18	4.8	15 (3.3)	27	4.7
Abdominal pain	1 (1.6)	1	2.5	3 (1.8)	4	2.5	10 (3.0)	13	3.4	14 (3.1)	18	3.1
Toothache	1 (1.6)	1	2.5	4 (2.4)	4	2.5	6 (1.8)	9	2.4	11 (2.4)	14	2.4
Abdominal pain upper	1 (1.6)	1	2.5	2 (1.2)	2	1.2	6 (1.8)	9	2.4	9 (2.0)	12	2.1
Dental caries	0			3 (1.8)	4	2.5	6 (1.8)	6	1.6	9 (2.0)	10	1.7
Dyspepsia	1 (1.6)	2	5.0	4 (2.4)	4	2.5	4 (1.2)	5	1.3	9 (2.0)	11	1.9
Gastritis	1 (1.6)	1	2.5	0			5 (1.5)	6	1.6	6 (1.3)	7	1.2
Gastrooesophageal reflux disease	1 (1.6)	1	2.5	1 (0.6)	1	0.6	4 (1.2)	4	1.1	6 (1.3)	6	1.0
Constipation	0			3 (1.8)	3	1.9	3 (0.9)	4	1.1	5 (1.1)	7	1.2

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Adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Abdominal tenderness	0			3 (1.8)	3	1.9	1 (0.3)	1	0.3	4 (0.9)	4	0.7
Large intestine polyp	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7
Stomatitis	0			1 (0.6)	1	0.6	3 (0.9)	6	1.6	4 (0.9)	7	1.2
Abdominal discomfort	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Abdominal distension	0			0			3 (0.9)	4	1.1	3 (0.7)	4	0.7
Food poisoning	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Colitis	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Dry mouth	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
Enteritis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Epigastric discomfort	0			0			2 (0.6)	5	1.3	2 (0.4)	5	0.9
Flatulence	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Gastric polyps	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Hiatus hernia	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Inguinal hernia	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Irritable bowel syndrome	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Lip swelling	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pancreatitis acute	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Abdominal hernia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Abdominal pain lower	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Abdominal wall mass	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ascites	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Barrett's oesophagus	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Chronic gastritis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Colitis ulcerative	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Dental cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Duodenal ulcer	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Faeces discoloured	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Faeces soft	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Gastrointestinal disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Haemorrhoids	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Intestinal ischaemia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Mouth ulceration	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Oesophagitis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

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Adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Oesophagitis ulcerative	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Poor dental condition	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Rectal polyp	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Reflux gastritis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Retching	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Short-bowel syndrome	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Spigelian hernia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Musculoskeletal and connective tissue disorders	10 (16.4)	14	35.1	45 (27.1)	78	48.4	85 (25.5)	132	34.9	130 (28.6)	224	38.7
Arthralgia	1 (1.6)	1	2.5	17 (10.2)	18	11.2	23 (6.9)	25	6.6	40 (8.8)	44	7.6
Back pain	2 (3.3)	2	5.0	6 (3.6)	8	5.0	21 (6.3)	23	6.1	29 (6.4)	33	5.7
Myalgia	3 (4.9)	3	7.5	8 (4.8)	8	5.0	7 (2.1)	9	2.4	18 (4.0)	20	3.5
Pain in extremity	1 (1.6)	1	2.5	6 (3.6)	8	5.0	7 (2.1)	7	1.9	14 (3.1)	16	2.8
Muscle spasms	1 (1.6)	2	5.0	0			7 (2.1)	7	1.9	8 (1.8)	9	1.6
Musculoskeletal pain	0			2 (1.2)	2	1.2	5 (1.5)	5	1.3	7 (1.5)	7	1.2
Osteoarthritis	0			3 (1.8)	4	2.5	3 (0.9)	3	0.8	6 (1.3)	7	1.2
Joint stiffness	0			3 (1.8)	3	1.9	2 (0.6)	2	0.5	5 (1.1)	5	0.9
Musculoskeletal stiffness	0			1 (0.6)	1	0.6	4 (1.2)	4	1.1	5 (1.1)	5	0.9
Neck pain	0			1 (0.6)	1	0.6	4 (1.2)	5	1.3	5 (1.1)	6	1.0
Joint swelling	0			4 (2.4)	5	3.1	0			4 (0.9)	5	0.9
Muscular weakness	0			1 (0.6)	1	0.6	3 (0.9)	6	1.6	4 (0.9)	7	1.2
Arthritis	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Bursitis	1 (1.6)	2	5.0	0			3 (0.9)	4	1.1	3 (0.7)	6	1.0
Musculoskeletal chest pain	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Pain in jaw	0			1 (0.6)	1	0.6	2 (0.6)	3	0.8	3 (0.7)	4	0.7
Tendonitis	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Tenosynovitis	1 (1.6)	1	2.5	1 (0.6)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	4	0.7
Intervertebral disc degeneration	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
Intervertebral disc protrusion	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Limb discomfort	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5
Muscle twitching	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Rotator cuff syndrome	0			2 (1.2)	3	1.9	0			2 (0.4)	3	0.5

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Coccydynia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Costochondritis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Exostosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Foot deformity	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Fracture pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Groin pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Joint effusion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Joint noise	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Limb deformity	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Lumbar spinal stenosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Muscle disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Muscle tightness	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Myositis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Neck deformity	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Nodal osteoarthritis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Osteoporosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Periarthritis	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Plantar fasciitis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Rheumatoid arthritis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Soft tissue disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Soft tissue mass	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Spinal pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Tendon pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Trigger finger	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Nervous system disorders	14 (23.0)	26	65.3	35 (21.1)	119	73.9	79 (23.7)	169	44.7	119 (26.2)	314	54.3
Headache	10 (16.4)	15	37.7	22 (13.3)	85	52.8	43 (12.9)	109	28.8	69 (15.2)	209	36.1
Dizziness	1 (1.6)	1	2.5	9 (5.4)	12	7.5	14 (4.2)	18	4.8	23 (5.1)	31	5.4
Hypoaesthesia	1 (1.6)	1	2.5	5 (3.0)	6	3.7	6 (1.8)	7	1.9	12 (2.6)	14	2.4
Paraesthesia	2 (3.3)	2	5.0	1 (0.6)	1	0.6	5 (1.5)	6	1.6	8 (1.8)	9	1.6
Sciatica	0			0			5 (1.5)	5	1.3	5 (1.1)	5	0.9
Migraine	1 (1.6)	3	7.5	1 (0.6)	1	0.6	3 (0.9)	4	1.1	4 (0.9)	8	1.4
Somnolence	0			2 (1.2)	2	1.2	2 (0.6)	3	0.8	4 (0.9)	5	0.9

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Adverse events by system organ class and preferred term - safety analysis set

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Intercostal neuralgia	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Carpal tunnel syndrome	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Disturbance in attention	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Dysgeusia	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Hypersomnia	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
Lethargy	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Syncope	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Tremor	1 (1.6)	1	2.5	1 (0.6)	2	1.2	0			2 (0.4)	3	0.5
Ataxia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Burning sensation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Depressed level of consciousness	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hydrocephalus	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hyposmia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Memory impairment	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Meralgia paraesthetica	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Neuralgia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Parosmia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Partial seizures	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Seizure	0			1 (0.6)	3	1.9	0			1 (0.2)	3	0.5
Vestibular migraine	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
General disorders and administration site conditions	9 (14.8)	13	32.6	41 (24.7)	65	40.4	74 (22.2)	124	32.8	114 (25.1)	202	34.9
Fatigue	2 (3.3)	2	5.0	13 (7.8)	13	8.1	19 (5.7)	23	6.1	34 (7.5)	38	6.6
Oedema peripheral	0			6 (3.6)	9	5.6	12 (3.6)	24	6.4	18 (4.0)	33	5.7
Asthenia	1 (1.6)	1	2.5	4 (2.4)	5	3.1	9 (2.7)	11	2.9	14 (3.1)	17	2.9
Pyrexia	0			1 (0.6)	2	1.2	11 (3.3)	13	3.4	12 (2.6)	15	2.6
Injection site bruising	2 (3.3)	3	7.5	6 (3.6)	6	3.7	1 (0.3)	1	0.3	9 (2.0)	10	1.7
Malaise	1 (1.6)	1	2.5	2 (1.2)	2	1.2	5 (1.5)	5	1.3	8 (1.8)	8	1.4
Pain	0			3 (1.8)	3	1.9	5 (1.5)	6	1.6	8 (1.8)	9	1.6
Peripheral swelling	1 (1.6)	1	2.5	3 (1.8)	3	1.9	4 (1.2)	4	1.1	8 (1.8)	8	1.4
Chest pain	1 (1.6)	1	2.5	3 (1.8)	3	1.9	3 (0.9)	3	0.8	7 (1.5)	7	1.2
Face oedema	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	5	0.9

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Adverse events by system organ class and preferred term - safety analysis set

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Influenza like illness	0			3 (1.8)	3	1.9	2 (0.6)	4	1.1	4 (0.9)	7	1.2
Injection site pain	1 (1.6)	1	2.5	1 (0.6)	1	0.6	2 (0.6)	3	0.8	4 (0.9)	5	0.9
Feeling hot	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Non-cardiac chest pain	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Fat tissue decreased	0			1 (0.6)	1	0.6	1 (0.3)	3	0.8	2 (0.4)	4	0.7
Injection site reaction	0			1 (0.6)	1	0.6	1 (0.3)	3	0.8	2 (0.4)	4	0.7
Nodule	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pre-existing condition improved	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5
Thirst	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Axillary pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Chest discomfort	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Chills	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Death	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Gait disturbance	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Hunger	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Inflammatory pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Injection site atrophy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Injection site haematoma	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Injection site haemorrhage	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Injection site hypertrophy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Oedema	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Oedema mucosal	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Retention cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Swelling	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vaccination site pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Vessel puncture site bruise	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Skin and subcutaneous tissue disorders	12 (19.7)	16	40.2	27 (16.3)	38	23.6	48 (14.4)	66	17.5	82 (18.1)	120	20.7
Rash	2 (3.3)	2	5.0	10 (6.0)	12	7.5	6 (1.8)	6	1.6	18 (4.0)	20	3.5
Dry skin	2 (3.3)	2	5.0	0			6 (1.8)	6	1.6	8 (1.8)	8	1.4
Pruritus	0			4 (2.4)	4	2.5	3 (0.9)	4	1.1	7 (1.5)	8	1.4

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Adverse events by system organ class and preferred term - safety analysis set

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Urticaria	0			2 (1.2)	2	1.2	5 (1.5)	6	1.6	7 (1.5)	8	1.4
Eczema	2 (3.3)	2	5.0	2 (1.2)	2	1.2	1 (0.3)	2	0.5	4 (0.9)	6	1.0
Acne	0			0			3 (0.9)	4	1.1	3 (0.7)	4	0.7
Alopecia	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Dermatitis	2 (3.3)	2	5.0	0			2 (0.6)	2	0.5	3 (0.7)	4	0.7
Dermatitis atopic	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Dermatitis contact	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Miliaria	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Rash generalised	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Acanthosis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Ecchymosis	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Haemorrhage subcutaneous	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Hyperkeratosis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Lipodystrophy acquired	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Lipohypertrophy	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Onychoclasis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Skin discolouration	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Asteatosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blister	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Dermal cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Dermatitis allergic	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Drug eruption	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eczema asteatotic	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Erythema	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Exfoliative rash	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hair disorder	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Ingrowing nail	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	1 (0.2)	2	0.3
Papule	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Prurigo	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Pruritus generalised	1 (1.6)	2	5.0	0			0			1 (0.2)	2	0.3
Pustular psoriasis	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Rash erythematous	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Rash macular	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

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Rash maculo-papular	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Rash papular	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Skin burning sensation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Skin erosion	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Skin hyperpigmentation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Skin lesion	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Skin mass	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Skin ulcer	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Skin warm	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Swelling face	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Investigations	7 (11.5)	10	25.1	26 (15.7)	47	29.2	43 (12.9)	90	23.8	70 (15.4)	147	25.4
Blood creatine phosphokinase increased	0			0			12 (3.6)	14	3.7	12 (2.6)	14	2.4
Weight increased	0			2 (1.2)	2	1.2	9 (2.7)	10	2.6	11 (2.4)	12	2.1
Blood testosterone decreased	0			3 (1.8)	3	1.9	3 (0.9)	3	0.8	6 (1.3)	6	1.0
Alanine aminotransferase increased	1 (1.6)	1	2.5	2 (1.2)	2	1.2	3 (0.9)	3	0.8	5 (1.1)	6	1.0
Thyroxine free decreased	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	4	1.1	5 (1.1)	6	1.0
Aspartate aminotransferase increased	1 (1.6)	1	2.5	0			4 (1.2)	5	1.3	4 (0.9)	6	1.0
Blood uric acid increased	0			2 (1.2)	2	1.2	2 (0.6)	2	0.5	4 (0.9)	4	0.7
Cortisol decreased	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7
Creatinine renal clearance decreased	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Gamma-glutamyltransferase increased	0			2 (1.2)	2	1.2	2 (0.6)	2	0.5	4 (0.9)	4	0.7
Glycosylated haemoglobin increased	0			1 (0.6)	2	1.2	3 (0.9)	4	1.1	4 (0.9)	6	1.0
Blood insulin increased	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Blood potassium decreased	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Blood thyroid stimulating hormone decreased	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Hepatic enzyme increased	2 (3.3)	2	5.0	0			1 (0.3)	1	0.3	3 (0.7)	3	0.5
Intraocular pressure increased	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5

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Blood alkaline phosphatase increased	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Blood glucose increased	0			1 (0.6)	3	1.9	1 (0.3)	1	0.3	2 (0.4)	4	0.7
Haematocrit increased	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Liver function test abnormal	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Platelet count increased	0			1 (0.6)	2	1.2	1 (0.3)	1	0.3	2 (0.4)	3	0.5
Weight decreased	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
White blood cell count increased	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Blood alkaline phosphatase decreased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood bilirubin increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood calcium decreased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood cholesterol increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood corticotrophin decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood creatinine decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood creatinine increased	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Blood insulin decreased	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Blood phosphorus increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood potassium increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood pressure decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood pressure increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood testosterone increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Body temperature increased	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Cardiac murmur	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cholangiogram	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cortisol increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Creatinine renal clearance increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Electrocardiogram PR prolongation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Electrocardiogram QT prolonged	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Electrocardiogram T wave abnormal	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Electrocardiogram T wave inversion	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Electrocardiogram abnormal	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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Adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Glomerular filtration rate decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Glomerular filtration rate increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Heart rate increased	0			1 (0.6)	3	1.9	0			1 (0.2)	3	0.5
Hormone level abnormal	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Lymph node palpable	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Normetanephrine urine increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Platelet count decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pulmonary function test decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Thyroid hormones decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Thyroxine decreased	0			0			1 (0.3)	3	0.8	1 (0.2)	3	0.5
Thyroxine increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tri-iodothyronine decreased	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Urine analysis abnormal	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Vitamin D decreased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Injury, poisoning and procedural complications	3 (4.9)	3	7.5	22 (13.3)	31	19.3	45 (13.5)	59	15.6	66 (14.5)	93	16.1
Contusion	1 (1.6)	1	2.5	5 (3.0)	7	4.3	3 (0.9)	4	1.1	9 (2.0)	12	2.1
Fall	0			3 (1.8)	4	2.5	5 (1.5)	6	1.6	8 (1.8)	10	1.7
Tooth fracture	1 (1.6)	1	2.5	2 (1.2)	2	1.2	3 (0.9)	3	0.8	6 (1.3)	6	1.0
Head injury	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7
Ligament sprain	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Arthropod bite	0			2 (1.2)	2	1.2	2 (0.6)	2	0.5	3 (0.7)	4	0.7
Foot fracture	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Muscle strain	0			1 (0.6)	1	0.6	2 (0.6)	4	1.1	3 (0.7)	5	0.9
Arthropod sting	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Chest injury	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Laceration	0			1 (0.6)	2	1.2	1 (0.3)	1	0.3	2 (0.4)	3	0.5
Limb injury	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Meniscus injury	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Post procedural complication	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5

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Procedural pain	1 (1.6)	1	2.5	0			1 (0.3)	2	0.5	2 (0.4)	3	0.5
Spinal compression fracture	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Animal bite	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Bone contusion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Concussion	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Corneal abrasion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Drug dispensing error	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hand fracture	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Heat illness	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Incorrect dose administered	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ligament rupture	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Multiple fractures	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Muscle injury	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Patella fracture	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Post-traumatic pain	0			0			1 (0.3)	3	0.8	1 (0.2)	3	0.5
Prescription drug used without a prescription	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Procedural complication	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Procedural dizziness	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Radius fracture	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Scratch	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Spinal column injury	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Thermal burn	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Tibia fracture	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Toxicity to various agents	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Wound	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Wrist fracture	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Respiratory, thoracic and mediastinal disorders	4 (6.6)	5	12.6	19 (11.4)	32	19.9	30 (9.0)	48	12.7	52 (11.5)	85	14.7
Cough	3 (4.9)	3	7.5	6 (3.6)	7	4.3	8 (2.4)	10	2.6	17 (3.7)	20	3.5
Oropharyngeal pain	2 (3.3)	2	5.0	3 (1.8)	3	1.9	11 (3.3)	11	2.9	15 (3.3)	16	2.8
Epistaxis	0			4 (2.4)	9	5.6	1 (0.3)	1	0.3	5 (1.1)	10	1.7

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Rhinitis allergic	0			3 (1.8)	4	2.5	2 (0.6)	2	0.5	5 (1.1)	6	1.0
Sleep apnoea syndrome	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Dyspnoea	0			3 (1.8)	3	1.9	1 (0.3)	1	0.3	3 (0.7)	4	0.7
Asthma	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Nasal congestion	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Sinus congestion	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Upper respiratory tract congestion	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5
Upper-airway cough syndrome	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Dyspnoea exertional	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Dyspnoea paroxysmal nocturnal	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Increased viscosity of upper respiratory secretion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Paranasal sinus hypersecretion	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Pharyngeal erythema	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pneumonia aspiration	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Respiratory disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Respiratory tract congestion	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Rhinorrhoea	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sinus polyp	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sneezing	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Snoring	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Upper respiratory tract inflammation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Metabolism and nutrition disorders	5 (8.2)	6	15.1	10 (6.0)	11	6.8	27 (8.1)	35	9.3	42 (9.3)	52	9.0
Hypokalaemia	0			0			5 (1.5)	5	1.3	5 (1.1)	5	0.9
Iron deficiency	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7
Vitamin D deficiency	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Diabetes mellitus	0			3 (1.8)	3	1.9	0			3 (0.7)	3	0.5
Gout	0			1 (0.6)	1	0.6	2 (0.6)	4	1.1	3 (0.7)	5	0.9
Hyperphosphataemia	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Hypocalcaemia	1 (1.6)	1	2.5	0			2 (0.6)	2	0.5	3 (0.7)	3	0.5
Dehydration	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3

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Dyslipidaemia	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Fluid retention	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
Hypercholesterolaemia	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Hyperkalaemia	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Hyperlipidaemia	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Hypoglycaemia	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Decreased appetite	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Fat redistribution	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hyperglycaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypertriglyceridaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hyponatraemia	1 (1.6)	2	5.0	0			0			1 (0.2)	2	0.3
Increased appetite	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Obesity	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Polydipsia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vitamin B complex deficiency	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Psychiatric disorders	2 (3.3)	2	5.0	6 (3.6)	7	4.3	22 (6.6)	28	7.4	29 (6.4)	37	6.4
Insomnia	0			1 (0.6)	1	0.6	7 (2.1)	9	2.4	8 (1.8)	10	1.7
Sleep disorder	1 (1.6)	1	2.5	1 (0.6)	1	0.6	5 (1.5)	5	1.3	7 (1.5)	7	1.2
Anxiety	1 (1.6)	1	2.5	0			4 (1.2)	7	1.9	5 (1.1)	8	1.4
Depression	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Attention deficit/hyperactivity disorder	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Adjustment disorder with depressed mood	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Delirium	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Emotional disorder	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Initial insomnia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Mood swings	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Nervousness	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Eye disorders	2 (3.3)	2	5.0	11 (6.6)	14	8.7	14 (4.2)	16	4.2	26 (5.7)	32	5.5
Dry eye	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7

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Vision blurred	1 (1.6)	1	2.5	1 (0.6)	1	0.6	2 (0.6)	2	0.5	4 (0.9)	4	0.7
Visual impairment	0			4 (2.4)	4	2.5	0			4 (0.9)	4	0.7
Cataract	0			3 (1.8)	3	1.9	0			3 (0.7)	3	0.5
Conjunctival haemorrhage	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Glaucoma	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Age-related macular degeneration	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Conjunctivitis allergic	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Diplopia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eye irritation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eye pruritus	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eye swelling	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Eyelid disorder	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Eyelid oedema	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Neovascular age-related macular degeneration	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ocular hyperaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Scleral disorder	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Visual acuity reduced	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Xerophthalmia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vascular disorders	1 (1.6)	1	2.5	8 (4.8)	9	5.6	17 (5.1)	17	4.5	25 (5.5)	27	4.7
Hypertension	1 (1.6)	1	2.5	7 (4.2)	7	4.3	10 (3.0)	10	2.6	18 (4.0)	18	3.1
Hot flush	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Hypotension	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Arteriosclerosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Orthostatic hypotension	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Vascular fragility	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Endocrine disorders	2 (3.3)	2	5.0	9 (5.4)	10	6.2	14 (4.2)	15	4.0	24 (5.3)	27	4.7
Hypothyroidism	1 (1.6)	1	2.5	4 (2.4)	4	2.5	2 (0.6)	2	0.5	7 (1.5)	7	1.2
Adrenocortical insufficiency acute	1 (1.6)	1	2.5	0			4 (1.2)	4	1.1	5 (1.1)	5	0.9
Adrenal insufficiency	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7
Secondary hypothyroidism	0			4 (2.4)	4	2.5	0			4 (0.9)	4	0.7

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Diabetes insipidus	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Glucocorticoid deficiency	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hyperthyroidism	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypopituitarism	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Secondary adrenocortical insufficiency	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Thyroid disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Thyroid mass	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ear and labyrinth disorders	0			8 (4.8)	10	6.2	15 (4.5)	16	4.2	21 (4.6)	26	4.5
Ear pain	0			5 (3.0)	6	3.7	3 (0.9)	3	0.8	7 (1.5)	9	1.6
Vertigo	0			2 (1.2)	2	1.2	5 (1.5)	5	1.3	7 (1.5)	7	1.2
Tinnitus	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Cerumen impaction	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ear discomfort	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Ear disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eustachian tube dysfunction	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
External ear pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Middle ear inflammation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vertigo positional	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood and lymphatic system disorders	0			6 (3.6)	8	5.0	12 (3.6)	15	4.0	18 (4.0)	23	4.0
Anaemia	0			3 (1.8)	3	1.9	7 (2.1)	7	1.9	10 (2.2)	10	1.7
Lymphadenopathy	0			0			3 (0.9)	6	1.6	3 (0.7)	6	1.0
Haemoconcentration	0			2 (1.2)	3	1.9	0			2 (0.4)	3	0.5
Iron deficiency anaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Polycythaemia	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Thrombocytopenia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Renal and urinary disorders	1 (1.6)	1	2.5	10 (6.0)	12	7.5	7 (2.1)	9	2.4	18 (4.0)	22	3.8
Pollakiuria	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Dysuria	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5
Haematuria	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3

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Adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Nephrolithiasis	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Nocturia	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Renal cyst	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Bladder pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Calculus urinary	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Chronic kidney disease	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Micturition disorder	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Polyuria	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ureterolithiasis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Urinary incontinence	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Urinary tract obstruction	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Reproductive system and breast disorders	2 (3.3)	2	5.0	4 (2.4)	4	2.5	11 (3.3)	12	3.2	17 (3.7)	18	3.1
Dysmenorrhoea	2 (3.3)	2	5.0	1 (0.6)	1	0.6	2 (0.6)	2	0.5	5 (1.1)	5	0.9
Gynaecomastia	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Menstruation irregular	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Breast disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cervical dysplasia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Menstruation delayed	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Nipple pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Prostatitis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Uterine polyp	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vaginal discharge	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Vaginal haemorrhage	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vulvovaginal pruritus	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Cardiac disorders	1 (1.6)	1	2.5	5 (3.0)	6	3.7	10 (3.0)	17	4.5	16 (3.5)	24	4.1
Palpitations	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Tachycardia	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Atrioventricular block first degree	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Angina unstable	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Aortic valve incompetence	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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Adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Atrial flutter	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Bradycardia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Bundle branch block right	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Cardiac discomfort	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cardiogenic shock	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cardiomyopathy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cardiovascular disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Left ventricular dysfunction	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Mitral valve incompetence	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Myocardial ischaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sinus arrhythmia	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Ventricular extrasystoles	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ventricular fibrillation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Immune system disorders	2 (3.3)	2	5.0	3 (1.8)	3	1.9	7 (2.1)	8	2.1	12 (2.6)	13	2.2
Seasonal allergy	1 (1.6)	1	2.5	1 (0.6)	1	0.6	6 (1.8)	7	1.9	8 (1.8)	9	1.6
Allergy to plants	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Allergy to vaccine	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Food allergy	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Multiple allergies	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			4 (2.4)	5	3.1	7 (2.1)	7	1.9	11 (2.4)	12	2.1
Lipoma	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pituitary tumour benign	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Angiomyolipoma	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Basal cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Bladder transitional cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Intraductal papillary mucinous neoplasm	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Melanocytic naevus	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pituitary tumour	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Plasma cell myeloma	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

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Adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Soft tissue neoplasm	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hepatobiliary disorders	0			2 (1.2)	3	1.9	7 (2.1)	7	1.9	9 (2.0)	10	1.7
Cholelithiasis	0			1 (0.6)	2	1.2	2 (0.6)	2	0.5	3 (0.7)	4	0.7
Biliary colic	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Hepatic cirrhosis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hepatic steatosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hepatomegaly	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Liver disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Surgical and medical procedures	1 (1.6)	1	2.5	2 (1.2)	2	1.2	5 (1.5)	7	1.9	8 (1.8)	10	1.7
Tooth extraction	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Arterial stent insertion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cholecystectomy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Dental care	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Dental operation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Mammoplasty	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Skin operation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Umbilical hernia repair	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Congenital, familial and genetic disorders	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Myotonia congenita	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Rathke's cleft cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Product issues	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Device malfunction	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2

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8 Serious adverse events by system organ class, preferred term, and treatment group - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All serious adverse events	5 (8.2)	7	17.6	16 (9.6)	22	13.7	29 (8.7)	50	13.2	47 (10.4)	79	13.7
Infections and infestations	1 (1.6)	1	2.5	5 (3.0)	7	4.3	8 (2.4)	11	2.9	13 (2.9)	19	3.3
Gastroenteritis	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Appendicitis	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Gastroenteritis viral	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Urinary tract infection	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Clostridium difficile infection	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Herpes simplex	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Influenza	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pneumonia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pneumonia viral	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sepsis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Urosepsis	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Viral infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Viral upper respiratory tract infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Gastrointestinal disorders	2 (3.3)	3	7.5	2 (1.2)	4	2.5	6 (1.8)	7	1.9	10 (2.2)	14	2.4
Vomiting	1 (1.6)	1	2.5	0			2 (0.6)	2	0.5	3 (0.7)	3	0.5
Inguinal hernia	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Pancreatitis acute	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Abdominal pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Dental cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Diarrhoea	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Intestinal ischaemia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Large intestine polyp	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Short-bowel syndrome	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Stomatitis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Injury, poisoning and procedural complications	0			2 (1.2)	3	1.9	6 (1.8)	6	1.6	8 (1.8)	9	1.6
Drug dispensing error	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Fall	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Head injury	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Patella fracture	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Procedural complication	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Spinal compression fracture	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tibia fracture	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Tooth fracture	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Toxicity to various agents	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Endocrine disorders	1 (1.6)	1	2.5	1 (0.6)	1	0.6	4 (1.2)	4	1.1	6 (1.3)	6	1.0
Adrenocortical insufficiency acute	1 (1.6)	1	2.5	0			2 (0.6)	2	0.5	3 (0.7)	3	0.5
Diabetes insipidus	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypopituitarism	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Secondary adrenocortical insufficiency	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
General disorders and administration site conditions	0			0			5 (1.5)	5	1.3	5 (1.1)	5	0.9
Fatigue	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Death	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Non-cardiac chest pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pyrexia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Investigations	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Blood testosterone increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Cholangiogram	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Electrocardiogram T wave abnormal	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Renal and urinary disorders	0			3 (1.8)	3	1.9	0			3 (0.7)	3	0.5
Nephrolithiasis	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Chronic kidney disease	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Respiratory, thoracic and mediastinal disorders	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Dyspnoea exertional	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pneumonia aspiration	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sleep apnoea syndrome	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cardiac disorders	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
Cardiogenic shock	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ventricular extrasystoles	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ventricular fibrillation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Bladder transitional cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Plasma cell myeloma	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Surgical and medical procedures	0			0			2 (0.6)	4	1.1	2 (0.4)	4	0.7
Arterial stent insertion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cholecystectomy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Mammoplasty	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Umbilical hernia repair	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood and lymphatic system disorders	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Haemoconcentration	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hepatobiliary disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cholelithiasis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Metabolism and nutrition disorders	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hyponatraemia	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Nervous system disorders	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Depressed level of consciousness	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Headache	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Psychiatric disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Delirium	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Skin and subcutaneous tissue disorders	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Dermatitis atopic	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Vascular disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypertension	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

9 Severe adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All severe adverse events	4 (6.6)	6	15.1	12 (7.2)	19	11.8	26 (7.8)	47	12.4	41 (9.0)	72	12.4
Gastrointestinal disorders	2 (3.3)	3	7.5	4 (2.4)	5	3.1	2 (0.6)	4	1.1	8 (1.8)	12	2.1
Vomiting	1 (1.6)	1	2.5	0			2 (0.6)	2	0.5	3 (0.7)	3	0.5
Toothache	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Abdominal pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Dental cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Diarrhoea	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Intestinal ischaemia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Nausea	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pancreatitis acute	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Short-bowel syndrome	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Infections and infestations	1 (1.6)	1	2.5	4 (2.4)	6	3.7	4 (1.2)	6	1.6	8 (1.8)	13	2.2
Appendicitis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Bronchitis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Clostridium difficile infection	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Device related sepsis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Gastroenteritis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Gastroenteritis viral	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Herpes simplex	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pneumonia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pneumonia viral	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sepsis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Urinary tract infection	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Urosepsis	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
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MedDRA version 21.0.

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
General disorders and administration site conditions	0			0			6 (1.8)	6	1.6	6 (1.3)	6	1.0
Asthenia	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Death	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Fatigue	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Non-cardiac chest pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pyrexia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Nervous system disorders	0			0			6 (1.8)	7	1.9	6 (1.3)	7	1.2
Headache	0			0			5 (1.5)	5	1.3	5 (1.1)	5	0.9
Dizziness	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sciatica	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Endocrine disorders	1 (1.6)	1	2.5	0			4 (1.2)	4	1.1	5 (1.1)	5	0.9
Adrenocortical insufficiency acute	1 (1.6)	1	2.5	0			3 (0.9)	3	0.8	4 (0.9)	4	0.7
Diabetes insipidus	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Injury, poisoning and procedural complications	0			1 (0.6)	2	1.2	3 (0.9)	3	0.8	4 (0.9)	5	0.9
Fall	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Procedural complication	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tibia fracture	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Tooth fracture	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Toxicity to various agents	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Musculoskeletal and connective tissue disorders	1 (1.6)	1	2.5	0			3 (0.9)	3	0.8	4 (0.9)	4	0.7
Intervertebral disc protrusion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Muscle spasms	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Muscle tightness	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Musculoskeletal pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Investigations	0			0			3 (0.9)	4	1.1	3 (0.7)	4	0.7

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MedDRA version 21.0.

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Blood creatine phosphokinase increased	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Cholangiogram	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cortisol decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Bladder transitional cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Plasma cell myeloma	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Renal and urinary disorders	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Nephrolithiasis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pollakiuria	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Respiratory, thoracic and mediastinal disorders	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pneumonia aspiration	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sleep apnoea syndrome	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Surgical and medical procedures	0			0			2 (0.6)	4	1.1	2 (0.4)	4	0.7
Arterial stent insertion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cholecystectomy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Mammoplasty	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Umbilical hernia repair	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood and lymphatic system disorders	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Haemoconcentration	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Cardiac disorders	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Cardiogenic shock	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ventricular fibrillation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hepatobiliary disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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MedDRA version 21.0.

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Cholelithiasis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Psychiatric disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Delirium	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Skin and subcutaneous tissue disorders	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Dermatitis atopic	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

10 Moderate adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All moderate adverse events	17 (27.9)	32	80.3	63 (38.0)	221	137.2	99 (29.7)	295	78.1	161 (35.5)	548	94.7
Infections and infestations	6 (9.8)	8	20.1	24 (14.5)	43	26.7	41 (12.3)	62	16.4	67 (14.8)	113	19.5
Nasopharyngitis	2 (3.3)	2	5.0	8 (4.8)	11	6.8	12 (3.6)	16	4.2	21 (4.6)	29	5.0
Gastroenteritis	0			2 (1.2)	3	1.9	6 (1.8)	6	1.6	8 (1.8)	9	1.6
Gastroenteritis viral	1 (1.6)	1	2.5	2 (1.2)	2	1.2	2 (0.6)	2	0.5	5 (1.1)	5	0.9
Tooth abscess	0			3 (1.8)	3	1.9	2 (0.6)	2	0.5	5 (1.1)	5	0.9
Upper respiratory tract infection	1 (1.6)	1	2.5	2 (1.2)	2	1.2	3 (0.9)	3	0.8	5 (1.1)	6	1.0
Influenza	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Tonsillitis	0			2 (1.2)	2	1.2	2 (0.6)	2	0.5	4 (0.9)	4	0.7
Cellulitis	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Cystitis	2 (3.3)	2	5.0	0			1 (0.3)	2	0.5	3 (0.7)	4	0.7
Lower respiratory tract infection	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Urinary tract infection	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Bronchitis	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Ear infection	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pharyngitis	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Respiratory tract infection	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
Respiratory tract infection viral	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Sinusitis	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Viral infection	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Acarodermatitis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Appendicitis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Gastrointestinal infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Gingivitis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Herpes virus infection	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Herpes zoster	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Oral candidiasis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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MedDRA version 21.0.

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Oral herpes	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Otitis externa	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Otitis media	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Periodontitis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pharyngitis streptococcal	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pilonidal cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pneumonia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pneumonia bacterial	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Post procedural infection	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pulmonary tuberculosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pulpitis dental	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Rotavirus infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tooth infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Viral upper respiratory tract infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Wound infection	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Nervous system disorders	5 (8.2)	5	12.6	12 (7.2)	70	43.5	25 (7.5)	59	15.6	41 (9.0)	134	23.2
Headache	4 (6.6)	4	10.0	9 (5.4)	58	36.0	12 (3.6)	40	10.6	25 (5.5)	102	17.6
Dizziness	0			3 (1.8)	3	1.9	4 (1.2)	6	1.6	7 (1.5)	9	1.6
Disturbance in attention	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Hypoaesthesia	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Migraine	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Paraesthesia	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Sciatica	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Ataxia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Carpal tunnel syndrome	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Depressed level of consciousness	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypersomnia	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Lethargy	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Parosmia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Seizure	0			1 (0.6)	3	1.9	0			1 (0.2)	3	0.5
Somnolence	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Syncope	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tremor	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Gastrointestinal disorders	3 (4.9)	4	10.0	15 (9.0)	24	14.9	16 (4.8)	24	6.4	33 (7.3)	52	9.0
Vomiting	1 (1.6)	1	2.5	6 (3.6)	7	4.3	2 (0.6)	2	0.5	9 (2.0)	10	1.7
Nausea	1 (1.6)	1	2.5	3 (1.8)	3	1.9	3 (0.9)	3	0.8	6 (1.3)	7	1.2
Abdominal pain	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	5	1.3	5 (1.1)	7	1.2
Toothache	0			2 (1.2)	2	1.2	3 (0.9)	5	1.3	5 (1.1)	7	1.2
Diarrhoea	1 (1.6)	1	2.5	2 (1.2)	2	1.2	0			3 (0.7)	3	0.5
Stomatitis	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Abdominal pain upper	0			1 (0.6)	1	0.6	1 (0.3)	4	1.1	2 (0.4)	5	0.9
Gastrooesophageal reflux disease	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Abdominal pain lower	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Abdominal tenderness	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Dental caries	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Haemorrhoids	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Inguinal hernia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Irritable bowel syndrome	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pancreatitis acute	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Musculoskeletal and connective tissue disorders	4 (6.6)	4	10.0	11 (6.6)	15	9.3	18 (5.4)	22	5.8	31 (6.8)	41	7.1
Arthralgia	1 (1.6)	1	2.5	3 (1.8)	3	1.9	3 (0.9)	4	1.1	6 (1.3)	8	1.4
Back pain	2 (3.3)	2	5.0	1 (0.6)	1	0.6	1 (0.3)	1	0.3	4 (0.9)	4	0.7
Osteoarthritis	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Muscle spasms	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Muscular weakness	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5
Myalgia	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pain in jaw	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Arthritis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Costochondritis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Foot deformity	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Intervertebral disc protrusion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Joint stiffness	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Joint swelling	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Limb deformity	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Muscle disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Musculoskeletal pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Osteoporosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pain in extremity	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Plantar fasciitis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Rotator cuff syndrome	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Spinal pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Tendonitis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tenosynovitis	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
General disorders and administration site conditions	1 (1.6)	2	5.0	9 (5.4)	11	6.8	16 (4.8)	32	8.5	26 (5.7)	45	7.8
Fatigue	0			2 (1.2)	2	1.2	6 (1.8)	6	1.6	8 (1.8)	8	1.4
Asthenia	0			1 (0.6)	1	0.6	5 (1.5)	5	1.3	6 (1.3)	6	1.0
Oedema peripheral	0			1 (0.6)	1	0.6	4 (1.2)	13	3.4	5 (1.1)	14	2.4
Pain	0			2 (1.2)	2	1.2	2 (0.6)	2	0.5	4 (0.9)	4	0.7
Chest pain	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pyrexia	0			1 (0.6)	2	1.2	1 (0.3)	2	0.5	2 (0.4)	4	0.7
Axillary pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Chills	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Influenza like illness	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Injection site bruising	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Injection site pain	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Injury, poisoning and procedural complications	0			8 (4.8)	12	7.5	14 (4.2)	19	5.0	22 (4.8)	31	5.4
Fall	0			2 (1.2)	2	1.2	2 (0.6)	3	0.8	4 (0.9)	5	0.9
Foot fracture	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Muscle strain	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5

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

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Spinal compression fracture	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Tooth fracture	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Bone contusion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Concussion	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Contusion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hand fracture	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Laceration	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Ligament rupture	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ligament sprain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Meniscus injury	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Multiple fractures	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Patella fracture	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Post procedural complication	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Post-traumatic pain	0			0			1 (0.3)	3	0.8	1 (0.2)	3	0.5
Radius fracture	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Wrist fracture	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Investigations	1 (1.6)	1	2.5	8 (4.8)	9	5.6	11 (3.3)	13	3.4	20 (4.4)	23	4.0
Blood creatine phosphokinase increased	0			0			5 (1.5)	5	1.3	5 (1.1)	5	0.9
Weight increased	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Hepatic enzyme increased	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Aspartate aminotransferase increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood corticotrophin decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood glucose increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood potassium decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood pressure decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood testosterone increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Electrocardiogram T wave inversion	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Glycosylated haemoglobin increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Heart rate increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Intraocular pressure increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

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

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Pulmonary function test decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vitamin D decreased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Weight decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Skin and subcutaneous tissue disorders	0			5 (3.0)	6	3.7	10 (3.0)	10	2.6	14 (3.1)	16	2.8
Dry skin	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Alopecia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blister	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Dermal cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Dermatitis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Dermatitis atopic	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eczema	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Lipodystrophy acquired	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pruritus	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pustular psoriasis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Rash generalised	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Skin burning sensation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Skin ulcer	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Urticaria	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Respiratory, thoracic and mediastinal disorders	1 (1.6)	2	5.0	2 (1.2)	3	1.9	8 (2.4)	9	2.4	11 (2.4)	14	2.4
Oropharyngeal pain	1 (1.6)	1	2.5	0			3 (0.9)	3	0.8	4 (0.9)	4	0.7
Cough	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Dyspnoea	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Dyspnoea exertional	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Respiratory disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sinus congestion	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Sinus polyp	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sleep apnoea syndrome	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Upper respiratory tract inflammation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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

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Ear and labyrinth disorders	0			1 (0.6)	1	0.6	6 (1.8)	6	1.6	7 (1.5)	7	1.2
Ear pain	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Cerumen impaction	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eustachian tube dysfunction	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Middle ear inflammation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vertigo	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vertigo positional	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Metabolism and nutrition disorders	2 (3.3)	2	5.0	1 (0.6)	1	0.6	4 (1.2)	4	1.1	7 (1.5)	7	1.2
Gout	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Hypercholesterolaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypocalcaemia	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Hypoglycaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hyponatraemia	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Psychiatric disorders	0			2 (1.2)	2	1.2	5 (1.5)	8	2.1	7 (1.5)	10	1.7
Anxiety	0			0			3 (0.9)	6	1.6	3 (0.7)	6	1.0
Attention deficit/hyperactivity disorder	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Depression	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Sleep disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cardiac disorders	0			2 (1.2)	3	1.9	4 (1.2)	6	1.6	6 (1.3)	9	1.6
Angina unstable	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Atrial flutter	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Atrioventricular block first degree	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cardiac discomfort	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cardiomyopathy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Palpitations	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Tachycardia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ventricular extrasystoles	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Endocrine disorders	0			2 (1.2)	2	1.2	4 (1.2)	5	1.3	6 (1.3)	7	1.2

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Adrenocortical insufficiency acute	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Glucocorticoid deficiency	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hypopituitarism	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypothyroidism	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Secondary adrenocortical insufficiency	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Thyroid disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Thyroid mass	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eye disorders	2 (3.3)	2	5.0	3 (1.8)	5	3.1	2 (0.6)	2	0.5	6 (1.3)	9	1.6
Cataract	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Age-related macular degeneration	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Dry eye	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eye swelling	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Neovascular age-related macular degeneration	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Scleral disorder	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Vision blurred	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Visual acuity reduced	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Vascular disorders	0			3 (1.8)	3	1.9	3 (0.9)	3	0.8	6 (1.3)	6	1.0
Hypertension	0			3 (1.8)	3	1.9	1 (0.3)	1	0.3	4 (0.9)	4	0.7
Arteriosclerosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypotension	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Renal and urinary disorders	0			5 (3.0)	5	3.1	0			5 (1.1)	5	0.9
Calculus urinary	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Chronic kidney disease	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Dysuria	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Nephrolithiasis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Ureterolithiasis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

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Reproductive system and breast disorders	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	3	0.8	5 (1.1)	5	0.9
Dysmenorrhoea	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Menstruation delayed	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Uterine polyp	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vulvovaginal pruritus	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Immune system disorders	1 (1.6)	1	2.5	2 (1.2)	2	1.2	0			3 (0.7)	3	0.5
Allergy to plants	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Allergy to vaccine	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Food allergy	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Pituitary tumour benign	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Basal cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Surgical and medical procedures	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Dental operation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Skin operation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Tooth extraction	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood and lymphatic system disorders	0			1 (0.6)	2	1.2	1 (0.3)	1	0.3	2 (0.4)	3	0.5
Anaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Haemoconcentration	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Hepatobiliary disorders	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Biliary colic	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3

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MedDRA version 21.0.

11 Mild adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All mild adverse events	41 (67.2)	144	361.5	115 (69.3)	499	309.9	250 (75.1)	1081	286.1	347 (76.4)	1724	297.9
Infections and infestations	31 (50.8)	41	102.9	65 (39.2)	109	67.7	147 (44.1)	285	75.4	216 (47.6)	435	75.2
Nasopharyngitis	8 (13.1)	10	25.1	33 (19.9)	42	26.1	74 (22.2)	113	29.9	108 (23.8)	165	28.5
Upper respiratory tract infection	6 (9.8)	6	15.1	11 (6.6)	17	10.6	19 (5.7)	22	5.8	33 (7.3)	45	7.8
Influenza	2 (3.3)	3	7.5	2 (1.2)	3	1.9	16 (4.8)	18	4.8	19 (4.2)	24	4.1
Gastroenteritis	2 (3.3)	2	5.0	1 (0.6)	1	0.6	12 (3.6)	14	3.7	15 (3.3)	17	2.9
Urinary tract infection	1 (1.6)	1	2.5	2 (1.2)	2	1.2	12 (3.6)	18	4.8	14 (3.1)	21	3.6
Sinusitis	3 (4.9)	6	15.1	3 (1.8)	3	1.9	8 (2.4)	10	2.6	13 (2.9)	19	3.3
Bronchitis	2 (3.3)	2	5.0	3 (1.8)	3	1.9	7 (2.1)	7	1.9	11 (2.4)	12	2.1
Tonsillitis	1 (1.6)	1	2.5	2 (1.2)	3	1.9	6 (1.8)	6	1.6	9 (2.0)	10	1.7
Pharyngitis	1 (1.6)	1	2.5	4 (2.4)	4	2.5	3 (0.9)	3	0.8	8 (1.8)	8	1.4
Herpes zoster	1 (1.6)	1	2.5	2 (1.2)	2	1.2	3 (0.9)	8	2.1	6 (1.3)	11	1.9
Respiratory tract infection	2 (3.3)	2	5.0	3 (1.8)	4	2.5	1 (0.3)	1	0.3	6 (1.3)	7	1.2
Rhinitis	0			2 (1.2)	2	1.2	4 (1.2)	4	1.1	6 (1.3)	6	1.0
Ear infection	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	6	1.6	5 (1.1)	8	1.4
Fungal infection	0			2 (1.2)	2	1.2	3 (0.9)	3	0.8	5 (1.1)	5	0.9
Viral infection	0			1 (0.6)	1	0.6	4 (1.2)	4	1.1	5 (1.1)	5	0.9
Lower respiratory tract infection	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Respiratory tract infection viral	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Viral upper respiratory tract infection	1 (1.6)	1	2.5	1 (0.6)	1	0.6	2 (0.6)	2	0.5	4 (0.9)	4	0.7
Gingivitis	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Hordeolum	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Oral herpes	0			1 (0.6)	1	0.6	2 (0.6)	3	0.8	3 (0.7)	4	0.7
Pharyngitis streptococcal	0			0			3 (0.9)	4	1.1	3 (0.7)	4	0.7
Tooth infection	0			2 (1.2)	3	1.9	1 (0.3)	1	0.3	3 (0.7)	4	0.7
Bronchitis viral	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Conjunctivitis	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Cystitis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Laryngitis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Otitis media	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Parotitis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Periodontitis	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pulpitis dental	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Tinea infection	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Abscess	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Candida infection	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Clostridium difficile infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Diverticulitis	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Escherichia infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eye infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Folliculitis	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Helicobacter infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Lung infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Meningitis viral	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Molluscum contagiosum	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Onychomycosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ophthalmic herpes zoster	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Paronychia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Periporitis staphylogenes	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pyoderma	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Tinea capitis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tinea cruris	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tinea pedis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tooth abscess	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Upper respiratory tract infection bacterial	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vaginal infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vulvovaginal candidiasis	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Vulvovaginal mycotic infection	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Musculoskeletal and connective tissue disorders	8 (13.1)	9	22.6	36 (21.7)	63	39.1	71 (21.3)	107	28.3	111 (24.4)	179	30.9
Arthralgia	0			14 (8.4)	15	9.3	20 (6.0)	21	5.6	34 (7.5)	36	6.2
Back pain	0			5 (3.0)	7	4.3	20 (6.0)	22	5.8	25 (5.5)	29	5.0
Myalgia	3 (4.9)	3	7.5	7 (4.2)	7	4.3	7 (2.1)	8	2.1	17 (3.7)	18	3.1
Pain in extremity	1 (1.6)	1	2.5	6 (3.6)	8	5.0	6 (1.8)	6	1.6	13 (2.9)	15	2.6
Muscle spasms	1 (1.6)	1	2.5	0			5 (1.5)	5	1.3	6 (1.3)	6	1.0
Musculoskeletal pain	0			2 (1.2)	2	1.2	3 (0.9)	3	0.8	5 (1.1)	5	0.9
Musculoskeletal stiffness	0			1 (0.6)	1	0.6	4 (1.2)	4	1.1	5 (1.1)	5	0.9
Neck pain	0			1 (0.6)	1	0.6	4 (1.2)	5	1.3	5 (1.1)	6	1.0
Joint stiffness	0			2 (1.2)	2	1.2	2 (0.6)	2	0.5	4 (0.9)	4	0.7
Bursitis	1 (1.6)	2	5.0	0			3 (0.9)	4	1.1	3 (0.7)	6	1.0
Joint swelling	0			3 (1.8)	4	2.5	0			3 (0.7)	4	0.7
Musculoskeletal chest pain	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Osteoarthritis	0			1 (0.6)	2	1.2	2 (0.6)	2	0.5	3 (0.7)	4	0.7
Arthritis	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Intervertebral disc degeneration	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
Limb discomfort	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5
Muscle twitching	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Muscular weakness	0			0			2 (0.6)	4	1.1	2 (0.4)	4	0.7
Pain in jaw	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Tendonitis	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Tenosynovitis	0			1 (0.6)	2	1.2	1 (0.3)	1	0.3	2 (0.4)	3	0.5
Coccydynia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Exostosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Fracture pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Groin pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Joint effusion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Joint noise	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Lumbar spinal stenosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Myositis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Neck deformity	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Nodal osteoarthritis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

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MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Periarthritis	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Rheumatoid arthritis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Rotator cuff syndrome	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Soft tissue disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Soft tissue mass	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tendon pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Trigger finger	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Gastrointestinal disorders	9 (14.8)	17	42.7	29 (17.5)	38	23.6	78 (23.4)	143	37.8	109 (24.0)	198	34.2
Diarrhoea	4 (6.6)	6	15.1	6 (3.6)	6	3.7	21 (6.3)	31	8.2	31 (6.8)	43	7.4
Vomiting	0			1 (0.6)	1	0.6	11 (3.3)	14	3.7	12 (2.6)	15	2.6
Abdominal pain	0			2 (1.2)	2	1.2	7 (2.1)	8	2.1	9 (2.0)	10	1.7
Dyspepsia	1 (1.6)	2	5.0	4 (2.4)	4	2.5	4 (1.2)	5	1.3	9 (2.0)	11	1.9
Nausea	0			4 (2.4)	5	3.1	6 (1.8)	14	3.7	9 (2.0)	19	3.3
Dental caries	0			2 (1.2)	2	1.2	6 (1.8)	6	1.6	8 (1.8)	8	1.4
Abdominal pain upper	1 (1.6)	1	2.5	1 (0.6)	1	0.6	5 (1.5)	5	1.3	7 (1.5)	7	1.2
Gastritis	1 (1.6)	1	2.5	0			5 (1.5)	6	1.6	6 (1.3)	7	1.2
Constipation	0			3 (1.8)	3	1.9	3 (0.9)	4	1.1	5 (1.1)	7	1.2
Gastrooesophageal reflux disease	1 (1.6)	1	2.5	0			3 (0.9)	3	0.8	4 (0.9)	4	0.7
Large intestine polyp	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7
Toothache	1 (1.6)	1	2.5	0			3 (0.9)	4	1.1	4 (0.9)	5	0.9
Abdominal discomfort	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Abdominal distension	0			0			3 (0.9)	4	1.1	3 (0.7)	4	0.7
Abdominal tenderness	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Food poisoning	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Colitis	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Dry mouth	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
Enteritis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Epigastric discomfort	0			0			2 (0.6)	5	1.3	2 (0.4)	5	0.9
Flatulence	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Gastric polyps	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Hiatus hernia	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Lip swelling	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3

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MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Abdominal hernia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Abdominal wall mass	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ascites	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Barrett's oesophagus	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Chronic gastritis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Colitis ulcerative	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Duodenal ulcer	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Faeces discoloured	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Faeces soft	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Gastrointestinal disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Inguinal hernia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Irritable bowel syndrome	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Mouth ulceration	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Oesophagitis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Oesophagitis ulcerative	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Poor dental condition	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Rectal polyp	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Reflux gastritis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Retching	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Spigelian hernia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Stomatitis	0			0			1 (0.3)	4	1.1	1 (0.2)	4	0.7
General disorders and administration site conditions	9 (14.8)	11	27.6	36 (21.7)	54	33.5	61 (18.3)	86	22.8	96 (21.1)	151	26.1
Fatigue	2 (3.3)	2	5.0	11 (6.6)	11	6.8	12 (3.6)	16	4.2	25 (5.5)	29	5.0
Oedema peripheral	0			6 (3.6)	8	5.0	9 (2.7)	11	2.9	15 (3.3)	19	3.3
Injection site bruising	2 (3.3)	2	5.0	6 (3.6)	6	3.7	1 (0.3)	1	0.3	9 (2.0)	9	1.6
Pyrexia	0			0			9 (2.7)	10	2.6	9 (2.0)	10	1.7
Asthenia	1 (1.6)	1	2.5	3 (1.8)	4	2.5	4 (1.2)	4	1.1	8 (1.8)	9	1.6
Malaise	1 (1.6)	1	2.5	2 (1.2)	2	1.2	5 (1.5)	5	1.3	8 (1.8)	8	1.4
Peripheral swelling	1 (1.6)	1	2.5	3 (1.8)	3	1.9	4 (1.2)	4	1.1	8 (1.8)	8	1.4
Chest pain	1 (1.6)	1	2.5	2 (1.2)	2	1.2	2 (0.6)	2	0.5	5 (1.1)	5	0.9
Face oedema	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	5	0.9

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Influenza like illness	0			3 (1.8)	3	1.9	2 (0.6)	2	0.5	4 (0.9)	5	0.9
Pain	0			1 (0.6)	1	0.6	3 (0.9)	4	1.1	4 (0.9)	5	0.9
Feeling hot	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Injection site pain	0			1 (0.6)	1	0.6	2 (0.6)	3	0.8	3 (0.7)	4	0.7
Fat tissue decreased	0			1 (0.6)	1	0.6	1 (0.3)	3	0.8	2 (0.4)	4	0.7
Injection site reaction	0			1 (0.6)	1	0.6	1 (0.3)	3	0.8	2 (0.4)	4	0.7
Nodule	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Non-cardiac chest pain	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Pre-existing condition improved	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5
Thirst	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Chest discomfort	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Chills	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Gait disturbance	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Hunger	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Inflammatory pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Injection site atrophy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Injection site haematoma	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Injection site haemorrhage	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Injection site hypertrophy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Oedema	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Oedema mucosal	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Retention cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Swelling	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vaccination site pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Vessel puncture site bruise	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Nervous system disorders	10 (16.4)	21	52.7	29 (17.5)	49	30.4	61 (18.3)	103	27.3	95 (20.9)	173	29.9
Headache	7 (11.5)	11	27.6	16 (9.6)	27	16.8	33 (9.9)	64	16.9	52 (11.5)	102	17.6
Dizziness	1 (1.6)	1	2.5	8 (4.8)	9	5.6	10 (3.0)	11	2.9	19 (4.2)	21	3.6
Hypoaesthesia	1 (1.6)	1	2.5	4 (2.4)	5	3.1	6 (1.8)	6	1.6	11 (2.4)	12	2.1
Paraesthesia	2 (3.3)	2	5.0	1 (0.6)	1	0.6	3 (0.9)	4	1.1	6 (1.3)	7	1.2
Intercostal neuralgia	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Somnolence	0			1 (0.6)	1	0.6	2 (0.6)	3	0.8	3 (0.7)	4	0.7

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

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Dysgeusia	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Migraine	1 (1.6)	3	7.5	0			2 (0.6)	3	0.8	2 (0.4)	6	1.0
Sciatica	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Tremor	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Burning sensation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Carpal tunnel syndrome	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hydrocephalus	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypersomnia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hyposmia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Lethargy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Memory impairment	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Meralgia paraesthetica	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Neuralgia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Partial seizures	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Syncope	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Vestibular migraine	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Skin and subcutaneous tissue disorders	12 (19.7)	16	40.2	23 (13.9)	31	19.3	40 (12.0)	56	14.8	71 (15.6)	103	17.8
Rash	2 (3.3)	2	5.0	10 (6.0)	12	7.5	6 (1.8)	6	1.6	18 (4.0)	20	3.5
Dry skin	2 (3.3)	2	5.0	0			4 (1.2)	4	1.1	6 (1.3)	6	1.0
Pruritus	0			3 (1.8)	3	1.9	3 (0.9)	4	1.1	6 (1.3)	7	1.2
Urticaria	0			2 (1.2)	2	1.2	4 (1.2)	5	1.3	6 (1.3)	7	1.2
Acne	0			0			3 (0.9)	4	1.1	3 (0.7)	4	0.7
Dermatitis contact	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Eczema	2 (3.3)	2	5.0	1 (0.6)	1	0.6	1 (0.3)	2	0.5	3 (0.7)	5	0.9
Miliaria	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Acanthosis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Alopecia	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Dermatitis	2 (3.3)	2	5.0	0			1 (0.3)	1	0.3	2 (0.4)	3	0.5
Ecchymosis	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Haemorrhage subcutaneous	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Hyperkeratosis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3

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Lipohypertrophy	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Onychoclasis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Rash generalised	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Skin discolouration	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Asteatosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Dermatitis allergic	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Dermatitis atopic	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Drug eruption	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eczema asteatotic	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Erythema	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Exfoliative rash	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hair disorder	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Ingrowing nail	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	1 (0.2)	2	0.3
Lipodystrophy acquired	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Papule	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Prurigo	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Pruritus generalised	1 (1.6)	2	5.0	0			0			1 (0.2)	2	0.3
Pustular psoriasis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Rash erythematous	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Rash macular	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Rash maculo-papular	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Rash papular	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Skin erosion	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Skin hyperpigmentation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Skin lesion	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Skin mass	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Skin warm	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Swelling face	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Investigations	6 (9.8)	9	22.6	21 (12.7)	38	23.6	32 (9.6)	73	19.3	53 (11.7)	120	20.7
Weight increased	0			0			8 (2.4)	9	2.4	8 (1.8)	9	1.6
Blood creatine phosphokinase increased	0			0			7 (2.1)	7	1.9	7 (1.5)	7	1.2

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Blood testosterone decreased	0			3 (1.8)	3	1.9	3 (0.9)	3	0.8	6 (1.3)	6	1.0
Alanine aminotransferase increased	1 (1.6)	1	2.5	2 (1.2)	2	1.2	3 (0.9)	3	0.8	5 (1.1)	6	1.0
Thyroxine free decreased	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	4	1.1	5 (1.1)	6	1.0
Blood uric acid increased	0			2 (1.2)	2	1.2	2 (0.6)	2	0.5	4 (0.9)	4	0.7
Creatinine renal clearance decreased	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Gamma-glutamyltransferase increased	0			2 (1.2)	2	1.2	2 (0.6)	2	0.5	4 (0.9)	4	0.7
Glycosylated haemoglobin increased	0			1 (0.6)	1	0.6	3 (0.9)	4	1.1	4 (0.9)	5	0.9
Aspartate aminotransferase increased	1 (1.6)	1	2.5	0			3 (0.9)	4	1.1	3 (0.7)	5	0.9
Blood insulin increased	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Blood thyroid stimulating hormone decreased	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Cortisol decreased	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Blood alkaline phosphatase increased	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Blood glucose increased	0			1 (0.6)	2	1.2	1 (0.3)	1	0.3	2 (0.4)	3	0.5
Blood potassium decreased	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Haematocrit increased	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Intraocular pressure increased	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Liver function test abnormal	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Platelet count increased	0			1 (0.6)	2	1.2	1 (0.3)	1	0.3	2 (0.4)	3	0.5
White blood cell count increased	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Blood alkaline phosphatase decreased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood bilirubin increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood calcium decreased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood cholesterol increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood creatinine decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood creatinine increased	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Blood insulin decreased	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Blood phosphorus increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood potassium increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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Blood pressure increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Body temperature increased	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Cardiac murmur	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cortisol increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Creatinine renal clearance increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Electrocardiogram PR prolongation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Electrocardiogram QT prolonged	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Electrocardiogram T wave abnormal	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Electrocardiogram abnormal	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Glomerular filtration rate decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Glomerular filtration rate increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Heart rate increased	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Hepatic enzyme increased	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Hormone level abnormal	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Lymph node palpable	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Normetanephrine urine increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Platelet count decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Thyroid hormones decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Thyroxine decreased	0			0			1 (0.3)	3	0.8	1 (0.2)	3	0.5
Thyroxine increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Tri-iodothyronine decreased	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Urine analysis abnormal	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Weight decreased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Injury, poisoning and procedural complications	3 (4.9)	3	7.5	15 (9.0)	17	10.6	32 (9.6)	37	9.8	48 (10.6)	57	9.8
Contusion	1 (1.6)	1	2.5	5 (3.0)	7	4.3	3 (0.9)	3	0.8	9 (2.0)	11	1.9
Fall	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Head injury	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7
Arthropod bite	0			2 (1.2)	2	1.2	2 (0.6)	2	0.5	3 (0.7)	4	0.7

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Ligament sprain	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Tooth fracture	1 (1.6)	1	2.5	0			2 (0.6)	2	0.5	3 (0.7)	3	0.5
Arthropod sting	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Chest injury	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Limb injury	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Procedural pain	1 (1.6)	1	2.5	0			1 (0.3)	2	0.5	2 (0.4)	3	0.5
Animal bite	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Corneal abrasion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Drug dispensing error	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Foot fracture	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Heat illness	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Incorrect dose administered	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Laceration	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Meniscus injury	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Muscle injury	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Muscle strain	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Post procedural complication	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Prescription drug used without a prescription	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Procedural dizziness	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Scratch	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Spinal column injury	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Thermal burn	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Wound	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Respiratory, thoracic and mediastinal disorders	3 (4.9)	3	7.5	16 (9.6)	28	17.4	23 (6.9)	38	10.1	41 (9.0)	69	11.9
Cough	2 (3.3)	2	5.0	5 (3.0)	6	3.7	8 (2.4)	10	2.6	15 (3.3)	18	3.1
Oropharyngeal pain	1 (1.6)	1	2.5	3 (1.8)	3	1.9	8 (2.4)	8	2.1	11 (2.4)	12	2.1
Epistaxis	0			4 (2.4)	9	5.6	1 (0.3)	1	0.3	5 (1.1)	10	1.7
Rhinitis allergic	0			3 (1.8)	4	2.5	2 (0.6)	2	0.5	5 (1.1)	6	1.0
Asthma	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Dyspnoea	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Nasal congestion	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Sleep apnoea syndrome	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Upper respiratory tract congestion	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5
Upper-airway cough syndrome	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Dyspnoea paroxysmal nocturnal	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Increased viscosity of upper respiratory secretion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Paranasal sinus hypersecretion	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Pharyngeal erythema	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Respiratory tract congestion	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Rhinorrhoea	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sinus congestion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sneezing	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Snoring	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Metabolism and nutrition disorders	4 (6.6)	4	10.0	9 (5.4)	10	6.2	25 (7.5)	31	8.2	38 (8.4)	45	7.8
Hypokalaemia	0			0			5 (1.5)	5	1.3	5 (1.1)	5	0.9
Iron deficiency	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7
Vitamin D deficiency	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Diabetes mellitus	0			3 (1.8)	3	1.9	0			3 (0.7)	3	0.5
Hyperphosphataemia	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Dehydration	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Dyslipidaemia	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Fluid retention	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
Hyperkalaemia	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Hyperlipidaemia	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Hypocalcaemia	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Decreased appetite	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Fat redistribution	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Gout	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Hypercholesterolaemia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hyperglycaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypertriglyceridaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hypoglycaemia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hyponatraemia	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Increased appetite	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Obesity	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Polydipsia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vitamin B complex deficiency	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Psychiatric disorders	2 (3.3)	2	5.0	4 (2.4)	5	3.1	16 (4.8)	19	5.0	21 (4.6)	26	4.5
Insomnia	0			1 (0.6)	1	0.6	7 (2.1)	9	2.4	8 (1.8)	10	1.7
Sleep disorder	1 (1.6)	1	2.5	1 (0.6)	1	0.6	4 (1.2)	4	1.1	6 (1.3)	6	1.0
Anxiety	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Depression	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Adjustment disorder with depressed mood	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Emotional disorder	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Initial insomnia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Mood swings	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Nervousness	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Vascular disorders	1 (1.6)	1	2.5	6 (3.6)	6	3.7	14 (4.2)	14	3.7	21 (4.6)	21	3.6
Hypertension	1 (1.6)	1	2.5	4 (2.4)	4	2.5	9 (2.7)	9	2.4	14 (3.1)	14	2.4
Hot flush	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Hypotension	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Orthostatic hypotension	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Vascular fragility	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eye disorders	0			8 (4.8)	9	5.6	12 (3.6)	14	3.7	20 (4.4)	23	4.0
Visual impairment	0			4 (2.4)	4	2.5	0			4 (0.9)	4	0.7
Dry eye	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Vision blurred	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Conjunctival haemorrhage	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Glaucoma	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Cataract	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Conjunctivitis allergic	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Diplopia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eye irritation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eye pruritus	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eyelid disorder	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Eyelid oedema	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Ocular hyperaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Xerophthalmia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood and lymphatic system disorders	0			4 (2.4)	5	3.1	11 (3.3)	14	3.7	15 (3.3)	19	3.3
Anaemia	0			3 (1.8)	3	1.9	6 (1.8)	6	1.6	9 (2.0)	9	1.6
Lymphadenopathy	0			0			3 (0.9)	6	1.6	3 (0.7)	6	1.0
Iron deficiency anaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Polycythaemia	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Thrombocytopenia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ear and labyrinth disorders	0			7 (4.2)	9	5.6	9 (2.7)	10	2.6	15 (3.3)	19	3.3
Vertigo	0			2 (1.2)	2	1.2	4 (1.2)	4	1.1	6 (1.3)	6	1.0
Ear pain	0			4 (2.4)	5	3.1	2 (0.6)	2	0.5	5 (1.1)	7	1.2
Tinnitus	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Ear discomfort	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Ear disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
External ear pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Endocrine disorders	1 (1.6)	1	2.5	8 (4.8)	8	5.0	6 (1.8)	6	1.6	14 (3.1)	15	2.6
Hypothyroidism	1 (1.6)	1	2.5	4 (2.4)	4	2.5	1 (0.3)	1	0.3	6 (1.3)	6	1.0
Adrenal insufficiency	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7
Secondary hypothyroidism	0			4 (2.4)	4	2.5	0			4 (0.9)	4	0.7
Hyperthyroidism	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Reproductive system and breast disorders	1 (1.6)	1	2.5	3 (1.8)	3	1.9	9 (2.7)	9	2.4	13 (2.9)	13	2.2
Dysmenorrhoea	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Gynaecomastia	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Menstruation irregular	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Breast disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Cervical dysplasia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Nipple pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Prostatitis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vaginal discharge	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Vaginal haemorrhage	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Renal and urinary disorders	1 (1.6)	1	2.5	4 (2.4)	5	3.1	7 (2.1)	9	2.4	12 (2.6)	15	2.6
Haematuria	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Nocturia	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pollakiuria	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Renal cyst	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Bladder pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Dysuria	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Micturition disorder	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Polyuria	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Urinary incontinence	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Urinary tract obstruction	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Cardiac disorders	1 (1.6)	1	2.5	3 (1.8)	3	1.9	6 (1.8)	9	2.4	10 (2.2)	13	2.2
Palpitations	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Tachycardia	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Aortic valve incompetence	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Atrioventricular block first degree	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Bradycardia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Bundle branch block right	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Cardiovascular disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Left ventricular dysfunction	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Mitral valve incompetence	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Myocardial ischaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Sinus arrhythmia	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2

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

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Immune system disorders	1 (1.6)	1	2.5	1 (0.6)	1	0.6	7 (2.1)	8	2.1	9 (2.0)	10	1.7
Seasonal allergy	1 (1.6)	1	2.5	1 (0.6)	1	0.6	6 (1.8)	7	1.9	8 (1.8)	9	1.6
Multiple allergies	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hepatobiliary disorders	0			2 (1.2)	3	1.9	4 (1.2)	4	1.1	6 (1.3)	7	1.2
Cholelithiasis	0			1 (0.6)	2	1.2	1 (0.3)	1	0.3	2 (0.4)	3	0.5
Hepatic cirrhosis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hepatic steatosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hepatomegaly	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Liver disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			3 (1.8)	4	2.5	3 (0.9)	3	0.8	6 (1.3)	7	1.2
Lipoma	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Angiomyolipoma	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Intraductal papillary mucinous neoplasm	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Melanocytic naevus	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pituitary tumour	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Soft tissue neoplasm	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Surgical and medical procedures	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Tooth extraction	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Dental care	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Congenital, familial and genetic disorders	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Myotonia congenita	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Rathke's cleft cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Product issues	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Device malfunction	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2

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12 Possibly or probably related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All possibly or probably related adverse events	12 (19.7)	19	47.7	48 (28.9)	110	68.3	85 (25.5)	247	65.4	133 (29.3)	376	65.0
General disorders and administration site conditions	4 (6.6)	7	17.6	24 (14.5)	31	19.3	31 (9.3)	52	13.8	55 (12.1)	90	15.6
Fatigue	1 (1.6)	1	2.5	7 (4.2)	7	4.3	9 (2.7)	11	2.9	17 (3.7)	19	3.3
Oedema peripheral	0			6 (3.6)	9	5.6	7 (2.1)	17	4.5	13 (2.9)	26	4.5
Injection site bruising	2 (3.3)	3	7.5	4 (2.4)	4	2.5	1 (0.3)	1	0.3	7 (1.5)	8	1.4
Asthenia	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Injection site pain	1 (1.6)	1	2.5	1 (0.6)	1	0.6	2 (0.6)	3	0.8	4 (0.9)	5	0.9
Peripheral swelling	0			2 (1.2)	2	1.2	2 (0.6)	2	0.5	4 (0.9)	4	0.7
Face oedema	1 (1.6)	1	2.5	1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	4	0.7
Fat tissue decreased	0			1 (0.6)	1	0.6	1 (0.3)	3	0.8	2 (0.4)	4	0.7
Injection site reaction	0			1 (0.6)	1	0.6	1 (0.3)	3	0.8	2 (0.4)	4	0.7
Malaise	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pain	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pre-existing condition improved	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5
Feeling hot	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Influenza like illness	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Injection site atrophy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Injection site haematoma	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Injection site hypertrophy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Musculoskeletal and connective tissue disorders	1 (1.6)	1	2.5	12 (7.2)	20	12.4	20 (6.0)	26	6.9	32 (7.0)	47	8.1
Arthralgia	1 (1.6)	1	2.5	6 (3.6)	6	3.7	9 (2.7)	11	2.9	15 (3.3)	18	3.1
Back pain	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Joint stiffness	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
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MedDRA version 21.0.

Possibly or probably related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Musculoskeletal stiffness	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Myalgia	0			3 (1.8)	3	1.9	0			3 (0.7)	3	0.5
Arthritis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Joint swelling	0			2 (1.2)	3	1.9	0			2 (0.4)	3	0.5
Limb discomfort	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5
Intervertebral disc protrusion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Joint noise	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Limb deformity	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Muscle spasms	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Muscular weakness	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Musculoskeletal pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pain in extremity	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Trigger finger	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Nervous system disorders	4 (6.6)	4	10.0	8 (4.8)	16	9.9	21 (6.3)	66	17.5	31 (6.8)	86	14.9
Headache	2 (3.3)	2	5.0	5 (3.0)	10	6.2	11 (3.3)	50	13.2	16 (3.5)	62	10.7
Dizziness	1 (1.6)	1	2.5	2 (1.2)	3	1.9	4 (1.2)	5	1.3	7 (1.5)	9	1.6
Hypoaesthesia	0			1 (0.6)	1	0.6	4 (1.2)	4	1.1	5 (1.1)	5	0.9
Paraesthesia	1 (1.6)	1	2.5	0			2 (0.6)	2	0.5	3 (0.7)	3	0.5
Disturbance in attention	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Somnolence	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5
Hypersomnia	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Investigations	3 (4.9)	3	7.5	7 (4.2)	13	8.1	15 (4.5)	30	7.9	24 (5.3)	46	7.9
Weight increased	0			2 (1.2)	2	1.2	4 (1.2)	4	1.1	6 (1.3)	6	1.0
Blood creatine phosphokinase increased	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7
Glycosylated haemoglobin increased	0			1 (0.6)	2	1.2	3 (0.9)	4	1.1	4 (0.9)	6	1.0
Alanine aminotransferase increased	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Thyroxine free decreased	1 (1.6)	1	2.5	0			2 (0.6)	3	0.8	3 (0.7)	4	0.7
Blood alkaline phosphatase increased	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Blood glucose increased	0			1 (0.6)	3	1.9	1 (0.3)	1	0.3	2 (0.4)	4	0.7

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MedDRA version 21.0.

Possibly or probably related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Gamma-glutamyltransferase increased	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Weight decreased	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Blood bilirubin increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood insulin decreased	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Blood insulin increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood testosterone decreased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood uric acid increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Creatinine renal clearance decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Electrocardiogram QT prolonged	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Electrocardiogram T wave inversion	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Glomerular filtration rate decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hormone level abnormal	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Liver function test abnormal	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Platelet count decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
White blood cell count increased	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Skin and subcutaneous tissue disorders	3 (4.9)	4	10.0	3 (1.8)	4	2.5	8 (2.4)	12	3.2	14 (3.1)	20	3.5
Ecchymosis	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Lipohypertrophy	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Acne	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Alopecia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Dry skin	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Exfoliative rash	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Haemorrhage subcutaneous	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Lipodystrophy acquired	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pruritus generalised	1 (1.6)	2	5.0	0			0			1 (0.2)	2	0.3
Pustular psoriasis	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Skin hyperpigmentation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Skin mass	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Swelling face	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3

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Possibly or probably related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Urticaria	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Gastrointestinal disorders	0			3 (1.8)	3	1.9	7 (2.1)	30	7.9	10 (2.2)	33	5.7
Diarrhoea	0			0			3 (0.9)	8	2.1	3 (0.7)	8	1.4
Nausea	0			1 (0.6)	1	0.6	2 (0.6)	10	2.6	3 (0.7)	11	1.9
Abdominal pain upper	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Abdominal discomfort	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Abdominal pain	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Constipation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Dry mouth	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Epigastric discomfort	0			0			1 (0.3)	3	0.8	1 (0.2)	3	0.5
Flatulence	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vomiting	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Metabolism and nutrition disorders	0			3 (1.8)	3	1.9	7 (2.1)	8	2.1	10 (2.2)	11	1.9
Hyperphosphataemia	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Diabetes mellitus	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Fat redistribution	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Fluid retention	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Hypercholesterolaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypokalaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Obesity	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Infections and infestations	0			3 (1.8)	7	4.3	3 (0.9)	3	0.8	6 (1.3)	10	1.7
Nasopharyngitis	0			2 (1.2)	5	3.1	2 (0.6)	2	0.5	4 (0.9)	7	1.2
Fungal infection	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Gastroenteritis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Oral herpes	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Injury, poisoning and procedural complications	0			2 (1.2)	2	1.2	4 (1.2)	6	1.6	6 (1.3)	8	1.4
Contusion	0			2 (1.2)	2	1.2	2 (0.6)	3	0.8	4 (0.9)	5	0.9
Ligament sprain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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Possibly or probably related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Post procedural complication	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Eye disorders	0			2 (1.2)	2	1.2	2 (0.6)	2	0.5	4 (0.9)	4	0.7
Dry eye	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Glaucoma	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Neovascular age-related macular degeneration	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vision blurred	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Vascular disorders	0			3 (1.8)	3	1.9	1 (0.3)	1	0.3	4 (0.9)	4	0.7
Hypertension	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Hot flush	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Orthostatic hypotension	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Basal cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Bladder transitional cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pituitary tumour benign	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood and lymphatic system disorders	0			2 (1.2)	3	1.9	0			2 (0.4)	3	0.5
Haemoconcentration	0			2 (1.2)	3	1.9	0			2 (0.4)	3	0.5
Endocrine disorders	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Adrenal insufficiency	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Hepatobiliary disorders	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Hepatic steatosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Liver disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Respiratory, thoracic and mediastinal disorders	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Sleep apnoea syndrome	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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Possibly or probably related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Snoring	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Ear and labyrinth disorders	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Ear pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Tinnitus	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Psychiatric disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Mood swings	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Renal and urinary disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Nocturia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Reproductive system and breast disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Nipple pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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13 Possibly or probably related serious adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All possibly or probably related serious adverse events	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Blood and lymphatic system disorders	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Haemoconcentration	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Bladder transitional cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

14 Possibly or probably related severe adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All possibly or probably related severe adverse events	0			1 (0.6)	1	0.6	5 (1.5)	5	1.3	6 (1.3)	6	1.0
Nervous system disorders	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Headache	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Blood and lymphatic system disorders	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Haemoconcentration	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
General disorders and administration site conditions	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Asthenia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Musculoskeletal and connective tissue disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Intervertebral disc protrusion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Bladder transitional cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
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15 Possibly related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All possibly related adverse events	9 (14.8)	13	32.6	34 (20.5)	68	42.2	65 (19.5)	180	47.6	101 (22.2)	261	45.1
General disorders and administration site conditions	2 (3.3)	2	5.0	11 (6.6)	15	9.3	20 (6.0)	30	7.9	33 (7.3)	47	8.1
Fatigue	1 (1.6)	1	2.5	3 (1.8)	3	1.9	7 (2.1)	8	2.1	11 (2.4)	12	2.1
Oedema peripheral	0			3 (1.8)	4	2.5	5 (1.5)	12	3.2	8 (1.8)	16	2.8
Injection site bruising	0			3 (1.8)	3	1.9	0			3 (0.7)	3	0.5
Face oedema	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Injection site pain	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
Peripheral swelling	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Asthenia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Feeling hot	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Influenza like illness	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Injection site atrophy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Injection site reaction	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Malaise	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pre-existing condition improved	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Nervous system disorders	4 (6.6)	4	10.0	6 (3.6)	11	6.8	15 (4.5)	56	14.8	23 (5.1)	71	12.3
Headache	2 (3.3)	2	5.0	4 (2.4)	9	5.6	8 (2.4)	44	11.6	12 (2.6)	55	9.5
Dizziness	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	4	1.1	5 (1.1)	6	1.0
Hypoaesthesia	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Paraesthesia	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Hypersomnia	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Somnolence	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
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MedDRA version 21.0.

Possibly related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Musculoskeletal and connective tissue disorders	1 (1.6)	1	2.5	6 (3.6)	13	8.1	14 (4.2)	18	4.8	21 (4.6)	32	5.5
Arthralgia	1 (1.6)	1	2.5	2 (1.2)	2	1.2	4 (1.2)	5	1.3	7 (1.5)	8	1.4
Myalgia	0			3 (1.8)	3	1.9	0			3 (0.7)	3	0.5
Arthritis	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Back pain	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Joint swelling	0			2 (1.2)	3	1.9	0			2 (0.4)	3	0.5
Musculoskeletal stiffness	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Intervertebral disc protrusion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Joint noise	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Joint stiffness	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Limb deformity	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Limb discomfort	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Muscle spasms	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Muscular weakness	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Musculoskeletal pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pain in extremity	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Trigger finger	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Investigations	2 (3.3)	2	5.0	7 (4.2)	11	6.8	10 (3.0)	18	4.8	19 (4.2)	31	5.4
Weight increased	0			1 (0.6)	1	0.6	4 (1.2)	4	1.1	5 (1.1)	5	0.9
Alanine aminotransferase increased	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Blood creatine phosphokinase increased	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Gamma-glutamyltransferase increased	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Glycosylated haemoglobin increased	0			1 (0.6)	2	1.2	1 (0.3)	2	0.5	2 (0.4)	4	0.7
Weight decreased	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Blood alkaline phosphatase increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood bilirubin increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood glucose increased	0			1 (0.6)	3	1.9	0			1 (0.2)	3	0.5
Blood insulin decreased	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Electrocardiogram QT prolonged	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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MedDRA version 21.0.

Possibly related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Electrocardiogram T wave inversion	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hormone level abnormal	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Liver function test abnormal	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Platelet count decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
White blood cell count increased	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Skin and subcutaneous tissue disorders	3 (4.9)	4	10.0	0			8 (2.4)	11	2.9	11 (2.4)	15	2.6
Lipohypertrophy	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Acne	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Alopecia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Dry skin	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Ecchymosis	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Lipodystrophy acquired	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pruritus generalised	1 (1.6)	2	5.0	0			0			1 (0.2)	2	0.3
Pustular psoriasis	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Skin mass	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Swelling face	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Urticaria	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Gastrointestinal disorders	0			3 (1.8)	3	1.9	6 (1.8)	26	6.9	9 (2.0)	29	5.0
Diarrhoea	0			0			3 (0.9)	8	2.1	3 (0.7)	8	1.4
Nausea	0			1 (0.6)	1	0.6	2 (0.6)	10	2.6	3 (0.7)	11	1.9
Abdominal discomfort	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Abdominal pain	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Abdominal pain upper	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Constipation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Dry mouth	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Flatulence	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vomiting	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Metabolism and nutrition disorders	0			2 (1.2)	2	1.2	5 (1.5)	5	1.3	7 (1.5)	7	1.2
Hyperphosphataemia	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3

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Possibly related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Diabetes mellitus	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Fluid retention	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypercholesterolaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hypokalaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Obesity	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Eye disorders	0			2 (1.2)	2	1.2	2 (0.6)	2	0.5	4 (0.9)	4	0.7
Dry eye	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Glaucoma	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Neovascular age-related macular degeneration	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vision blurred	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Injury, poisoning and procedural complications	0			2 (1.2)	2	1.2	2 (0.6)	3	0.8	4 (0.9)	5	0.9
Contusion	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Ligament sprain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Post procedural complication	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Basal cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Bladder transitional cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pituitary tumour benign	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Vascular disorders	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Hypertension	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Hot flush	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hepatobiliary disorders	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Hepatic steatosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Liver disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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MedDRA version 21.0.

Possibly related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Infections and infestations	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Fungal infection	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Nasopharyngitis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Respiratory, thoracic and mediastinal disorders	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Sleep apnoea syndrome	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Snoring	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood and lymphatic system disorders	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Haemoconcentration	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Ear and labyrinth disorders	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Ear pain	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Tinnitus	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Endocrine disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Adrenal insufficiency	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Psychiatric disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Mood swings	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Renal and urinary disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Nocturia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Reproductive system and breast disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Nipple pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

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16 Possibly related serious adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All possibly related serious adverse events	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Bladder transitional cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
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MedDRA version 21.0.

17 Possibly related severe adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All possibly related severe adverse events	0			0			5 (1.5)	5	1.3	5 (1.1)	5	0.9
Nervous system disorders	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Headache	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
General disorders and administration site conditions	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Asthenia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Musculoskeletal and connective tissue disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Intervertebral disc protrusion	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Bladder transitional cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
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MedDRA version 21.0.

18 Probably related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All probably related adverse events	4 (6.6)	6	15.1	20 (12.0)	42	26.1	37 (11.1)	67	17.7	57 (12.6)	115	19.9
General disorders and administration site conditions	3 (4.9)	5	12.6	14 (8.4)	16	9.9	13 (3.9)	22	5.8	27 (5.9)	43	7.4
Fatigue	0			4 (2.4)	4	2.5	3 (0.9)	3	0.8	7 (1.5)	7	1.2
Oedema peripheral	0			3 (1.8)	5	3.1	3 (0.9)	5	1.3	6 (1.3)	10	1.7
Injection site bruising	2 (3.3)	3	7.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	4 (0.9)	5	0.9
Asthenia	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Face oedema	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Fat tissue decreased	0			1 (0.6)	1	0.6	1 (0.3)	3	0.8	2 (0.4)	4	0.7
Injection site pain	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Peripheral swelling	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Injection site haematoma	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Injection site hypertrophy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Injection site reaction	0			0			1 (0.3)	3	0.8	1 (0.2)	3	0.5
Malaise	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pre-existing condition improved	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Musculoskeletal and connective tissue disorders	0			6 (3.6)	7	4.3	7 (2.1)	8	2.1	12 (2.6)	15	2.6
Arthralgia	0			4 (2.4)	4	2.5	5 (1.5)	6	1.6	8 (1.8)	10	1.7
Joint stiffness	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Back pain	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Limb discomfort	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Musculoskeletal stiffness	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Investigations	1 (1.6)	1	2.5	2 (1.2)	2	1.2	7 (2.1)	12	3.2	10 (2.2)	15	2.6

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Probably related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Thyroxine free decreased	1 (1.6)	1	2.5	0			2 (0.6)	3	0.8	3 (0.7)	4	0.7
Glycosylated haemoglobin increased	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Blood alkaline phosphatase increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood creatine phosphokinase increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood glucose increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood insulin increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood testosterone decreased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood uric acid increased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Creatinine renal clearance decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Glomerular filtration rate decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Weight increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Nervous system disorders	0			2 (1.2)	5	3.1	7 (2.1)	10	2.6	9 (2.0)	15	2.6
Headache	0			1 (0.6)	1	0.6	4 (1.2)	6	1.6	5 (1.1)	7	1.2
Disturbance in attention	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Dizziness	0			1 (0.6)	2	1.2	1 (0.3)	1	0.3	2 (0.4)	3	0.5
Hypoaesthesia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Paraesthesia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Somnolence	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Infections and infestations	0			1 (0.6)	5	3.1	3 (0.9)	3	0.8	4 (0.9)	8	1.4
Nasopharyngitis	0			1 (0.6)	4	2.5	2 (0.6)	2	0.5	3 (0.7)	6	1.0
Gastroenteritis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Oral herpes	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Metabolism and nutrition disorders	0			1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	4	0.7
Diabetes mellitus	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Fat redistribution	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Fluid retention	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

Probably related adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hyperphosphataemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Skin and subcutaneous tissue disorders	0			3 (1.8)	4	2.5	1 (0.3)	1	0.3	4 (0.9)	5	0.9
Ecchymosis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Exfoliative rash	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Haemorrhage subcutaneous	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Skin hyperpigmentation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Swelling face	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Injury, poisoning and procedural complications	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
Contusion	0			0			2 (0.6)	3	0.8	2 (0.4)	3	0.5
Blood and lymphatic system disorders	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Haemoconcentration	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Endocrine disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Adrenal insufficiency	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Gastrointestinal disorders	0			0			1 (0.3)	4	1.1	1 (0.2)	4	0.7
Abdominal pain upper	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Epigastric discomfort	0			0			1 (0.3)	3	0.8	1 (0.2)	3	0.5
Vascular disorders	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Orthostatic hypotension	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

19 Probably related serious adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All probably related serious adverse events	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood and lymphatic system disorders	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Haemoconcentration	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

20 Probably related severe adverse events by system organ class and preferred term - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All probably related severe adverse events	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Blood and lymphatic system disorders	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Haemoconcentration	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

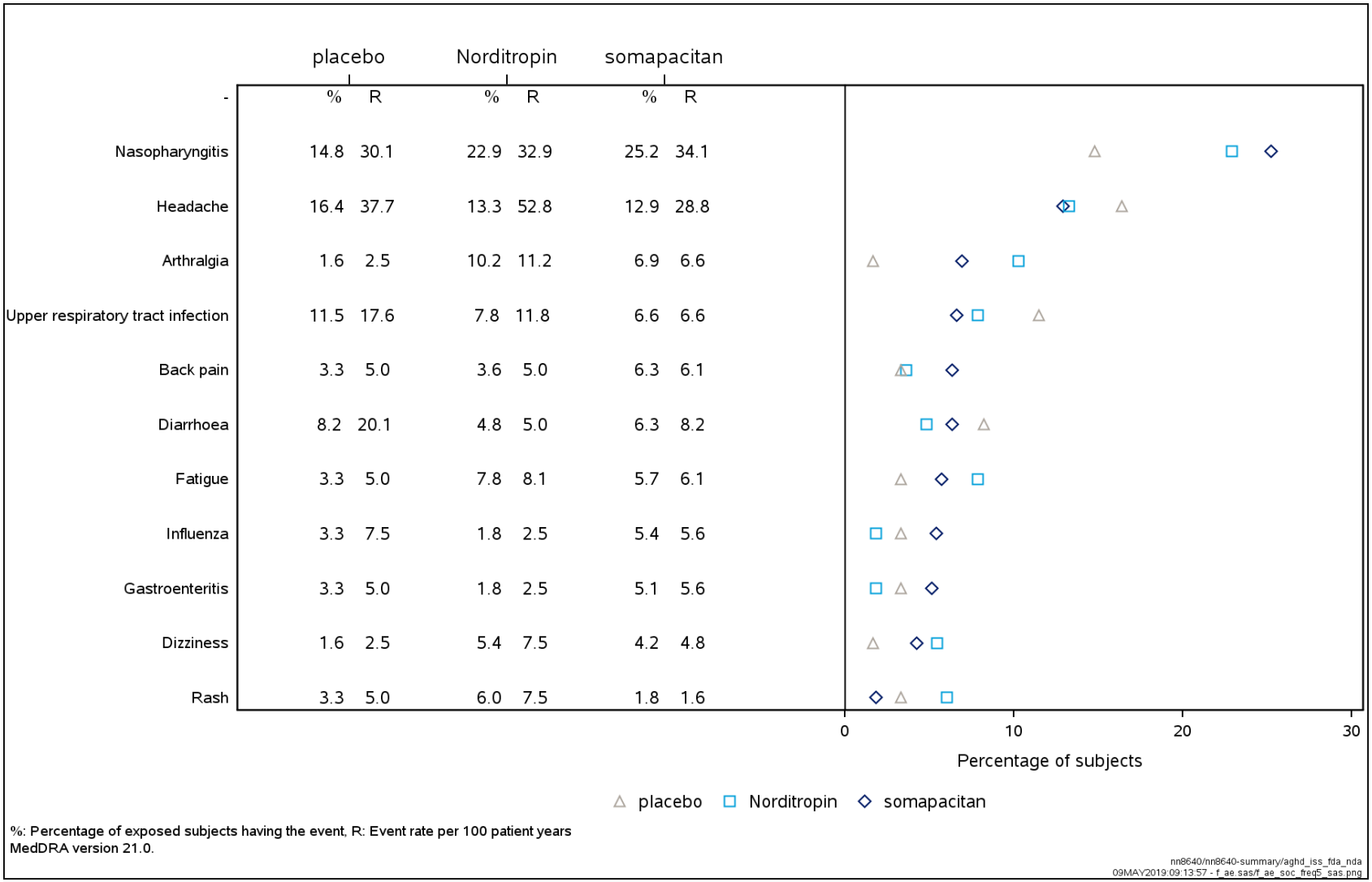
%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

21 Most frequent adverse events (>=5%) by system organ class and preferred term - safety analysis

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
Infections and infestations												
Nasopharyngitis	9 (14.8)	12	30.1	38 (22.9)	53	32.9	84 (25.2)	129	34.1	121 (26.7)	194	33.5
Upper respiratory tract infection	7 (11.5)	7	17.6	13 (7.8)	19	11.8	22 (6.6)	25	6.6	37 (8.1)	51	8.8
Gastroenteritis	2 (3.3)	2	5.0	3 (1.8)	4	2.5	17 (5.1)	21	5.6	22 (4.8)	27	4.7
Influenza	2 (3.3)	3	7.5	3 (1.8)	4	2.5	18 (5.4)	21	5.6	22 (4.8)	28	4.8
Nervous system disorders												
Headache	10 (16.4)	15	37.7	22 (13.3)	85	52.8	43 (12.9)	109	28.8	69 (15.2)	209	36.1
Dizziness	1 (1.6)	1	2.5	9 (5.4)	12	7.5	14 (4.2)	18	4.8	23 (5.1)	31	5.4
Musculoskeletal and connective tissue disorders												
Arthralgia	1 (1.6)	1	2.5	17 (10.2)	18	11.2	23 (6.9)	25	6.6	40 (8.8)	44	7.6
Back pain	2 (3.3)	2	5.0	6 (3.6)	8	5.0	21 (6.3)	23	6.1	29 (6.4)	33	5.7
General disorders and administration site conditions												
Fatigue	2 (3.3)	2	5.0	13 (7.8)	13	8.1	19 (5.7)	23	6.1	34 (7.5)	38	6.6
Gastrointestinal disorders												
Diarrhoea	5 (8.2)	8	20.1	8 (4.8)	8	5.0	21 (6.3)	31	8.2	33 (7.3)	47	8.1
Skin and subcutaneous tissue disorders												
Rash	2 (3.3)	2	5.0	10 (6.0)	12	7.5	6 (1.8)	6	1.6	18 (4.0)	20	3.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

22 Most frequent adverse events by preferred term (>=5%) - safety analysis set



23 Serious adverse events onset by 3 month periods - summary - safety analysis set

	placebo		Norditropin		somapacitan		total	
	N (%)	E	N (%)	E	N (%)	E	N (%)	E
Subjects Exposed	61		166		333		454	
All serious adverse events	5 (100.0)	7	16 (100.0)	22	29 (100.0)	50	47 (100.0)	79
Time after start of exposure								
0-<3 months	1 (20.0)	3	7 (43.8)	9	7 (24.1)	11	15 (31.9)	23
3-<6 months	4 (80.0)	4	5 (31.3)	5	8 (27.6)	11	16 (34.0)	20
6-<9 months	0		1 (6.3)	2	6 (20.7)	7	7 (14.9)	9
9-<12 months	0		1 (6.3)	1	7 (24.1)	13	8 (17.0)	14
12-<15 months	0		2 (12.5)	4	1 (3.4)	2	3 (6.4)	6
15-<18 months	0		1 (6.3)	1	3 (10.3)	3	4 (8.5)	4
18-<21 months	0		0		1 (3.4)	3	1 (2.1)	3

N: Number of subjects, %: Percentage of subjects having serious adverse events, E: Number of events
For subjects in 4054 time is calculated from start of current treatment.
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
Exposure to placebo was only done in 4054 and for no more than 35 weeks.
Month = 30 days.

24 Adverse events by system organ class and preferred term - Hypothyroidism - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All hypothyroidism events	1 (1.6)	1	2.5	8 (4.8)	8	5.0	2 (0.6)	2	0.5	11 (2.4)	11	1.9
Endocrine disorders	1 (1.6)	1	2.5	8 (4.8)	8	5.0	2 (0.6)	2	0.5	11 (2.4)	11	1.9
Hypothyroidism	1 (1.6)	1	2.5	4 (2.4)	4	2.5	2 (0.6)	2	0.5	7 (1.5)	7	1.2
Secondary hypothyroidism	0			4 (2.4)	4	2.5	0			4 (0.9)	4	0.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

25 Adverse events by system organ class and preferred term - Pancreaitis - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All pancreaitis events	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Gastrointestinal disorders	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Pancreatitis acute	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

26 Adverse events by system organ class and preferred term - Peripheral oedema - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All peripheral oedema events	1 (1.6)	1	2.5	8 (4.8)	12	7.5	15 (4.5)	28	7.4	24 (5.3)	41	7.1
General disorders and administration site conditions	1 (1.6)	1	2.5	8 (4.8)	12	7.5	15 (4.5)	28	7.4	24 (5.3)	41	7.1
Oedema peripheral	0			6 (3.6)	9	5.6	12 (3.6)	24	6.4	18 (4.0)	33	5.7
Peripheral swelling	1 (1.6)	1	2.5	3 (1.8)	3	1.9	4 (1.2)	4	1.1	8 (1.8)	8	1.4

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

27 Adverse events by system organ class and preferred term - Fatigue/Asthenia - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All fatigue/asthenia events	4 (6.6)	4	10.0	19 (11.4)	20	12.4	33 (9.9)	39	10.3	56 (12.3)	63	10.9
General disorders and administration site conditions	4 (6.6)	4	10.0	19 (11.4)	20	12.4	33 (9.9)	39	10.3	56 (12.3)	63	10.9
Fatigue	2 (3.3)	2	5.0	13 (7.8)	13	8.1	19 (5.7)	23	6.1	34 (7.5)	38	6.6
Asthenia	1 (1.6)	1	2.5	4 (2.4)	5	3.1	9 (2.7)	11	2.9	14 (3.1)	17	2.9
Malaise	1 (1.6)	1	2.5	2 (1.2)	2	1.2	5 (1.5)	5	1.3	8 (1.8)	8	1.4

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

28 Adverse events by system organ class and preferred term - Allergic reactions (non-anaphylactic reactions) - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All allergic reaction (non-anaphylactic reaction) events	9 (14.8)	10	25.1	25 (15.1)	30	18.6	27 (8.1)	33	8.7	56 (12.3)	73	12.6
Skin and subcutaneous tissue disorders	7 (11.5)	7	17.6	19 (11.4)	23	14.3	20 (6.0)	25	6.6	43 (9.5)	55	9.5
Rash	2 (3.3)	2	5.0	10 (6.0)	12	7.5	6 (1.8)	6	1.6	18 (4.0)	20	3.5
Urticaria	0			2 (1.2)	2	1.2	5 (1.5)	6	1.6	7 (1.5)	8	1.4
Eczema	2 (3.3)	2	5.0	2 (1.2)	2	1.2	1 (0.3)	2	0.5	4 (0.9)	6	1.0
Dermatitis	2 (3.3)	2	5.0	0			2 (0.6)	2	0.5	3 (0.7)	4	0.7
Dermatitis atopic	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Dermatitis contact	1 (1.6)	1	2.5	1 (0.6)	1	0.6	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Rash generalised	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Dermatitis allergic	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Drug eruption	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Exfoliative rash	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Rash erythematous	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Rash macular	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Rash maculo-papular	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Swelling face	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Respiratory, thoracic and mediastinal disorders	0			3 (1.8)	4	2.5	2 (0.6)	2	0.5	5 (1.1)	6	1.0
Rhinitis allergic	0			3 (1.8)	4	2.5	2 (0.6)	2	0.5	5 (1.1)	6	1.0
General disorders and administration site conditions	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	5	0.9
Face oedema	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	5	0.9

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

Adverse events by system organ class and preferred term - Allergic reactions (non-anaphylactic reactions) - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Eye disorders	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Conjunctivitis allergic	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eye swelling	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Eyelid oedema	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Gastrointestinal disorders	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Lip swelling	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Immune system disorders	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Allergy to vaccine	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Multiple allergies	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

29 Adverse events by system organ class and preferred term - Injection site reactions - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All injection site reaction events	3 (4.9)	5	12.6	9 (5.4)	9	5.6	5 (1.5)	9	2.4	16 (3.5)	23	4.0
General disorders and administration site conditions	3 (4.9)	5	12.6	9 (5.4)	9	5.6	5 (1.5)	9	2.4	16 (3.5)	23	4.0
Injection site bruising	2 (3.3)	3	7.5	6 (3.6)	6	3.7	1 (0.3)	1	0.3	9 (2.0)	10	1.7
Injection site pain	1 (1.6)	1	2.5	1 (0.6)	1	0.6	2 (0.6)	3	0.8	4 (0.9)	5	0.9
Injection site reaction	0			1 (0.6)	1	0.6	1 (0.3)	3	0.8	2 (0.4)	4	0.7
Injection site atrophy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Injection site haematoma	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Injection site haemorrhage	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Injection site hypertrophy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

30 Adverse events by system organ class and preferred term - Lipohypertrophy - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All lipohypertrophy events	0			0			5 (1.5)	5	1.3	5 (1.1)	5	0.9
Skin and subcutaneous tissue disorders	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7
Lipodystrophy acquired	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Lipohypertrophy	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
General disorders and administration site conditions	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Injection site hypertrophy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

31 Adverse events by system organ class and preferred term - Lipoatrophy - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All lipoatrophy events	0			1 (0.6)	1	0.6	2 (0.6)	4	1.1	3 (0.7)	5	0.9
General disorders and administration site conditions	0			1 (0.6)	1	0.6	2 (0.6)	4	1.1	3 (0.7)	5	0.9
Fat tissue decreased	0			1 (0.6)	1	0.6	1 (0.3)	3	0.8	2 (0.4)	4	0.7
Injection site atrophy	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

32 Adverse events by system organ class and preferred term - Blood alkaline phosphatase increased (bone) - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All blood alkaline phosphatase increased (bone) events	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Investigations	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Blood alkaline phosphatase increased	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

33 Adverse events by system organ class and preferred term - Drug specific antibodies present - safety analysis set

There are no data for this output

34 Adverse events by system organ class and preferred term - High level group terms Cardiac and vascular investigations incl. arrhythmia - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All cardiac and vascular investigations and cardiac arrhythmia	2 (3.3)	2	5.0	7 (4.2)	10	6.2	9 (2.7)	11	2.9	18 (4.0)	23	4.0
Cardiac disorders	1 (1.6)	1	2.5	3 (1.8)	4	2.5	6 (1.8)	7	1.9	10 (2.2)	12	2.1
Tachycardia	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Atrioventricular block first degree	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Atrial flutter	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Bradycardia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Bundle branch block right	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Sinus arrhythmia	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Ventricular extrasystoles	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ventricular fibrillation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Investigations	1 (1.6)	1	2.5	4 (2.4)	6	3.7	4 (1.2)	4	1.1	9 (2.0)	11	1.9
Blood pressure decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Blood pressure increased	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Cardiac murmur	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Electrocardiogram PR prolongation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Electrocardiogram QT prolonged	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Electrocardiogram T wave abnormal	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Electrocardiogram T wave inversion	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Electrocardiogram abnormal	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Heart rate increased	0			1 (0.6)	3	1.9	0			1 (0.2)	3	0.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

35 Adverse events by system organ class and preferred term - Weight increased - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All weight increased events	0			2 (1.2)	2	1.2	9 (2.7)	10	2.6	11 (2.4)	12	2.1
Investigations	0			2 (1.2)	2	1.2	9 (2.7)	10	2.6	11 (2.4)	12	2.1
Weight increased	0			2 (1.2)	2	1.2	9 (2.7)	10	2.6	11 (2.4)	12	2.1

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

36 Adverse events by system organ class and preferred term - Hyperglycaemia - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All hyperglycemia events	0			1 (0.6)	5	3.1	4 (1.2)	6	1.6	5 (1.1)	11	1.9
Investigations	0			1 (0.6)	5	3.1	3 (0.9)	5	1.3	4 (0.9)	10	1.7
Glycosylated haemoglobin increased	0			1 (0.6)	2	1.2	3 (0.9)	4	1.1	4 (0.9)	6	1.0
Blood glucose increased	0			1 (0.6)	3	1.9	1 (0.3)	1	0.3	2 (0.4)	4	0.7
Metabolism and nutrition disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Hyperglycaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

37 Adverse events by system organ class and preferred term - Type 2 diabetes - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All type 2 diabetes events	0			5 (3.0)	9	5.6	5 (1.5)	8	2.1	10 (2.2)	17	2.9
Investigations	0			2 (1.2)	6	3.7	4 (1.2)	7	1.9	6 (1.3)	13	2.2
Glycosylated haemoglobin increased	0			1 (0.6)	2	1.2	3 (0.9)	4	1.1	4 (0.9)	6	1.0
Blood insulin increased	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Blood glucose increased	0			1 (0.6)	3	1.9	1 (0.3)	1	0.3	2 (0.4)	4	0.7
Metabolism and nutrition disorders	0			3 (1.8)	3	1.9	1 (0.3)	1	0.3	4 (0.9)	4	0.7
Diabetes mellitus	0			3 (1.8)	3	1.9	0			3 (0.7)	3	0.5
Hyperglycaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

38 Adverse events by system organ class and preferred term - Arthralgia - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All athralgia events	1 (1.6)	1	2.5	17 (10.2)	18	11.2	23 (6.9)	25	6.6	40 (8.8)	44	7.6
Musculoskeletal and connective tissue disorders	1 (1.6)	1	2.5	17 (10.2)	18	11.2	23 (6.9)	25	6.6	40 (8.8)	44	7.6
Arthralgia	1 (1.6)	1	2.5	17 (10.2)	18	11.2	23 (6.9)	25	6.6	40 (8.8)	44	7.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

39 Adverse events by system organ class and preferred term - Myalgia - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All myalgia events	3 (4.9)	3	7.5	8 (4.8)	8	5.0	7 (2.1)	9	2.4	18 (4.0)	20	3.5
Musculoskeletal and connective tissue disorders	3 (4.9)	3	7.5	8 (4.8)	8	5.0	7 (2.1)	9	2.4	18 (4.0)	20	3.5
Myalgia	3 (4.9)	3	7.5	8 (4.8)	8	5.0	7 (2.1)	9	2.4	18 (4.0)	20	3.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

40 Adverse events by system organ class and preferred term - Scoliosis - safety analysis set

There are no data for this output

41 Adverse events by system organ class and preferred term - All benign, malignant and unspecified neoplasms - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All benign, malignant and unspecified neoplasm events	0			4 (2.4)	5	3.1	7 (2.1)	7	1.9	11 (2.4)	12	2.1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			4 (2.4)	5	3.1	7 (2.1)	7	1.9	11 (2.4)	12	2.1
Lipoma	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pituitary tumour benign	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Angiomyolipoma	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Basal cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Bladder transitional cell carcinoma	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Intraductal papillary mucinous neoplasm	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Melanocytic naevus	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pituitary tumour	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Plasma cell myeloma	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Soft tissue neoplasm	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

42 Adverse events by system organ class and preferred term - Headache - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All headache events	10 (16.4)	15	37.7	22 (13.3)	85	52.8	43 (12.9)	109	28.8	69 (15.2)	209	36.1
Nervous system disorders	10 (16.4)	15	37.7	22 (13.3)	85	52.8	43 (12.9)	109	28.8	69 (15.2)	209	36.1
Headache	10 (16.4)	15	37.7	22 (13.3)	85	52.8	43 (12.9)	109	28.8	69 (15.2)	209	36.1

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

43 Adverse events by system organ class and preferred term - Paraesthesia - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All paraesthesia events	2 (3.3)	2	5.0	1 (0.6)	1	0.6	5 (1.5)	6	1.6	8 (1.8)	9	1.6
Nervous system disorders	2 (3.3)	2	5.0	1 (0.6)	1	0.6	5 (1.5)	6	1.6	8 (1.8)	9	1.6
Paraesthesia	2 (3.3)	2	5.0	1 (0.6)	1	0.6	5 (1.5)	6	1.6	8 (1.8)	9	1.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

44 Adverse events by system organ class and preferred term - Stroke - safety analysis set

There are no data for this output

45 Adverse events by system organ class and preferred term - Carpal tunnel syndrome - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All carpal tunnel syndrome events	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Nervous system disorders	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Carpal tunnel syndrome	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

46 Adverse events by system organ class and preferred term - Benign intracranial hypertension - safety analysis set

There are no data for this output

47 Adverse events by system organ class and preferred term - Rare events - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All rare events	5 (8.2)	5	12.6	13 (7.8)	18	11.2	21 (6.3)	24	6.4	37 (8.1)	47	8.1
Cardiac disorders	1 (1.6)	1	2.5	5 (3.0)	6	3.7	6 (1.8)	8	2.1	12 (2.6)	15	2.6
Palpitations	0			2 (1.2)	2	1.2	1 (0.3)	1	0.3	3 (0.7)	3	0.5
Tachycardia	0			0			3 (0.9)	3	0.8	3 (0.7)	3	0.5
Atrioventricular block first degree	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Atrial flutter	0			1 (0.6)	2	1.2	0			1 (0.2)	2	0.3
Bradycardia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Bundle branch block right	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Sinus arrhythmia	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Ventricular extrasystoles	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ventricular fibrillation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Gastrointestinal disorders	2 (3.3)	2	5.0	2 (1.2)	2	1.2	1 (0.3)	1	0.3	5 (1.1)	5	0.9
Lip swelling	1 (1.6)	1	2.5	0			1 (0.3)	1	0.3	2 (0.4)	2	0.3
Pancreatitis acute	1 (1.6)	1	2.5	1 (0.6)	1	0.6	0			2 (0.4)	2	0.3
Ascites	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Investigations	0			2 (1.2)	4	2.5	3 (0.9)	3	0.8	5 (1.1)	7	1.2
Electrocardiogram PR prolongation	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Electrocardiogram QT prolonged	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Electrocardiogram abnormal	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Heart rate increased	0			1 (0.6)	3	1.9	0			1 (0.2)	3	0.5
Platelet count decreased	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
General disorders and administration site conditions	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	5	0.9
Face oedema	1 (1.6)	1	2.5	1 (0.6)	1	0.6	3 (0.9)	3	0.8	4 (0.9)	5	0.9

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

Adverse events by system organ class and preferred term - Rare events - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hepatobiliary disorders	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Hepatic cirrhosis	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Hepatic steatosis	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Liver disorder	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Congenital, familial and genetic disorders	0			0			2 (0.6)	2	0.5	2 (0.4)	2	0.3
Myotonia congenita	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Rathke's cleft cyst	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Infections and infestations	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Clostridium difficile infection	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Nervous system disorders	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Syncope	0			1 (0.6)	1	0.6	1 (0.3)	1	0.3	2 (0.4)	2	0.3
Skin and subcutaneous tissue disorders	0			1 (0.6)	1	0.6	1 (0.3)	2	0.5	2 (0.4)	3	0.5
Exfoliative rash	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Swelling face	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Blood and lymphatic system disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Thrombocytopenia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Eye disorders	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Eyelid oedema	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Renal and urinary disorders	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Urinary tract obstruction	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

48 Adverse events by system organ class and preferred term - Fatal outcome - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All fatal events	1 (1.6)	1	2.5	2 (1.2)	2	1.2	2 (0.6)	4	1.1	5 (1.1)	7	1.2
Infections and infestations	0			2 (1.2)	2	1.2	0			2 (0.4)	2	0.3
Influenza	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Pneumonia	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Cardiac disorders	0			0			1 (0.3)	2	0.5	1 (0.2)	2	0.3
Cardiogenic shock	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Ventricular fibrillation	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Endocrine disorders	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Adrenocortical insufficiency acute	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
General disorders and administration site conditions	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Death	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Respiratory, thoracic and mediastinal disorders	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2
Pneumonia aspiration	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

49 Adverse events by system organ class and preferred term - Hypersensitivity (Anaphylactic reactions) - safety analysis set

There are no data for this output

50 Adverse events by system organ class and preferred term - Adrenocortical insufficiency (secondary) - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All adrenocortical insufficiency (secondary) events	1 (1.6)	1	2.5	2 (1.2)	2	1.2	8 (2.4)	8	2.1	11 (2.4)	11	1.9
Endocrine disorders	1 (1.6)	1	2.5	2 (1.2)	2	1.2	8 (2.4)	8	2.1	11 (2.4)	11	1.9
Adrenocortical insufficiency acute	1 (1.6)	1	2.5	0			4 (1.2)	4	1.1	5 (1.1)	5	0.9
Adrenal insufficiency	0			0			4 (1.2)	4	1.1	4 (0.9)	4	0.7
Glucocorticoid deficiency	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2
Secondary adrenocortical insufficiency	0			1 (0.6)	1	0.6	0			1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

51 Adverse events by system organ class and preferred term - metabolism disorders - glycaemic control - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			166			333			454		
Total patient years	39.8			161.0			377.8			578.7		
All metabolism disorders - glyceamic control - events	1 (1.6)	1	2.5	5 (3.0)	9	5.6	5 (1.5)	8	2.1	11 (2.4)	18	3.1
Investigations	1 (1.6)	1	2.5	2 (1.2)	6	3.7	4 (1.2)	7	1.9	7 (1.5)	14	2.4
Glycosylated haemoglobin increased	0			1 (0.6)	2	1.2	3 (0.9)	4	1.1	4 (0.9)	6	1.0
Blood insulin increased	0			1 (0.6)	1	0.6	2 (0.6)	2	0.5	3 (0.7)	3	0.5
Blood glucose increased	0			1 (0.6)	3	1.9	1 (0.3)	1	0.3	2 (0.4)	4	0.7
Blood insulin decreased	1 (1.6)	1	2.5	0			0			1 (0.2)	1	0.2
Metabolism and nutrition disorders	0			3 (1.8)	3	1.9	1 (0.3)	1	0.3	4 (0.9)	4	0.7
Diabetes mellitus	0			3 (1.8)	3	1.9	0			3 (0.7)	3	0.5
Hyperglycaemia	0			0			1 (0.3)	1	0.3	1 (0.2)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

52 Adverse Events - Male - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	29			84			164			228		
Total patient years	18.5			79.6			181.0			279.1		
All adverse events	18 (62.1)	56	302.4	61 (72.6)	371	466.0	125 (76.2)	508	280.6	178 (78.1)	935	334.9
Serious adverse events	2 (6.9)	2	10.8	11 (13.1)	16	20.1	17 (10.4)	30	16.6	29 (12.7)	48	17.2
Medical events of special interest	0			0			0			0		
Severity												
Mild	18 (62.1)	52	280.8	55 (65.5)	239	300.2	114 (69.5)	368	203.3	163 (71.5)	659	236.1
Moderate	2 (6.9)	4	21.6	28 (33.3)	115	144.5	38 (23.2)	115	63.5	66 (28.9)	234	83.8
Severe	0			10 (11.9)	17	21.4	14 (8.5)	25	13.8	24 (10.5)	42	15.0
Causality												
Unlikely	17 (58.6)	53	286.2	58 (69.0)	311	390.6	116 (70.7)	406	224.3	167 (73.2)	770	275.8
Possible	1 (3.4)	1	5.4	21 (25.0)	39	49.0	28 (17.1)	71	39.2	49 (21.5)	111	39.8
Probable	2 (6.9)	2	10.8	10 (11.9)	21	26.4	17 (10.4)	31	17.1	29 (12.7)	54	19.3
Outcome												
Recovered/Resolved	18 (62.1)	51	275.4	59 (70.2)	295	370.6	113 (68.9)	400	221.0	168 (73.7)	746	267.2
Recovering/Resolving	0			6 (7.1)	10	12.6	12 (7.3)	16	8.8	18 (7.9)	26	9.3
Recovered/Resolved With Sequelae	0			3 (3.6)	4	5.0	1 (0.6)	1	0.6	4 (1.8)	5	1.8
Not Recovered/Not Resolved	3 (10.3)	5	27.0	28 (33.3)	60	75.4	47 (28.7)	87	48.1	74 (32.5)	152	54.5
Fatal	0			2 (2.4)	2	2.5	2 (1.2)	4	2.2	4 (1.8)	6	2.1

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Adverse Events - Male - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Action												
Drug Interrupted	2	(6.9)	4 21.6	3	(3.6)	5 6.3	2	(1.2)	4 2.2	7	(3.1)	13 4.7
Drug Withdrawn	1	(3.4)	1 5.4	3	(3.6)	3 3.8	4	(2.4)	5 2.8	8	(3.5)	9 3.2
Dose Reduced	0			4	(4.8)	6 7.5	2	(1.2)	5 2.8	6	(2.6)	11 3.9
Dose Not Changed	18	(62.1)	51 275.4	58	(69.0)	340 427.1	124	(75.6)	464 256.3	174	(76.3)	855 306.3
Not Applicable	0			9	(10.7)	17 21.4	16	(9.8)	30 16.6	25	(11.0)	47 16.8
Treatment discontinuations due to adverse events*	1	(3.4)	1 5.4	4	(4.8)	4 5.0	4	(2.4)	5 2.8	9	(3.9)	10 3.6

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

53 Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	29			84			164			228		
Total patient years	18.5			79.6			181.0			279.1		
All adverse events	18 (62.1)	56	302.4	61 (72.6)	371	466.0	125 (76.2)	508	280.6	178 (78.1)	935	334.9
Infections and infestations	14 (48.3)	17	91.8	41 (48.8)	78	98.0	71 (43.3)	115	63.5	113 (49.6)	210	75.2
Nasopharyngitis	4 (13.8)	5	27.0	20 (23.8)	28	35.2	35 (21.3)	45	24.9	55 (24.1)	78	27.9
Upper respiratory tract infection	5 (17.2)	5	27.0	6 (7.1)	10	12.6	9 (5.5)	10	5.5	18 (7.9)	25	9.0
Influenza	1 (3.4)	1	5.4	1 (1.2)	1	1.3	7 (4.3)	7	3.9	8 (3.5)	9	3.2
Pharyngitis	1 (3.4)	1	5.4	4 (4.8)	6	7.5	2 (1.2)	2	1.1	7 (3.1)	9	3.2
Tonsillitis	1 (3.4)	1	5.4	3 (3.6)	4	5.0	3 (1.8)	3	1.7	7 (3.1)	8	2.9
Gastroenteritis	0			0			5 (3.0)	5	2.8	5 (2.2)	5	1.8
Herpes zoster	1 (3.4)	1	5.4	2 (2.4)	2	2.5	1 (0.6)	1	0.6	4 (1.8)	4	1.4
Lower respiratory tract infection	0			1 (1.2)	2	2.5	3 (1.8)	3	1.7	4 (1.8)	5	1.8
Sinusitis	0			1 (1.2)	1	1.3	3 (1.8)	3	1.7	4 (1.8)	4	1.4
Tooth abscess	0			2 (2.4)	2	2.5	2 (1.2)	2	1.1	4 (1.8)	4	1.4
Bronchitis	1 (3.4)	1	5.4	0			2 (1.2)	2	1.1	3 (1.3)	3	1.1
Rhinitis	0			2 (2.4)	2	2.5	1 (0.6)	1	0.6	3 (1.3)	3	1.1
Urinary tract infection	0			1 (1.2)	2	2.5	2 (1.2)	2	1.1	3 (1.3)	4	1.4
Viral upper respiratory tract infection	1 (3.4)	1	5.4	1 (1.2)	1	1.3	1 (0.6)	1	0.6	3 (1.3)	3	1.1
Ear infection	0			1 (1.2)	1	1.3	1 (0.6)	2	1.1	2 (0.9)	3	1.1
Gastroenteritis viral	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Hordeolum	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Pneumonia	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Pulpitis dental	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Respiratory tract infection	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Respiratory tract infection viral	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Tooth infection	0			1 (1.2)	1	1.3	1 (0.6)	2	1.1	2 (0.9)	3	1.1
Viral infection	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Bronchitis viral	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Clostridium difficile infection	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Conjunctivitis	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Device related sepsis	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Fungal infection	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Gastrointestinal infection	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Gingivitis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Herpes simplex	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Lung infection	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Oral candidiasis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Oral herpes	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Otitis externa	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Otitis media	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Paronychia	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Parotitis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Periodontitis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Periporitis staphylogenes	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Pharyngitis streptococcal	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Pneumonia bacterial	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4
Pulmonary tuberculosis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Sepsis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Tinea capitis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Tinea cruris	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Tinea pedis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Urosepsis	0			1 (1.2)	2	2.5	0			1 (0.4)	2	0.7
Gastrointestinal disorders	3 (10.3)	5	27.0	15 (17.9)	29	36.4	38 (23.2)	54	29.8	56 (24.6)	88	31.5
Diarrhoea	1 (3.4)	1	5.4	6 (7.1)	6	7.5	8 (4.9)	10	5.5	15 (6.6)	17	6.1
Abdominal pain	0			2 (2.4)	3	3.8	3 (1.8)	4	2.2	5 (2.2)	7	2.5
Dental caries	0			2 (2.4)	3	3.8	3 (1.8)	3	1.7	5 (2.2)	6	2.1
Toothache	1 (3.4)	1	5.4	2 (2.4)	2	2.5	2 (1.2)	3	1.7	5 (2.2)	6	2.1
Large intestine polyp	0			0			4 (2.4)	4	2.2	4 (1.8)	4	1.4
Vomiting	0			2 (2.4)	3	3.8	1 (0.6)	2	1.1	3 (1.3)	5	1.8
Abdominal discomfort	1 (3.4)	1	5.4	1 (1.2)	1	1.3	0			2 (0.9)	2	0.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Abdominal distension	0			0			2 (1.2)	3	1.7	2 (0.9)	3	1.1
Abdominal pain upper	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Abdominal tenderness	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Constipation	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Dyspepsia	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Enteritis	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Flatulence	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Food poisoning	1 (3.4)	1	5.4	1 (1.2)	1	1.3	0			2 (0.9)	2	0.7
Gastritis	1 (3.4)	1	5.4	0			1 (0.6)	1	0.6	2 (0.9)	2	0.7
Gastrooesophageal reflux disease	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Ascites	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Chronic gastritis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Colitis	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Colitis ulcerative	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Dry mouth	0			0			1 (0.6)	2	1.1	1 (0.4)	2	0.7
Duodenal ulcer	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Faeces discoloured	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Faeces soft	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Gastric polyps	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Haemorrhoids	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Inguinal hernia	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Intestinal ischaemia	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Irritable bowel syndrome	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Nausea	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Oesophagitis	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Retching	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Short-bowel syndrome	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Spigelian hernia	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Stomatitis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
General disorders and administration site conditions	3 (10.3)	3	16.2	24 (28.6)	34	42.7	31 (18.9)	51	28.2	53 (23.2)	88	31.5
Fatigue	1 (3.4)	1	5.4	8 (9.5)	8	10.0	8 (4.9)	10	5.5	17 (7.5)	19	6.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Oedema peripheral	0			3 (3.6)	5	6.3	4 (2.4)	4	2.2	7 (3.1)	9	3.2
Asthenia	0			1 (1.2)	2	2.5	5 (3.0)	5	2.8	6 (2.6)	7	2.5
Injection site bruising	0			4 (4.8)	4	5.0	1 (0.6)	1	0.6	5 (2.2)	5	1.8
Pain	0			2 (2.4)	2	2.5	3 (1.8)	3	1.7	5 (2.2)	5	1.8
Pyrexia	0			0			5 (3.0)	5	2.8	5 (2.2)	5	1.8
Malaise	0			2 (2.4)	2	2.5	2 (1.2)	2	1.1	4 (1.8)	4	1.4
Chest pain	0			2 (2.4)	2	2.5	1 (0.6)	1	0.6	3 (1.3)	3	1.1
Peripheral swelling	0			1 (1.2)	1	1.3	2 (1.2)	2	1.1	3 (1.3)	3	1.1
Face oedema	0			1 (1.2)	1	1.3	2 (1.2)	2	1.1	2 (0.9)	3	1.1
Injection site pain	0			1 (1.2)	1	1.3	1 (0.6)	2	1.1	2 (0.9)	3	1.1
Injection site reaction	0			1 (1.2)	1	1.3	1 (0.6)	3	1.7	2 (0.9)	4	1.4
Non-cardiac chest pain	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Pre-existing condition improved	0			1 (1.2)	1	1.3	1 (0.6)	2	1.1	2 (0.9)	3	1.1
Axillary pain	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Cyst	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Death	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Feeling hot	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Gait disturbance	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4
Influenza like illness	0			0			1 (0.6)	3	1.7	1 (0.4)	3	1.1
Injection site haematoma	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4
Injection site haemorrhage	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Nodule	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Thirst	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Vessel puncture site bruise	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Musculoskeletal and connective tissue disorders	2 (6.9)	2	10.8	22 (26.2)	40	50.2	31 (18.9)	42	23.2	53 (23.2)	84	30.1
Arthralgia	0			6 (7.1)	7	8.8	5 (3.0)	5	2.8	11 (4.8)	12	4.3
Back pain	0			5 (6.0)	7	8.8	4 (2.4)	4	2.2	9 (3.9)	11	3.9
Pain in extremity	0			4 (4.8)	6	7.5	4 (2.4)	4	2.2	8 (3.5)	10	3.6
Myalgia	1 (3.4)	1	5.4	4 (4.8)	4	5.0	2 (1.2)	3	1.7	7 (3.1)	8	2.9
Muscle spasms	0			0			3 (1.8)	3	1.7	3 (1.3)	3	1.1
Muscular weakness	0			1 (1.2)	1	1.3	2 (1.2)	3	1.7	3 (1.3)	4	1.4

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Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Musculoskeletal pain	0			1 (1.2)	1	1.3	2 (1.2)	2	1.1	3 (1.3)	3	1.1
Neck pain	0			1 (1.2)	1	1.3	2 (1.2)	2	1.1	3 (1.3)	3	1.1
Osteoarthritis	0			1 (1.2)	1	1.3	2 (1.2)	2	1.1	3 (1.3)	3	1.1
Arthritis	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Joint swelling	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Musculoskeletal chest pain	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Musculoskeletal stiffness	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Bursitis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Foot deformity	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Groin pain	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Joint noise	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Joint stiffness	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Limb discomfort	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Lumbar spinal stenosis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Muscle twitching	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Myositis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Neck deformity	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Pain in jaw	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Periarthritis	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4
Rotator cuff syndrome	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Soft tissue mass	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Spinal pain	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Tendon pain	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Tendonitis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Tenosynovitis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Trigger finger	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Nervous system disorders	4 (13.8)	8	43.2	16 (19.0)	72	90.4	25 (15.2)	58	32.0	44 (19.3)	138	49.4
Headache	3 (10.3)	5	27.0	12 (14.3)	64	80.4	12 (7.3)	41	22.6	26 (11.4)	110	39.4
Dizziness	0			4 (4.8)	5	6.3	3 (1.8)	3	1.7	7 (3.1)	8	2.9
Paraesthesia	1 (3.4)	1	5.4	0			3 (1.8)	4	2.2	4 (1.8)	5	1.8
Hypoaesthesia	1 (3.4)	1	5.4	0			2 (1.2)	3	1.7	3 (1.3)	4	1.4
Sciatica	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7

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Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Somnolence	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Burning sensation	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Carpal tunnel syndrome	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Disturbance in attention	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Hypersomnia	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Hyposmia	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Meralgia paraesthetica	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Tremor	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4
Investigations	5 (17.2)	8	43.2	11 (13.1)	17	21.4	23 (14.0)	47	26.0	35 (15.4)	72	25.8
Blood creatine phosphokinase increased	0			0			8 (4.9)	9	5.0	8 (3.5)	9	3.2
Blood testosterone decreased	0			3 (3.6)	3	3.8	3 (1.8)	3	1.7	6 (2.6)	6	2.1
Thyroxine free decreased	1 (3.4)	1	5.4	0			3 (1.8)	4	2.2	4 (1.8)	5	1.8
Weight increased	0			1 (1.2)	1	1.3	3 (1.8)	3	1.7	4 (1.8)	4	1.4
Alanine aminotransferase increased	1 (3.4)	1	5.4	2 (2.4)	2	2.5	1 (0.6)	1	0.6	3 (1.3)	4	1.4
Aspartate aminotransferase increased	1 (3.4)	1	5.4	0			3 (1.8)	4	2.2	3 (1.3)	5	1.8
Hepatic enzyme increased	2 (6.9)	2	10.8	0			1 (0.6)	1	0.6	3 (1.3)	3	1.1
Blood potassium decreased	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Blood thyroid stimulating hormone decreased	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Gamma-glutamyltransferase increased	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Glycosylated haemoglobin increased	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Weight decreased	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Blood alkaline phosphatase increased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Blood bilirubin increased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Blood calcium decreased	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Blood corticotrophin decreased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Blood creatinine decreased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Blood creatinine increased	0			0			1 (0.6)	2	1.1	1 (0.4)	2	0.7
Blood glucose increased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4

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Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Blood insulin increased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Blood phosphorus increased	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Blood pressure increased	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Blood testosterone increased	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Blood uric acid increased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Cholangiogram	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Cortisol decreased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Cortisol increased	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Creatinine renal clearance decreased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Creatinine renal clearance increased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Electrocardiogram T wave abnormal	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4
Glomerular filtration rate decreased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Haematocrit increased	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4
Platelet count decreased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Pulmonary function test decreased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Thyroid hormones decreased	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Vitamin D decreased	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
White blood cell count increased	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4
Skin and subcutaneous tissue disorders	1 (3.4)	3	16.2	15 (17.9)	19	23.9	15 (9.1)	19	10.5	29 (12.7)	41	14.7
Rash	0			4 (4.8)	4	5.0	0			4 (1.8)	4	1.4
Acne	0			0			3 (1.8)	4	2.2	3 (1.3)	4	1.4
Dry skin	0			0			3 (1.8)	3	1.7	3 (1.3)	3	1.1
Dermatitis contact	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Eczema	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Pruritus	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Urticaria	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Acanthosis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Blister	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4

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Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Dermatitis	1 (3.4)	1	5.4	0			1 (0.6)	1	0.6	1 (0.4)	2	0.7
Dermatitis atopic	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Ecchymosis	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Exfoliative rash	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Haemorrhage subcutaneous	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Ingrowing nail	1 (3.4)	1	5.4	0			1 (0.6)	1	0.6	1 (0.4)	2	0.7
Lipodystrophy acquired	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Miliaria	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Rash erythematous	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Rash macular	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Rash maculo-papular	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Skin discolouration	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Skin hyperpigmentation	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Skin lesion	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4
Skin mass	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Skin ulcer	0			1 (1.2)	2	2.5	0			1 (0.4)	2	0.7
Skin warm	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Injury, poisoning and procedural complications	0			8 (9.5)	11	13.8	20 (12.2)	24	13.3	28 (12.3)	35	12.5
Fall	0			2 (2.4)	3	3.8	3 (1.8)	4	2.2	5 (2.2)	7	2.5
Contusion	0			1 (1.2)	1	1.3	2 (1.2)	2	1.1	3 (1.3)	3	1.1
Arthropod sting	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Head injury	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Ligament sprain	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Tooth fracture	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Arthropod bite	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Bone contusion	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Chest injury	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Concussion	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Laceration	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Limb injury	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Meniscus injury	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4

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Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Multiple fractures	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Muscle strain	0			0			1 (0.6)	2	1.1	1 (0.4)	2	0.7
Patella fracture	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Prescription drug used without a prescription	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Procedural dizziness	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Tibia fracture	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Toxicity to various agents	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Wound	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Wrist fracture	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Respiratory, thoracic and mediastinal disorders	2 (6.9)	2	10.8	10 (11.9)	17	21.4	14 (8.5)	18	9.9	26 (11.4)	37	13.3
Cough	2 (6.9)	2	10.8	4 (4.8)	5	6.3	3 (1.8)	5	2.8	9 (3.9)	12	4.3
Oropharyngeal pain	0			1 (1.2)	1	1.3	3 (1.8)	3	1.7	4 (1.8)	4	1.4
Sleep apnoea syndrome	0			1 (1.2)	1	1.3	3 (1.8)	3	1.7	4 (1.8)	4	1.4
Dyspnoea	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Dyspnoea exertional	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Dyspnoea paroxysmal nocturnal	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Epistaxis	0			1 (1.2)	4	5.0	0			1 (0.4)	4	1.4
Nasal congestion	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Pneumonia aspiration	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Respiratory disorder	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Rhinitis allergic	0			1 (1.2)	2	2.5	0			1 (0.4)	2	0.7
Sinus congestion	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Sinus polyp	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Snoring	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Upper respiratory tract congestion	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Upper respiratory tract inflammation	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Metabolism and nutrition disorders	3 (10.3)	4	21.6	6 (7.1)	7	8.8	10 (6.1)	15	8.3	19 (8.3)	26	9.3
Gout	0			1 (1.2)	1	1.3	2 (1.2)	4	2.2	3 (1.3)	5	1.8

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Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Dehydration	1 (3.4)	1	5.4	0			1 (0.6)	1	0.6	2 (0.9)	2	0.7
Diabetes mellitus	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Hypercholesterolaemia	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Hyperkalaemia	1 (3.4)	1	5.4	1 (1.2)	1	1.3	0			2 (0.9)	2	0.7
Hyperphosphataemia	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Hypokalaemia	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Fluid retention	0			0			1 (0.6)	2	1.1	1 (0.4)	2	0.7
Hyperglycaemia	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Hypertriglyceridaemia	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Hypoglycaemia	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Hyponatraemia	1 (3.4)	2	10.8	0			0			1 (0.4)	2	0.7
Polydipsia	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Vitamin D deficiency	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Psychiatric disorders	0			4 (4.8)	5	6.3	10 (6.1)	10	5.5	14 (6.1)	15	5.4
Insomnia	0			0			3 (1.8)	3	1.7	3 (1.3)	3	1.1
Sleep disorder	0			1 (1.2)	1	1.3	2 (1.2)	2	1.1	3 (1.3)	3	1.1
Anxiety	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Attention deficit/hyperactivity disorder	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Adjustment disorder with depressed mood	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Delirium	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Depression	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Mood swings	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Nervousness	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Vascular disorders	1 (3.4)	1	5.4	4 (4.8)	4	5.0	7 (4.3)	7	3.9	12 (5.3)	12	4.3
Hypertension	1 (3.4)	1	5.4	4 (4.8)	4	5.0	4 (2.4)	4	2.2	9 (3.9)	9	3.2
Hypotension	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Arteriosclerosis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Endocrine disorders	0			5 (6.0)	5	6.3	7 (4.3)	7	3.9	11 (4.8)	12	4.3

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Adrenocortical insufficiency acute	0			0			3 (1.8)	3	1.7	3 (1.3)	3	1.1
Hypothyroidism	0			2 (2.4)	2	2.5	1 (0.6)	1	0.6	3 (1.3)	3	1.1
Secondary hypothyroidism	0			3 (3.6)	3	3.8	0			3 (1.3)	3	1.1
Adrenal insufficiency	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Hyperthyroidism	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Renal and urinary disorders	1 (3.4)	1	5.4	7 (8.3)	8	10.0	3 (1.8)	4	2.2	11 (4.8)	13	4.7
Pollakiuria	0			2 (2.4)	2	2.5	1 (0.6)	1	0.6	3 (1.3)	3	1.1
Nephrolithiasis	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Nocturia	0			1 (1.2)	1	1.3	1 (0.6)	1	0.6	2 (0.9)	2	0.7
Bladder pain	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Calculus urinary	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Dysuria	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Polyuria	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Ureterolithiasis	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Urinary tract obstruction	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4
Eye disorders	0			4 (4.8)	7	8.8	5 (3.0)	7	3.9	9 (3.9)	14	5.0
Vision blurred	0			1 (1.2)	1	1.3	2 (1.2)	2	1.1	3 (1.3)	3	1.1
Cataract	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Dry eye	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Visual impairment	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Age-related macular degeneration	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Conjunctival haemorrhage	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Diplopia	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Eye pruritus	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Visual acuity reduced	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Cardiac disorders	1 (3.4)	1	5.4	3 (3.6)	4	5.0	4 (2.4)	7	3.9	8 (3.5)	12	4.3
Angina unstable	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Atrial flutter	0			1 (1.2)	2	2.5	0			1 (0.4)	2	0.7
Atrioventricular block first degree	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Bundle branch block right	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Cardiogenic shock	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Cardiomyopathy	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Cardiovascular disorder	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Palpitations	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Sinus arrhythmia	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4
Ventricular extrasystoles	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Ventricular fibrillation	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Ear and labyrinth disorders	0			3 (3.6)	4	5.0	5 (3.0)	5	2.8	8 (3.5)	9	3.2
Ear pain	0			3 (3.6)	3	3.8	0			3 (1.3)	3	1.1
Vertigo	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Eustachian tube dysfunction	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
External ear pain	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Middle ear inflammation	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Tinnitus	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			1 (1.2)	1	1.3	5 (3.0)	5	2.8	6 (2.6)	6	2.1
Pituitary tumour benign	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Bladder transitional cell carcinoma	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Lipoma	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Pituitary tumour	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Plasma cell myeloma	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Blood and lymphatic system disorders	0			3 (3.6)	5	6.3	2 (1.2)	2	1.1	5 (2.2)	7	2.5
Haemoconcentration	0			2 (2.4)	3	3.8	0			2 (0.9)	3	1.1
Anaemia	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Polycythaemia	0			1 (1.2)	2	2.5	0			1 (0.4)	2	0.7
Thrombocytopenia	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Hepatobiliary disorders	0			2 (2.4)	3	3.8	2 (1.2)	2	1.1	4 (1.8)	5	1.8
Cholelithiasis	0			1 (1.2)	2	2.5	1 (0.6)	1	0.6	2 (0.9)	3	1.1
Biliary colic	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Male - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hepatic cirrhosis	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Surgical and medical procedures	0			1 (1.2)	1	1.3	3 (1.8)	5	2.8	4 (1.8)	6	2.1
Arterial stent insertion	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Cholecystectomy	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Dental care	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Dental operation	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Tooth extraction	0			1 (1.2)	1	1.3	0			1 (0.4)	1	0.4
Umbilical hernia repair	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Reproductive system and breast disorders	0			0			3 (1.8)	3	1.7	3 (1.3)	3	1.1
Gynaecomastia	0			0			2 (1.2)	2	1.1	2 (0.9)	2	0.7
Prostatitis	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Congenital, familial and genetic disorders	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Myotonia congenita	0			0			1 (0.6)	1	0.6	1 (0.4)	1	0.4
Immune system disorders	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4
Seasonal allergy	1 (3.4)	1	5.4	0			0			1 (0.4)	1	0.4

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MedDRA version 21.0.

54 Adverse Events - Female - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Subjects Exposed	32			82			169			226		
Total patient years	21.3			81.4			196.8			299.6		
All adverse events	28	(87.5)	126 590.9	69	(84.1)	368 451.9	150	(88.8)	915 464.9	204	(90.3)	1409 470.4
Serious adverse events	3	(9.4)	5 23.4	5	(6.1)	6 7.4	12	(7.1)	20 10.2	18	(8.0)	31 10.3
Medical events of special interest	0			0			0			0		
Severity												
Mild	23	(71.9)	92 431.5	60	(73.2)	260 319.3	136	(80.5)	713 362.3	184	(81.4)	1065 355.5
Moderate	15	(46.9)	28 131.3	35	(42.7)	106 130.2	61	(36.1)	180 91.5	95	(42.0)	314 104.8
Severe	4	(12.5)	6 28.1	2	(2.4)	2 2.5	12	(7.1)	22 11.2	17	(7.5)	30 10.0
Causality												
Unlikely	28	(87.5)	110 515.9	67	(81.7)	318 390.5	141	(83.4)	770 391.3	195	(86.3)	1198 399.9
Possible	8	(25.0)	12 56.3	13	(15.9)	29 35.6	37	(21.9)	109 55.4	52	(23.0)	150 50.1
Probable	2	(6.3)	4 18.8	10	(12.2)	21 25.8	20	(11.8)	36 18.3	28	(12.4)	61 20.4
Outcome												
Recovered/Resolved	25	(78.1)	109 511.2	62	(75.6)	299 367.2	141	(83.4)	769 390.7	191	(84.5)	1177 392.9
Recovering/Resolving	1	(3.1)	2 9.4	7	(8.5)	9 11.1	13	(7.7)	18 9.1	21	(9.3)	29 9.7
Recovered/Resolved With Sequelae	1	(3.1)	1 4.7	1	(1.2)	1 1.2	2	(1.2)	2 1.0	3	(1.3)	4 1.3
Not Recovered/Not Resolved	10	(31.3)	13 61.0	30	(36.6)	56 68.8	61	(36.1)	125 63.5	91	(40.3)	194 64.8
Fatal	1	(3.1)	1 4.7	0			0			1	(0.4)	1 0.3
Unknown	0			1	(1.2)	3 3.7	1	(0.6)	1 0.5	2	(0.9)	4 1.3
Action												

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MedDRA version 21.0.

Adverse Events - Female - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Drug Interrupted	1	(3.1)	1 4.7	3	(3.7)	5 6.1	1	(0.6)	2 1.0	5	(2.2)	8 2.7
Drug Withdrawn	0			3	(3.7)	6 7.4	2	(1.2)	3 1.5	5	(2.2)	9 3.0
Dose Reduced	0			1	(1.2)	1 1.2	8	(4.7)	9 4.6	9	(4.0)	10 3.3
Dose Not Changed	27	(84.4)	119 558.1	68	(82.9)	349 428.6	149	(88.2)	863 438.5	202	(89.4)	1331 444.3
Not Applicable	3	(9.4)	6 28.1	6	(7.3)	7 8.6	22	(13.0)	38 19.3	31	(13.7)	51 17.0
Treatment discontinuations due to adverse events	0			3	(3.7)	6 7.4	2	(1.2)	3 1.5	5	(2.2)	9 3.0

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
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55 Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	32			82			169			226		
Total patient years	21.3			81.4			196.8			299.6		
All adverse events	28 (87.5)	126	590.9	69 (84.1)	368	451.9	150 (88.8)	915	464.9	204 (90.3)	1409	470.4
Infections and infestations	22 (68.8)	33	154.8	42 (51.2)	80	98.2	100 (59.2)	238	120.9	141 (62.4)	351	117.2
Nasopharyngitis	5 (15.6)	7	32.8	18 (22.0)	25	30.7	49 (29.0)	84	42.7	66 (29.2)	116	38.7
Upper respiratory tract infection	2 (6.3)	2	9.4	7 (8.5)	9	11.1	13 (7.7)	15	7.6	19 (8.4)	26	8.7
Gastroenteritis	2 (6.3)	2	9.4	3 (3.7)	4	4.9	12 (7.1)	16	8.1	17 (7.5)	22	7.3
Influenza	1 (3.1)	2	9.4	2 (2.4)	3	3.7	11 (6.5)	14	7.1	14 (6.2)	19	6.3
Urinary tract infection	1 (3.1)	1	4.7	2 (2.4)	2	2.5	12 (7.1)	18	9.1	14 (6.2)	21	7.0
Bronchitis	2 (6.3)	2	9.4	4 (4.9)	4	4.9	6 (3.6)	6	3.0	11 (4.9)	12	4.0
Sinusitis	3 (9.4)	6	28.1	3 (3.7)	3	3.7	6 (3.6)	8	4.1	11 (4.9)	17	5.7
Respiratory tract infection	2 (6.3)	2	9.4	1 (1.2)	2	2.5	3 (1.8)	4	2.0	6 (2.7)	8	2.7
Tonsillitis	0			1 (1.2)	1	1.2	5 (3.0)	5	2.5	6 (2.7)	6	2.0
Cystitis	2 (6.3)	2	9.4	0			3 (1.8)	4	2.0	5 (2.2)	6	2.0
Ear infection	1 (3.1)	1	4.7	1 (1.2)	1	1.2	3 (1.8)	5	2.5	5 (2.2)	7	2.3
Viral infection	0			1 (1.2)	1	1.2	4 (2.4)	4	2.0	5 (2.2)	5	1.7
Fungal infection	0			1 (1.2)	1	1.2	3 (1.8)	3	1.5	4 (1.8)	4	1.3
Gastroenteritis viral	2 (6.3)	2	9.4	2 (2.4)	2	2.5	0			4 (1.8)	4	1.3
Respiratory tract infection viral	0			2 (2.4)	2	2.5	2 (1.2)	2	1.0	4 (1.8)	4	1.3
Cellulitis	0			2 (2.4)	2	2.5	1 (0.6)	1	0.5	3 (1.3)	3	1.0
Gingivitis	0			1 (1.2)	1	1.2	2 (1.2)	2	1.0	3 (1.3)	3	1.0
Herpes zoster	0			0			3 (1.8)	8	4.1	3 (1.3)	8	2.7
Oral herpes	0			0			3 (1.8)	4	2.0	3 (1.3)	4	1.3
Pharyngitis streptococcal	0			0			3 (1.8)	4	2.0	3 (1.3)	4	1.3
Rhinitis	0			0			3 (1.8)	3	1.5	3 (1.3)	3	1.0
Appendicitis	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7
Laryngitis	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Lower respiratory tract infection	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Otitis media	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7

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Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Periodontitis	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7
Tinea infection	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7
Tooth abscess	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7
Viral upper respiratory tract infection	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Abscess	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Acarodermatitis	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Bronchitis viral	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Candida infection	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Clostridium difficile infection	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Conjunctivitis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Diverticulitis	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Escherichia infection	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Eye infection	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Folliculitis	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Helicobacter infection	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Herpes virus infection	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Hordeolum	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Meningitis viral	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Molluscum contagiosum	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Onychomycosis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Ophthalmic herpes zoster	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Parotitis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Pharyngitis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Pilonidal cyst	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Pneumonia viral	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Post procedural infection	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Pulpitis dental	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Pyoderma	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Rotavirus infection	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Tooth infection	0			1 (1.2)	2	2.5	0			1 (0.4)	2	0.7
Upper respiratory tract infection bacterial	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Vaginal infection	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Vulvovaginal candidiasis	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Vulvovaginal mycotic infection	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Wound infection	0			1 (1.2)	2	2.5	0			1 (0.4)	2	0.7
Gastrointestinal disorders	10 (31.3)	19	89.1	23 (28.0)	38	46.7	52 (30.8)	117	59.4	77 (34.1)	174	58.1
Vomiting	1 (3.1)	2	9.4	4 (4.9)	5	6.1	14 (8.3)	16	8.1	19 (8.4)	23	7.7
Diarrhoea	4 (12.5)	7	32.8	2 (2.4)	2	2.5	13 (7.7)	21	10.7	18 (8.0)	30	10.0
Nausea	1 (3.1)	1	4.7	6 (7.3)	8	9.8	8 (4.7)	17	8.6	14 (6.2)	26	8.7
Abdominal pain	1 (3.1)	1	4.7	1 (1.2)	1	1.2	7 (4.1)	9	4.6	9 (4.0)	11	3.7
Abdominal pain upper	1 (3.1)	1	4.7	2 (2.4)	2	2.5	4 (2.4)	7	3.6	7 (3.1)	10	3.3
Dyspepsia	1 (3.1)	2	9.4	3 (3.7)	3	3.7	3 (1.8)	4	2.0	7 (3.1)	9	3.0
Toothache	0			2 (2.4)	2	2.5	4 (2.4)	6	3.0	6 (2.7)	8	2.7
Dental caries	0			1 (1.2)	1	1.2	3 (1.8)	3	1.5	4 (1.8)	4	1.3
Gastritis	0			0			4 (2.4)	5	2.5	4 (1.8)	5	1.7
Gastrooesophageal reflux disease	1 (3.1)	1	4.7	1 (1.2)	1	1.2	2 (1.2)	2	1.0	4 (1.8)	4	1.3
Constipation	0			3 (3.7)	3	3.7	1 (0.6)	2	1.0	3 (1.3)	5	1.7
Stomatitis	0			1 (1.2)	1	1.2	2 (1.2)	5	2.5	3 (1.3)	6	2.0
Abdominal tenderness	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Epigastric discomfort	0			0			2 (1.2)	5	2.5	2 (0.9)	5	1.7
Hiatus hernia	1 (3.1)	1	4.7	1 (1.2)	1	1.2	0			2 (0.9)	2	0.7
Lip swelling	1 (3.1)	1	4.7	0			1 (0.6)	1	0.5	2 (0.9)	2	0.7
Pancreatitis acute	1 (3.1)	1	4.7	1 (1.2)	1	1.2	0			2 (0.9)	2	0.7
Abdominal discomfort	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Abdominal distension	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Abdominal hernia	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Abdominal pain lower	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Abdominal wall mass	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Barrett's oesophagus	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Colitis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Dental cyst	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Dry mouth	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Food poisoning	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Gastric polyps	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Gastrointestinal disorder	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Inguinal hernia	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Irritable bowel syndrome	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Mouth ulceration	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Oesophagitis ulcerative	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Poor dental condition	0			0			1 (0.6)	2	1.0	1 (0.4)	2	0.7
Rectal polyp	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Reflux gastritis	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Musculoskeletal and connective tissue disorders	8 (25.0)	12	56.3	23 (28.0)	38	46.7	54 (32.0)	90	45.7	77 (34.1)	140	46.7
Arthralgia	1 (3.1)	1	4.7	11 (13.4)	11	13.5	18 (10.7)	20	10.2	29 (12.8)	32	10.7
Back pain	2 (6.3)	2	9.4	1 (1.2)	1	1.2	17 (10.1)	19	9.7	20 (8.8)	22	7.3
Myalgia	2 (6.3)	2	9.4	4 (4.9)	4	4.9	5 (3.0)	6	3.0	11 (4.9)	12	4.0
Pain in extremity	1 (3.1)	1	4.7	2 (2.4)	2	2.5	3 (1.8)	3	1.5	6 (2.7)	6	2.0
Muscle spasms	1 (3.1)	2	9.4	0			4 (2.4)	4	2.0	5 (2.2)	6	2.0
Joint stiffness	0			3 (3.7)	3	3.7	1 (0.6)	1	0.5	4 (1.8)	4	1.3
Musculoskeletal pain	0			1 (1.2)	1	1.2	3 (1.8)	3	1.5	4 (1.8)	4	1.3
Musculoskeletal stiffness	0			1 (1.2)	1	1.2	2 (1.2)	2	1.0	3 (1.3)	3	1.0
Osteoarthritis	0			2 (2.4)	3	3.7	1 (0.6)	1	0.5	3 (1.3)	4	1.3
Bursitis	1 (3.1)	2	9.4	0			2 (1.2)	3	1.5	2 (0.9)	5	1.7
Intervertebral disc degeneration	0			0			2 (1.2)	3	1.5	2 (0.9)	3	1.0
Intervertebral disc protrusion	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Joint swelling	0			2 (2.4)	3	3.7	0			2 (0.9)	3	1.0
Neck pain	0			0			2 (1.2)	3	1.5	2 (0.9)	3	1.0
Pain in jaw	0			1 (1.2)	1	1.2	1 (0.6)	2	1.0	2 (0.9)	3	1.0
Tendonitis	1 (3.1)	1	4.7	1 (1.2)	1	1.2	0			2 (0.9)	2	0.7
Tenosynovitis	1 (3.1)	1	4.7	1 (1.2)	2	2.5	0			2 (0.9)	3	1.0
Arthritis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Coccydynia	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Costochondritis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Exostosis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3

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Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Fracture pain	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Joint effusion	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Limb deformity	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Limb discomfort	0			0			1 (0.6)	2	1.0	1 (0.4)	2	0.7
Muscle disorder	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Muscle tightness	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Muscle twitching	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Muscular weakness	0			0			1 (0.6)	3	1.5	1 (0.4)	3	1.0
Musculoskeletal chest pain	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Nodal osteoarthritis	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Osteoporosis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Plantar fasciitis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Rheumatoid arthritis	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Rotator cuff syndrome	0			1 (1.2)	2	2.5	0			1 (0.4)	2	0.7
Soft tissue disorder	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Nervous system disorders	10 (31.3)	18	84.4	19 (23.2)	47	57.7	54 (32.0)	111	56.4	75 (33.2)	176	58.8
Headache	7 (21.9)	10	46.9	10 (12.2)	21	25.8	31 (18.3)	68	34.6	43 (19.0)	99	33.0
Dizziness	1 (3.1)	1	4.7	5 (6.1)	7	8.6	11 (6.5)	15	7.6	16 (7.1)	23	7.7
Hypoaesthesia	0			5 (6.1)	6	7.4	4 (2.4)	4	2.0	9 (4.0)	10	3.3
Migraine	1 (3.1)	3	14.1	1 (1.2)	1	1.2	3 (1.8)	4	2.0	4 (1.8)	8	2.7
Paraesthesia	1 (3.1)	1	4.7	1 (1.2)	1	1.2	2 (1.2)	2	1.0	4 (1.8)	4	1.3
Intercostal neuralgia	0			0			3 (1.8)	3	1.5	3 (1.3)	3	1.0
Sciatica	0			0			3 (1.8)	3	1.5	3 (1.3)	3	1.0
Dysgeusia	1 (3.1)	1	4.7	1 (1.2)	1	1.2	0			2 (0.9)	2	0.7
Lethargy	1 (3.1)	1	4.7	0			1 (0.6)	1	0.5	2 (0.9)	2	0.7
Somnolence	0			1 (1.2)	1	1.2	1 (0.6)	2	1.0	2 (0.9)	3	1.0
Syncope	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7
Ataxia	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Carpal tunnel syndrome	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Depressed level of consciousness	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Disturbance in attention	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Hydrocephalus	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3

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Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hypersomnia	0			0			1 (0.6)	2	1.0	1 (0.4)	2	0.7
Memory impairment	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Neuralgia	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Parosmia	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Partial seizures	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Seizure	0			1 (1.2)	3	3.7	0			1 (0.4)	3	1.0
Tremor	0			1 (1.2)	2	2.5	0			1 (0.4)	2	0.7
Vestibular migraine	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
General disorders and administration site conditions	6 (18.8)	10	46.9	17 (20.7)	31	38.1	43 (25.4)	73	37.1	61 (27.0)	114	38.1
Fatigue	1 (3.1)	1	4.7	5 (6.1)	5	6.1	11 (6.5)	13	6.6	17 (7.5)	19	6.3
Oedema peripheral	0			3 (3.7)	4	4.9	8 (4.7)	20	10.2	11 (4.9)	24	8.0
Asthenia	1 (3.1)	1	4.7	3 (3.7)	3	3.7	4 (2.4)	6	3.0	8 (3.5)	10	3.3
Pyrexia	0			1 (1.2)	2	2.5	6 (3.6)	8	4.1	7 (3.1)	10	3.3
Peripheral swelling	1 (3.1)	1	4.7	2 (2.4)	2	2.5	2 (1.2)	2	1.0	5 (2.2)	5	1.7
Chest pain	1 (3.1)	1	4.7	1 (1.2)	1	1.2	2 (1.2)	2	1.0	4 (1.8)	4	1.3
Injection site bruising	2 (6.3)	3	14.1	2 (2.4)	2	2.5	0			4 (1.8)	5	1.7
Malaise	1 (3.1)	1	4.7	0			3 (1.8)	3	1.5	4 (1.8)	4	1.3
Influenza like illness	0			3 (3.7)	3	3.7	1 (0.6)	1	0.5	3 (1.3)	4	1.3
Pain	0			1 (1.2)	1	1.2	2 (1.2)	3	1.5	3 (1.3)	4	1.3
Face oedema	1 (3.1)	1	4.7	0			1 (0.6)	1	0.5	2 (0.9)	2	0.7
Fat tissue decreased	0			1 (1.2)	1	1.2	1 (0.6)	3	1.5	2 (0.9)	4	1.3
Feeling hot	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7
Injection site pain	1 (3.1)	1	4.7	0			1 (0.6)	1	0.5	2 (0.9)	2	0.7
Chest discomfort	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Chills	0			1 (1.2)	2	2.5	0			1 (0.4)	2	0.7
Hunger	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Inflammatory pain	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Injection site atrophy	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Injection site hypertrophy	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Nodule	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Non-cardiac chest pain	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3

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Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Oedema	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Oedema mucosal	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Retention cyst	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Swelling	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Thirst	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Vaccination site pain	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Skin and subcutaneous tissue disorders	11 (34.4)	13	61.0	12 (14.6)	19	23.3	33 (19.5)	47	23.9	53 (23.5)	79	26.4
Rash	2 (6.3)	2	9.4	6 (7.3)	8	9.8	6 (3.6)	6	3.0	14 (6.2)	16	5.3
Dry skin	2 (6.3)	2	9.4	0			3 (1.8)	3	1.5	5 (2.2)	5	1.7
Pruritus	0			3 (3.7)	3	3.7	2 (1.2)	3	1.5	5 (2.2)	6	2.0
Urticaria	0			1 (1.2)	1	1.2	4 (2.4)	5	2.5	5 (2.2)	6	2.0
Alopecia	0			0			3 (1.8)	3	1.5	3 (1.3)	3	1.0
Rash generalised	0			2 (2.4)	2	2.5	1 (0.6)	1	0.5	3 (1.3)	3	1.0
Dermatitis	1 (3.1)	1	4.7	0			1 (0.6)	1	0.5	2 (0.9)	2	0.7
Dermatitis atopic	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Eczema	2 (6.3)	2	9.4	0			1 (0.6)	2	1.0	2 (0.9)	4	1.3
Hyperkeratosis	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Lipohypertrophy	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Miliaria	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Onychoclasis	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Acanthosis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Asteatosis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Dermal cyst	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Dermatitis allergic	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Dermatitis contact	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Drug eruption	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Ecchymosis	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Eczema asteatotic	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Erythema	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Haemorrhage subcutaneous	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Hair disorder	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Lipodystrophy acquired	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Papule	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Prurigo	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Pruritus generalised	1 (3.1)	2	9.4	0			0			1 (0.4)	2	0.7
Pustular psoriasis	0			0			1 (0.6)	2	1.0	1 (0.4)	2	0.7
Rash papular	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Skin burning sensation	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Skin discolouration	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Skin erosion	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Swelling face	0			0			1 (0.6)	2	1.0	1 (0.4)	2	0.7
Injury, poisoning and procedural complications	3 (9.4)	3	14.1	14 (17.1)	20	24.6	25 (14.8)	35	17.8	38 (16.8)	58	19.4
Contusion	1 (3.1)	1	4.7	4 (4.9)	6	7.4	1 (0.6)	2	1.0	6 (2.7)	9	3.0
Tooth fracture	1 (3.1)	1	4.7	1 (1.2)	1	1.2	2 (1.2)	2	1.0	4 (1.8)	4	1.3
Fall	0			1 (1.2)	1	1.2	2 (1.2)	2	1.0	3 (1.3)	3	1.0
Foot fracture	0			2 (2.4)	2	2.5	1 (0.6)	1	0.5	3 (1.3)	3	1.0
Arthropod bite	0			1 (1.2)	1	1.2	2 (1.2)	2	1.0	2 (0.9)	3	1.0
Head injury	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Ligament sprain	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Muscle strain	0			1 (1.2)	1	1.2	1 (0.6)	2	1.0	2 (0.9)	3	1.0
Post procedural complication	0			1 (1.2)	1	1.2	1 (0.6)	2	1.0	2 (0.9)	3	1.0
Procedural pain	1 (3.1)	1	4.7	0			1 (0.6)	2	1.0	2 (0.9)	3	1.0
Spinal compression fracture	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Animal bite	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Chest injury	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Corneal abrasion	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Drug dispensing error	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Hand fracture	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Heat illness	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Incorrect dose administered	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Laceration	0			1 (1.2)	2	2.5	0			1 (0.4)	2	0.7
Ligament rupture	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3

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Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Limb injury	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Meniscus injury	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Muscle injury	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Post-traumatic pain	0			0			1 (0.6)	3	1.5	1 (0.4)	3	1.0
Procedural complication	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Radius fracture	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Scratch	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Spinal column injury	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Thermal burn	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Investigations	2 (6.3)	2	9.4	15 (18.3)	30	36.8	20 (11.8)	43	21.8	35 (15.5)	75	25.0
Weight increased	0			1 (1.2)	1	1.2	6 (3.6)	7	3.6	7 (3.1)	8	2.7
Blood creatine phosphokinase increased	0			0			4 (2.4)	5	2.5	4 (1.8)	5	1.7
Blood uric acid increased	0			2 (2.4)	2	2.5	1 (0.6)	1	0.5	3 (1.3)	3	1.0
Cortisol decreased	0			0			3 (1.8)	3	1.5	3 (1.3)	3	1.0
Creatinine renal clearance decreased	0			1 (1.2)	1	1.2	2 (1.2)	2	1.0	3 (1.3)	3	1.0
Intraocular pressure increased	0			2 (2.4)	2	2.5	1 (0.6)	1	0.5	3 (1.3)	3	1.0
Alanine aminotransferase increased	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Blood insulin increased	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7
Gamma-glutamyltransferase increased	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Glycosylated haemoglobin increased	0			1 (1.2)	2	2.5	1 (0.6)	2	1.0	2 (0.9)	4	1.3
Liver function test abnormal	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7
Platelet count increased	0			1 (1.2)	2	2.5	1 (0.6)	1	0.5	2 (0.9)	3	1.0
Aspartate aminotransferase increased	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Blood alkaline phosphatase decreased	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Blood alkaline phosphatase increased	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Blood cholesterol increased	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Blood glucose increased	0			1 (1.2)	3	3.7	0			1 (0.4)	3	1.0

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Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Blood insulin decreased	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Blood potassium decreased	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Blood potassium increased	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Blood pressure decreased	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Blood thyroid stimulating hormone decreased	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Body temperature increased	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Cardiac murmur	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Electrocardiogram PR prolongation	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Electrocardiogram QT prolonged	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Electrocardiogram T wave inversion	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Electrocardiogram abnormal	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Glomerular filtration rate increased	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Haematocrit increased	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Heart rate increased	0			1 (1.2)	3	3.7	0			1 (0.4)	3	1.0
Hormone level abnormal	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Lymph node palpable	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Normetanephrine urine increased	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Thyroxine decreased	0			0			1 (0.6)	3	1.5	1 (0.4)	3	1.0
Thyroxine free decreased	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Thyroxine increased	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Tri-iodothyronine decreased	0			1 (1.2)	2	2.5	0			1 (0.4)	2	0.7
Urine analysis abnormal	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
White blood cell count increased	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Respiratory, thoracic and mediastinal disorders	2 (6.3)	3	14.1	9 (11.0)	15	18.4	16 (9.5)	30	15.2	26 (11.5)	48	16.0
Oropharyngeal pain	2 (6.3)	2	9.4	2 (2.4)	2	2.5	8 (4.7)	8	4.1	11 (4.9)	12	4.0
Cough	1 (3.1)	1	4.7	2 (2.4)	2	2.5	5 (3.0)	5	2.5	8 (3.5)	8	2.7
Epistaxis	0			3 (3.7)	5	6.1	1 (0.6)	1	0.5	4 (1.8)	6	2.0
Rhinitis allergic	0			2 (2.4)	2	2.5	2 (1.2)	2	1.0	4 (1.8)	4	1.3
Asthma	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7

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Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Dyspnoea	0			2 (2.4)	2	2.5	1 (0.6)	1	0.5	2 (0.9)	3	1.0
Upper-airway cough syndrome	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Increased viscosity of upper respiratory secretion	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Nasal congestion	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Paranasal sinus hypersecretion	0			0			1 (0.6)	2	1.0	1 (0.4)	2	0.7
Pharyngeal erythema	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Respiratory tract congestion	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Rhinorrhoea	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Sinus congestion	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Sneezing	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Upper respiratory tract congestion	0			0			1 (0.6)	2	1.0	1 (0.4)	2	0.7
Metabolism and nutrition disorders	2 (6.3)	2	9.4	4 (4.9)	4	4.9	17 (10.1)	20	10.2	23 (10.2)	26	8.7
Iron deficiency	0			0			4 (2.4)	4	2.0	4 (1.8)	4	1.3
Hypocalcaemia	1 (3.1)	1	4.7	0			2 (1.2)	2	1.0	3 (1.3)	3	1.0
Hypokalaemia	0			0			3 (1.8)	3	1.5	3 (1.3)	3	1.0
Vitamin D deficiency	0			0			3 (1.8)	3	1.5	3 (1.3)	3	1.0
Dyslipidaemia	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Hyperlipidaemia	1 (3.1)	1	4.7	0			1 (0.6)	1	0.5	2 (0.9)	2	0.7
Decreased appetite	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Diabetes mellitus	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Fat redistribution	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Fluid retention	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Hyperphosphataemia	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Hypoglycaemia	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Increased appetite	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Obesity	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Vitamin B complex deficiency	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Eye disorders	2 (6.3)	2	9.4	7 (8.5)	7	8.6	9 (5.3)	9	4.6	17 (7.5)	18	6.0
Dry eye	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Glaucoma	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7

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Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Visual impairment	0			2 (2.4)	2	2.5	0			2 (0.9)	2	0.7
Cataract	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Conjunctival haemorrhage	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Conjunctivitis allergic	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Eye irritation	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Eye swelling	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Eyelid disorder	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Eyelid oedema	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Neovascular age-related macular degeneration	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Ocular hyperaemia	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Scleral disorder	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Vision blurred	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Xerophthalmia	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Psychiatric disorders	2 (6.3)	2	9.4	2 (2.4)	2	2.5	12 (7.1)	18	9.1	15 (6.6)	22	7.3
Insomnia	0			1 (1.2)	1	1.2	4 (2.4)	6	3.0	5 (2.2)	7	2.3
Sleep disorder	1 (3.1)	1	4.7	0			3 (1.8)	3	1.5	4 (1.8)	4	1.3
Anxiety	1 (3.1)	1	4.7	0			2 (1.2)	5	2.5	3 (1.3)	6	2.0
Depression	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7
Emotional disorder	0			0			1 (0.6)	2	1.0	1 (0.4)	2	0.7
Initial insomnia	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Reproductive system and breast disorders	2 (6.3)	2	9.4	4 (4.9)	4	4.9	8 (4.7)	9	4.6	14 (6.2)	15	5.0
Dysmenorrhoea	2 (6.3)	2	9.4	1 (1.2)	1	1.2	2 (1.2)	2	1.0	5 (2.2)	5	1.7
Menstruation irregular	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Breast disorder	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Cervical dysplasia	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Menstruation delayed	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Nipple pain	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Uterine polyp	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Vaginal discharge	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3

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Adverse events by system organ class and preferred term - Female - safety analysis set

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Vaginal haemorrhage	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Vulvovaginal pruritus	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Blood and lymphatic system disorders	0			3 (3.7)	3	3.7	10 (5.9)	13	6.6	13 (5.8)	16	5.3
Anaemia	0			3 (3.7)	3	3.7	6 (3.6)	6	3.0	9 (4.0)	9	3.0
Lymphadenopathy	0			0			3 (1.8)	6	3.0	3 (1.3)	6	2.0
Iron deficiency anaemia	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Ear and labyrinth disorders	0			5 (6.1)	6	7.4	10 (5.9)	11	5.6	13 (5.8)	17	5.7
Vertigo	0			2 (2.4)	2	2.5	3 (1.8)	3	1.5	5 (2.2)	5	1.7
Ear pain	0			2 (2.4)	3	3.7	3 (1.8)	3	1.5	4 (1.8)	6	2.0
Tinnitus	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Cerumen impaction	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Ear discomfort	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Ear disorder	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Vertigo positional	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Endocrine disorders	2 (6.3)	2	9.4	4 (4.9)	5	6.1	7 (4.1)	8	4.1	13 (5.8)	15	5.0
Hypothyroidism	1 (3.1)	1	4.7	2 (2.4)	2	2.5	1 (0.6)	1	0.5	4 (1.8)	4	1.3
Adrenal insufficiency	0			0			2 (1.2)	2	1.0	2 (0.9)	2	0.7
Adrenocortical insufficiency acute	1 (3.1)	1	4.7	0			1 (0.6)	1	0.5	2 (0.9)	2	0.7
Diabetes insipidus	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Glucocorticoid deficiency	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Hypopituitarism	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Secondary adrenocortical insufficiency	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Secondary hypothyroidism	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Thyroid disorder	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Thyroid mass	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Vascular disorders	0			4 (4.9)	5	6.1	10 (5.9)	10	5.1	13 (5.8)	15	5.0
Hypertension	0			3 (3.7)	3	3.7	6 (3.6)	6	3.0	9 (4.0)	9	3.0
Hot flush	0			1 (1.2)	1	1.2	3 (1.8)	3	1.5	4 (1.8)	4	1.3

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Orthostatic hypotension	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Vascular fragility	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Immune system disorders	1 (3.1)	1	4.7	3 (3.7)	3	3.7	7 (4.1)	8	4.1	11 (4.9)	12	4.0
Seasonal allergy	0			1 (1.2)	1	1.2	6 (3.6)	7	3.6	7 (3.1)	8	2.7
Allergy to plants	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Allergy to vaccine	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Food allergy	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Multiple allergies	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Cardiac disorders	0			2 (2.4)	2	2.5	6 (3.6)	10	5.1	8 (3.5)	12	4.0
Tachycardia	0			0			3 (1.8)	3	1.5	3 (1.3)	3	1.0
Palpitations	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7
Aortic valve incompetence	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Atrioventricular block first degree	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Bradycardia	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Cardiac discomfort	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Left ventricular dysfunction	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Mitral valve incompetence	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Myocardial ischaemia	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Renal and urinary disorders	0			3 (3.7)	4	4.9	4 (2.4)	5	2.5	7 (3.1)	9	3.0
Haematuria	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7
Renal cyst	0			1 (1.2)	1	1.2	1 (0.6)	1	0.5	2 (0.9)	2	0.7
Chronic kidney disease	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Dysuria	0			0			1 (0.6)	2	1.0	1 (0.4)	2	0.7
Micturition disorder	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Urinary incontinence	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Hepatobiliary disorders	0			0			5 (3.0)	5	2.5	5 (2.2)	5	1.7
Biliary colic	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Cholelithiasis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Hepatic steatosis	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Female - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hepatomegaly	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Liver disorder	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			3 (3.7)	4	4.9	2 (1.2)	2	1.0	5 (2.2)	6	2.0
Angiomyolipoma	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Basal cell carcinoma	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Intraductal papillary mucinous neoplasm	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Lipoma	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Melanocytic naevus	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Soft tissue neoplasm	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Surgical and medical procedures	1 (3.1)	1	4.7	1 (1.2)	1	1.2	2 (1.2)	2	1.0	4 (1.8)	4	1.3
Tooth extraction	1 (3.1)	1	4.7	0			1 (0.6)	1	0.5	2 (0.9)	2	0.7
Mammoplasty	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Skin operation	0			1 (1.2)	1	1.2	0			1 (0.4)	1	0.3
Congenital, familial and genetic disorders	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Rathke's cleft cyst	0			0			1 (0.6)	1	0.5	1 (0.4)	1	0.3
Product issues	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3
Device malfunction	1 (3.1)	1	4.7	0			0			1 (0.4)	1	0.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
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MedDRA version 21.0.

56 Adverse Events - Childhood onset - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	20			45			103			136		
Total patient years	12.5			43.6			116.1			172.2		
All adverse events	11 (55.0)	31	247.6	32 (71.1)	189	433.5	79 (76.7)	377	324.6	105 (77.2)	597	346.6
Serious adverse events	0			2 (4.4)	2	4.6	9 (8.7)	11	9.5	10 (7.4)	13	7.5
Medical events of special interest	0			0			0			0		
Severity												
Mild	10 (50.0)	29	231.6	31 (68.9)	98	224.8	71 (68.9)	266	229.1	99 (72.8)	393	228.2
Moderate	2 (10.0)	2	16.0	15 (33.3)	91	208.7	33 (32.0)	98	84.4	46 (33.8)	191	110.9
Severe	0			0			9 (8.7)	13	11.2	9 (6.6)	13	7.5
Causality												
Unlikely	11 (55.0)	28	223.6	31 (68.9)	168	385.3	73 (70.9)	313	269.5	99 (72.8)	509	295.5
Possible	2 (10.0)	2	16.0	6 (13.3)	16	36.7	24 (23.3)	45	38.8	31 (22.8)	63	36.6
Probable	1 (5.0)	1	8.0	3 (6.7)	5	11.5	11 (10.7)	19	16.4	14 (10.3)	25	14.5
Outcome												
Recovered/Resolved	11 (55.0)	30	239.6	32 (71.1)	175	401.3	74 (71.8)	309	266.1	102 (75.0)	514	298.4
Recovering/Resolving	0			3 (6.7)	4	9.2	8 (7.8)	10	8.6	11 (8.1)	14	8.1
Recovered/Resolved With Sequelae	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Not Recovered/Not Resolved	1 (5.0)	1	8.0	7 (15.6)	10	22.9	31 (30.1)	57	49.1	37 (27.2)	68	39.5
Action												
Drug Interrupted	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Drug Withdrawn	0			1 (2.2)	1	2.3	1 (1.0)	2	1.7	2 (1.5)	3	1.7

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
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AE causality is based on judgement of investigators.
MedDRA version 21.0.

Adverse Events - Childhood onset - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Dose Reduced	0			1	(2.2)	2 4.6	5	(4.9)	9 7.8	6	(4.4)	11 6.4
Dose Not Changed	11	(55.0)	31 247.6	32	(71.1)	183 419.7	78	(75.7)	350 301.4	105	(77.2)	564 327.4
Not Applicable	0			2	(4.4)	3 6.9	10	(9.7)	15 12.9	12	(8.8)	18 10.4
Treatment discontinuations due to adverse events	0			1	(2.2)	1 2.3	1	(1.0)	2 1.7	2	(1.5)	3 1.7

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
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AE causality is based on judgement of investigators.
MedDRA version 21.0.

57 Adverse events by system organ class and preferred term - Childhood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	20			45			103			136		
Total patient years	12.5			43.6			116.1			172.2		
All adverse events	11 (55.0)	31	247.6	32 (71.1)	189	433.5	79 (76.7)	377	324.6	105 (77.2)	597	346.6
Infections and infestations	8 (40.0)	9	71.9	23 (51.1)	52	119.3	50 (48.5)	110	94.7	75 (55.1)	171	99.3
Nasopharyngitis	1 (5.0)	1	8.0	9 (20.0)	18	41.3	26 (25.2)	36	31.0	34 (25.0)	55	31.9
Upper respiratory tract infection	2 (10.0)	2	16.0	4 (8.9)	6	13.8	8 (7.8)	11	9.5	13 (9.6)	19	11.0
Gastroenteritis	1 (5.0)	1	8.0	2 (4.4)	3	6.9	6 (5.8)	8	6.9	9 (6.6)	12	7.0
Influenza	2 (10.0)	3	24.0	0			7 (6.8)	7	6.0	8 (5.9)	10	5.8
Tonsillitis	1 (5.0)	1	8.0	2 (4.4)	2	4.6	4 (3.9)	4	3.4	7 (5.1)	7	4.1
Respiratory tract infection	1 (5.0)	1	8.0	2 (4.4)	2	4.6	2 (1.9)	3	2.6	5 (3.7)	6	3.5
Respiratory tract infection viral	0			3 (6.7)	3	6.9	2 (1.9)	2	1.7	5 (3.7)	5	2.9
Bronchitis	0			1 (2.2)	1	2.3	3 (2.9)	3	2.6	4 (2.9)	4	2.3
Viral infection	0			0			4 (3.9)	4	3.4	4 (2.9)	4	2.3
Cellulitis	0			2 (4.4)	2	4.6	1 (1.0)	1	0.9	3 (2.2)	3	1.7
Gastroenteritis viral	0			2 (4.4)	2	4.6	1 (1.0)	1	0.9	3 (2.2)	3	1.7
Pharyngitis streptococcal	0			0			3 (2.9)	4	3.4	3 (2.2)	4	2.3
Tooth abscess	0			1 (2.2)	1	2.3	2 (1.9)	2	1.7	3 (2.2)	3	1.7
Cystitis	0			0			2 (1.9)	3	2.6	2 (1.5)	3	1.7
Herpes zoster	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Lower respiratory tract infection	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Pharyngitis	0			1 (2.2)	2	4.6	1 (1.0)	1	0.9	2 (1.5)	3	1.7
Rhinitis	0			2 (4.4)	2	4.6	0			2 (1.5)	2	1.2
Sinusitis	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Urinary tract infection	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Viral upper respiratory tract infection	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Acarodermatitis	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Appendicitis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Candida infection	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6

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Adverse events by system organ class and preferred term - Childhood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Fungal infection	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Gingivitis	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Herpes virus infection	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Hordeolum	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Laryngitis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Oral herpes	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Otitis media	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Paronychia	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Periporitis staphylogenes	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Pneumonia	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Pulmonary tuberculosis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Pulpitis dental	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Tinea capitis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Tinea pedis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Vulvovaginal mycotic infection	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Nervous system disorders	3 (15.0)	5	39.9	11 (24.4)	73	167.4	23 (22.3)	29	25.0	36 (26.5)	107	62.1
Headache	3 (15.0)	5	39.9	7 (15.6)	61	139.9	13 (12.6)	16	13.8	22 (16.2)	82	47.6
Hypoaesthesia	0			2 (4.4)	2	4.6	3 (2.9)	3	2.6	5 (3.7)	5	2.9
Dizziness	0			1 (2.2)	1	2.3	3 (2.9)	4	3.4	4 (2.9)	5	2.9
Somnolence	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Ataxia	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Carpal tunnel syndrome	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Dysgeusia	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Hypersomnia	0			0			1 (1.0)	2	1.7	1 (0.7)	2	1.2
Intercostal neuralgia	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Migraine	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Paraesthesia	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Partial seizures	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Sciatica	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Seizure	0			1 (2.2)	3	6.9	0			1 (0.7)	3	1.7

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Adverse events by system organ class and preferred term - Childhood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Musculoskeletal and connective tissue disorders	1 (5.0)	1	8.0	6 (13.3)	6	13.8	23 (22.3)	33	28.4	29 (21.3)	40	23.2
Arthralgia	0			3 (6.7)	3	6.9	5 (4.9)	6	5.2	7 (5.1)	9	5.2
Musculoskeletal pain	0			0			3 (2.9)	3	2.6	3 (2.2)	3	1.7
Myalgia	1 (5.0)	1	8.0	1 (2.2)	1	2.3	1 (1.0)	1	0.9	3 (2.2)	3	1.7
Pain in extremity	0			0			3 (2.9)	3	2.6	3 (2.2)	3	1.7
Back pain	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Intervertebral disc protrusion	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Neck pain	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Bursitis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Coccydynia	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Intervertebral disc degeneration	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Joint stiffness	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Limb deformity	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Muscle twitching	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Muscular weakness	0			0			1 (1.0)	2	1.7	1 (0.7)	2	1.2
Musculoskeletal stiffness	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Myositis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Osteoarthritis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Osteoporosis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Pain in jaw	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Plantar fasciitis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Tendonitis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Trigger finger	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Gastrointestinal disorders	1 (5.0)	2	16.0	6 (13.3)	6	13.8	21 (20.4)	34	29.3	28 (20.6)	42	24.4
Diarrhoea	1 (5.0)	1	8.0	2 (4.4)	2	4.6	6 (5.8)	7	6.0	9 (6.6)	10	5.8
Abdominal pain	0			0			3 (2.9)	3	2.6	3 (2.2)	3	1.7
Abdominal pain upper	0			0			3 (2.9)	6	5.2	3 (2.2)	6	3.5
Dyspepsia	0			2 (4.4)	2	4.6	1 (1.0)	1	0.9	3 (2.2)	3	1.7
Gastritis	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Gastrooesophageal reflux disease	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Toothache	1 (5.0)	1	8.0	1 (2.2)	1	2.3	0			2 (1.5)	2	1.2

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Childhood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Vomiting	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Abdominal distension	0			0			1 (1.0)	2	1.7	1 (0.7)	2	1.2
Abdominal tenderness	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Dental caries	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Enteritis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Epigastric discomfort	0			0			1 (1.0)	3	2.6	1 (0.7)	3	1.7
Inguinal hernia	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Irritable bowel syndrome	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Nausea	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Stomatitis	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Skin and subcutaneous tissue disorders	4 (20.0)	6	47.9	5 (11.1)	7	16.1	20 (19.4)	28	24.1	27 (19.9)	41	23.8
Rash	1 (5.0)	1	8.0	2 (4.4)	3	6.9	3 (2.9)	3	2.6	6 (4.4)	7	4.1
Urticaria	0			0			3 (2.9)	4	3.4	3 (2.2)	4	2.3
Acanthosis	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Acne	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Alopecia	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Dry skin	1 (5.0)	1	8.0	0			1 (1.0)	1	0.9	2 (1.5)	2	1.2
Dermal cyst	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Dermatitis	1 (5.0)	1	8.0	0			1 (1.0)	1	0.9	1 (0.7)	2	1.2
Dermatitis allergic	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Dermatitis atopic	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Dermatitis contact	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Ingrowing nail	1 (5.0)	1	8.0	0			1 (1.0)	1	0.9	1 (0.7)	2	1.2
Lipodystrophy acquired	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Lipohypertrophy	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Onychoclasis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Prurigo	1 (5.0)	1	8.0	0			0			1 (0.7)	1	0.6
Pruritus	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Pustular psoriasis	0			0			1 (1.0)	2	1.7	1 (0.7)	2	1.2
Rash generalised	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Rash maculo-papular	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Childhood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Skin discolouration	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Skin lesion	1 (5.0)	1	8.0	0			0			1 (0.7)	1	0.6
Skin warm	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Swelling face	0			0			1 (1.0)	2	1.7	1 (0.7)	2	1.2
General disorders and administration site conditions	2 (10.0)	3	24.0	7 (15.6)	14	32.1	17 (16.5)	30	25.8	26 (19.1)	47	27.3
Fatigue	0			4 (8.9)	4	9.2	5 (4.9)	5	4.3	9 (6.6)	9	5.2
Oedema peripheral	0			2 (4.4)	5	11.5	4 (3.9)	6	5.2	6 (4.4)	11	6.4
Asthenia	0			1 (2.2)	2	4.6	4 (3.9)	6	5.2	5 (3.7)	8	4.6
Influenza like illness	0			2 (4.4)	2	4.6	1 (1.0)	3	2.6	3 (2.2)	5	2.9
Peripheral swelling	0			1 (2.2)	1	2.3	2 (1.9)	2	1.7	3 (2.2)	3	1.7
Malaise	1 (5.0)	1	8.0	0			1 (1.0)	1	0.9	2 (1.5)	2	1.2
Non-cardiac chest pain	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Face oedema	1 (5.0)	1	8.0	0			0			1 (0.7)	1	0.6
Injection site haematoma	1 (5.0)	1	8.0	0			0			1 (0.7)	1	0.6
Injection site pain	0			0			1 (1.0)	2	1.7	1 (0.7)	2	1.2
Pain	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Pyrexia	0			0			1 (1.0)	2	1.7	1 (0.7)	2	1.2
Investigations	1 (5.0)	1	8.0	6 (13.3)	7	16.1	17 (16.5)	33	28.4	23 (16.9)	41	23.8
Blood creatine phosphokinase increased	0			0			5 (4.9)	6	5.2	5 (3.7)	6	3.5
Weight increased	0			0			5 (4.9)	6	5.2	5 (3.7)	6	3.5
Blood testosterone decreased	0			1 (2.2)	1	2.3	2 (1.9)	2	1.7	3 (2.2)	3	1.7
Aspartate aminotransferase increased	0			0			2 (1.9)	3	2.6	2 (1.5)	3	1.7
Blood insulin increased	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Gamma-glutamyltransferase increased	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Glycosylated haemoglobin increased	0			0			2 (1.9)	3	2.6	2 (1.5)	3	1.7
Thyroxine free decreased	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Alanine aminotransferase increased	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6

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Adverse events by system organ class and preferred term - Childhood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Blood alkaline phosphatase increased	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Blood creatinine decreased	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Blood potassium decreased	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Blood pressure decreased	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Blood thyroid stimulating hormone decreased	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Body temperature increased	1 (5.0)	1	8.0	0			0			1 (0.7)	1	0.6
Cortisol decreased	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Cortisol increased	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Electrocardiogram abnormal	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Glomerular filtration rate increased	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Hepatic enzyme increased	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Liver function test abnormal	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Weight decreased	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Metabolism and nutrition disorders	1 (5.0)	1	8.0	2 (4.4)	2	4.6	11 (10.7)	15	12.9	14 (10.3)	18	10.4
Hyperphosphataemia	0			0			3 (2.9)	3	2.6	3 (2.2)	3	1.7
Hypokalaemia	0			0			3 (2.9)	3	2.6	3 (2.2)	3	1.7
Hypercholesterolaemia	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Hypocalcaemia	1 (5.0)	1	8.0	0			1 (1.0)	1	0.9	2 (1.5)	2	1.2
Fat redistribution	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Fluid retention	0			0			1 (1.0)	2	1.7	1 (0.7)	2	1.2
Hypertriglyceridaemia	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Hypoglycaemia	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Increased appetite	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Obesity	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Vitamin D deficiency	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Injury, poisoning and procedural complications	0			5 (11.1)	5	11.5	8 (7.8)	11	9.5	13 (9.6)	16	9.3
Contusion	0			0			2 (1.9)	3	2.6	2 (1.5)	3	1.7

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Adverse events by system organ class and preferred term - Childhood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Ligament sprain	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Limb injury	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Arthropod bite	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Ligament rupture	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Multiple fractures	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Muscle strain	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Prescription drug used without a prescription	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Spinal column injury	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Spinal compression fracture	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Thermal burn	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Toxicity to various agents	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Cardiac disorders	1 (5.0)	1	8.0	2 (4.4)	2	4.6	6 (5.8)	10	8.6	9 (6.6)	13	7.5
Palpitations	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Tachycardia	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Aortic valve incompetence	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Atrioventricular block first degree	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Bradycardia	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Cardiac discomfort	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Cardiovascular disorder	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Left ventricular dysfunction	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Mitral valve incompetence	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Myocardial ischaemia	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Sinus arrhythmia	1 (5.0)	1	8.0	0			0			1 (0.7)	1	0.6
Respiratory, thoracic and mediastinal disorders	1 (5.0)	1	8.0	2 (4.4)	2	4.6	5 (4.9)	6	5.2	8 (5.9)	9	5.2
Oropharyngeal pain	0			1 (2.2)	1	2.3	2 (1.9)	2	1.7	3 (2.2)	3	1.7
Asthma	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Cough	1 (5.0)	1	8.0	0			1 (1.0)	1	0.9	2 (1.5)	2	1.2
Dyspnoea paroxysmal nocturnal	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Rhinitis allergic	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6

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MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Endocrine disorders	0			4 (8.9)	5	11.5	4 (3.9)	4	3.4	7 (5.1)	9	5.2
Hypothyroidism	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Secondary hypothyroidism	0			2 (4.4)	2	4.6	0			2 (1.5)	2	1.2
Adrenal insufficiency	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Glucocorticoid deficiency	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Hyperthyroidism	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Hypopituitarism	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Secondary adrenocortical insufficiency	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Eye disorders	0			3 (6.7)	3	6.9	4 (3.9)	4	3.4	7 (5.1)	7	4.1
Visual impairment	0			2 (4.4)	2	4.6	0			2 (1.5)	2	1.2
Conjunctival haemorrhage	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Conjunctivitis allergic	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Dry eye	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Eye swelling	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Vision blurred	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Psychiatric disorders	0			0			5 (4.9)	8	6.9	5 (3.7)	8	4.6
Anxiety	0			0			1 (1.0)	4	3.4	1 (0.7)	4	2.3
Delirium	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Depression	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Insomnia	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Sleep disorder	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Reproductive system and breast disorders	1 (5.0)	1	8.0	0			4 (3.9)	4	3.4	5 (3.7)	5	2.9
Dysmenorrhoea	1 (5.0)	1	8.0	0			2 (1.9)	2	1.7	3 (2.2)	3	1.7
Breast disorder	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Menstruation irregular	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Vascular disorders	0			0			5 (4.9)	5	4.3	5 (3.7)	5	2.9
Hypertension	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2

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Adverse events by system organ class and preferred term - Childhood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Arteriosclerosis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Hot flush	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Hypotension	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Hepatobiliary disorders	0			0			4 (3.9)	4	3.4	4 (2.9)	4	2.3
Cholelithiasis	0			0			2 (1.9)	2	1.7	2 (1.5)	2	1.2
Biliary colic	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Hepatic steatosis	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Blood and lymphatic system disorders	0			1 (2.2)	1	2.3	2 (1.9)	2	1.7	3 (2.2)	3	1.7
Anaemia	0			1 (2.2)	1	2.3	2 (1.9)	2	1.7	3 (2.2)	3	1.7
Ear and labyrinth disorders	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Vertigo	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			1 (2.2)	2	4.6	1 (1.0)	1	0.9	2 (1.5)	3	1.7
Lipoma	0			1 (2.2)	1	2.3	1 (1.0)	1	0.9	2 (1.5)	2	1.2
Soft tissue neoplasm	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Renal and urinary disorders	0			1 (2.2)	1	2.3	1 (1.0)	2	1.7	2 (1.5)	3	1.7
Chronic kidney disease	0			1 (2.2)	1	2.3	0			1 (0.7)	1	0.6
Dysuria	0			0			1 (1.0)	2	1.7	1 (0.7)	2	1.2
Congenital, familial and genetic disorders	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Myotonia congenita	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Immune system disorders	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Seasonal allergy	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Surgical and medical procedures	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6
Mammoplasty	0			0			1 (1.0)	1	0.9	1 (0.7)	1	0.6

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58 Adverse Events - Adulthood onset - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	41			121			230			318		
Total patient years	27.3			117.4			261.7			406.5		
All adverse events	35 (85.4)	151	552.7	98 (81.0)	550	468.3	196 (85.2)	1046	399.7	277 (87.1)	1747	429.8
Serious adverse events	5 (12.2)	7	25.6	14 (11.6)	20	17.0	20 (8.7)	39	14.9	37 (11.6)	66	16.2
Medical events of special interest	0			0			0			0		
Severity												
Mild	31 (75.6)	115	421.0	84 (69.4)	401	341.5	179 (77.8)	815	311.4	248 (78.0)	1331	327.5
Moderate	15 (36.6)	30	109.8	48 (39.7)	130	110.7	66 (28.7)	197	75.3	115 (36.2)	357	87.8
Severe	4 (9.8)	6	22.0	12 (9.9)	19	16.2	17 (7.4)	34	13.0	32 (10.1)	59	14.5
Causality												
Unlikely	34 (82.9)	135	494.2	94 (77.7)	461	392.6	184 (80.0)	863	329.8	263 (82.7)	1459	359.0
Possible	7 (17.1)	11	40.3	28 (23.1)	52	44.3	41 (17.8)	135	51.6	70 (22.0)	198	48.7
Probable	3 (7.3)	5	18.3	17 (14.0)	37	31.5	26 (11.3)	48	18.3	43 (13.5)	90	22.1
Outcome												
Recovered/Resolved	32 (78.0)	130	475.9	89 (73.6)	419	356.8	180 (78.3)	860	328.6	257 (80.8)	1409	346.7
Recovering/Resolving	1 (2.4)	2	7.3	10 (8.3)	15	12.8	17 (7.4)	24	9.2	28 (8.8)	41	10.1
Recovered/Resolved With Sequelae	1 (2.4)	1	3.7	4 (3.3)	5	4.3	2 (0.9)	2	0.8	6 (1.9)	8	2.0
Not Recovered/Not Resolved	12 (29.3)	17	62.2	51 (42.1)	106	90.3	77 (33.5)	155	59.2	128 (40.3)	278	68.4
Fatal	1 (2.4)	1	3.7	2 (1.7)	2	1.7	2 (0.9)	4	1.5	5 (1.6)	7	1.7

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
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AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Adverse Events - Adulthood onset - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Unknown	0			1	(0.8)	3 2.6	1	(0.4)	1 0.4	2	(0.6)	4 1.0
Action												
Drug Interrupted	3	(7.3)	5 18.3	6	(5.0)	10 8.5	2	(0.9)	5 1.9	11	(3.5)	20 4.9
Drug Withdrawn	1	(2.4)	1 3.7	5	(4.1)	8 6.8	5	(2.2)	6 2.3	11	(3.5)	15 3.7
Dose Reduced	0			4	(3.3)	5 4.3	5	(2.2)	5 1.9	9	(2.8)	10 2.5
Dose Not Changed	34	(82.9)	139 508.8	94	(77.7)	506 430.9	195	(84.8)	977 373.3	271	(85.2)	1622 399.1
Not Applicable	3	(7.3)	6 22.0	13	(10.7)	21 17.9	28	(12.2)	53 20.3	44	(13.8)	80 19.7
Treatment discontinuations due to adverse events*	1	(2.4)	1 3.7	6	(5.0)	9 7.7	5	(2.2)	6 2.3	12	(3.8)	16 3.9

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
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59 Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	41			121			230			318		
Total patient years	27.3			117.4			261.7			406.5		
All adverse events	35 (85.4)	151	552.7	98 (81.0)	550	468.3	196 (85.2)	1046	399.7	277 (87.1)	1747	429.8
Infections and infestations	28 (68.3)	41	150.1	60 (49.6)	106	90.3	121 (52.6)	243	92.9	179 (56.3)	390	96.0
Nasopharyngitis	8 (19.5)	11	40.3	29 (24.0)	35	29.8	58 (25.2)	93	35.5	87 (27.4)	139	34.2
Upper respiratory tract infection	5 (12.2)	5	18.3	9 (7.4)	13	11.1	14 (6.1)	14	5.3	24 (7.5)	32	7.9
Urinary tract infection	1 (2.4)	1	3.7	3 (2.5)	4	3.4	12 (5.2)	18	6.9	15 (4.7)	23	5.7
Influenza	0			3 (2.5)	4	3.4	11 (4.8)	14	5.3	14 (4.4)	18	4.4
Gastroenteritis	1 (2.4)	1	3.7	1 (0.8)	1	0.9	11 (4.8)	13	5.0	13 (4.1)	15	3.7
Sinusitis	3 (7.3)	6	22.0	3 (2.5)	3	2.6	8 (3.5)	10	3.8	13 (4.1)	19	4.7
Bronchitis	3 (7.3)	3	11.0	3 (2.5)	3	2.6	5 (2.2)	5	1.9	10 (3.1)	11	2.7
Ear infection	1 (2.4)	1	3.7	2 (1.7)	2	1.7	4 (1.7)	7	2.7	7 (2.2)	10	2.5
Pharyngitis	1 (2.4)	1	3.7	3 (2.5)	4	3.4	2 (0.9)	2	0.8	6 (1.9)	7	1.7
Tonsillitis	0			2 (1.7)	3	2.6	4 (1.7)	4	1.5	6 (1.9)	7	1.7
Herpes zoster	1 (2.4)	1	3.7	2 (1.7)	2	1.7	2 (0.9)	7	2.7	5 (1.6)	10	2.5
Fungal infection	0			2 (1.7)	2	1.7	2 (0.9)	2	0.8	4 (1.3)	4	1.0
Lower respiratory tract infection	0			1 (0.8)	2	1.7	3 (1.3)	3	1.1	4 (1.3)	5	1.2
Rhinitis	0			0			4 (1.7)	4	1.5	4 (1.3)	4	1.0
Cystitis	2 (4.9)	2	7.3	0			1 (0.4)	1	0.4	3 (0.9)	3	0.7
Gastroenteritis viral	2 (4.9)	2	7.3	0			1 (0.4)	1	0.4	3 (0.9)	3	0.7
Gingivitis	0			0			3 (1.3)	3	1.1	3 (0.9)	3	0.7
Oral herpes	0			1 (0.8)	1	0.9	2 (0.9)	3	1.1	3 (0.9)	4	1.0
Periodontitis	0			1 (0.8)	1	0.9	2 (0.9)	2	0.8	3 (0.9)	3	0.7
Respiratory tract infection	1 (2.4)	1	3.7	1 (0.8)	2	1.7	1 (0.4)	1	0.4	3 (0.9)	4	1.0
Tooth abscess	0			2 (1.7)	2	1.7	1 (0.4)	1	0.4	3 (0.9)	3	0.7
Tooth infection	0			2 (1.7)	3	2.6	1 (0.4)	2	0.8	3 (0.9)	5	1.2
Viral infection	0			1 (0.8)	1	0.9	2 (0.9)	2	0.8	3 (0.9)	3	0.7
Viral upper respiratory tract infection	1 (2.4)	1	3.7	0			2 (0.9)	2	0.8	3 (0.9)	3	0.7

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Bronchitis viral	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Clostridium difficile infection	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Conjunctivitis	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Hordeolum	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Otitis media	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Parotitis	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Pulpitis dental	0			2 (1.7)	2	1.7	0			2 (0.6)	2	0.5
Tinea infection	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Abscess	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Appendicitis	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Device related sepsis	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Diverticulitis	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Escherichia infection	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Eye infection	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Folliculitis	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Gastrointestinal infection	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Helicobacter infection	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Herpes simplex	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Laryngitis	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Lung infection	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Meningitis viral	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Molluscum contagiosum	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Onychomycosis	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Ophthalmic herpes zoster	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Oral candidiasis	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Otitis externa	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Pharyngitis streptococcal	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Pilonidal cyst	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Pneumonia	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Pneumonia bacterial	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Pneumonia viral	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Post procedural infection	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Pyoderma	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Respiratory tract infection viral	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Rotavirus infection	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Sepsis	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Tinea cruris	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Upper respiratory tract infection bacterial	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Urosepsis	0			1 (0.8)	2	1.7	0			1 (0.3)	2	0.5
Vaginal infection	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Vulvovaginal candidiasis	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Wound infection	0			1 (0.8)	2	1.7	0			1 (0.3)	2	0.5
Gastrointestinal disorders	12 (29.3)	22	80.5	32 (26.4)	61	51.9	69 (30.0)	137	52.3	105 (33.0)	220	54.1
Diarrhoea	4 (9.8)	7	25.6	6 (5.0)	6	5.1	15 (6.5)	24	9.2	24 (7.5)	37	9.1
Vomiting	1 (2.4)	2	7.3	6 (5.0)	8	6.8	13 (5.7)	16	6.1	20 (6.3)	26	6.4
Nausea	1 (2.4)	1	3.7	6 (5.0)	8	6.8	8 (3.5)	17	6.5	14 (4.4)	26	6.4
Abdominal pain	1 (2.4)	1	3.7	3 (2.5)	4	3.4	7 (3.0)	10	3.8	11 (3.5)	15	3.7
Toothache	0			3 (2.5)	3	2.6	6 (2.6)	9	3.4	9 (2.8)	12	3.0
Dental caries	0			3 (2.5)	4	3.4	5 (2.2)	5	1.9	8 (2.5)	9	2.2
Abdominal pain upper	1 (2.4)	1	3.7	2 (1.7)	2	1.7	3 (1.3)	3	1.1	6 (1.9)	6	1.5
Dyspepsia	1 (2.4)	2	7.3	2 (1.7)	2	1.7	3 (1.3)	4	1.5	6 (1.9)	8	2.0
Constipation	0			3 (2.5)	3	2.6	3 (1.3)	4	1.5	5 (1.6)	7	1.7
Gastritis	1 (2.4)	1	3.7	0			3 (1.3)	4	1.5	4 (1.3)	5	1.2
Gastrooesophageal reflux disease	1 (2.4)	1	3.7	1 (0.8)	1	0.9	2 (0.9)	2	0.8	4 (1.3)	4	1.0
Large intestine polyp	0			0			4 (1.7)	4	1.5	4 (1.3)	4	1.0
Abdominal discomfort	1 (2.4)	1	3.7	1 (0.8)	1	0.9	1 (0.4)	1	0.4	3 (0.9)	3	0.7
Abdominal tenderness	0			3 (2.5)	3	2.6	0			3 (0.9)	3	0.7
Food poisoning	1 (2.4)	1	3.7	1 (0.8)	1	0.9	1 (0.4)	1	0.4	3 (0.9)	3	0.7
Stomatitis	0			0			3 (1.3)	6	2.3	3 (0.9)	6	1.5
Abdominal distension	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Colitis	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Dry mouth	0			0			2 (0.9)	3	1.1	2 (0.6)	3	0.7
Flatulence	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Gastric polyps	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5

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Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hiatus hernia	1 (2.4)	1	3.7	1 (0.8)	1	0.9	0			2 (0.6)	2	0.5
Lip swelling	1 (2.4)	1	3.7	0			1 (0.4)	1	0.4	2 (0.6)	2	0.5
Pancreatitis acute	1 (2.4)	1	3.7	1 (0.8)	1	0.9	0			2 (0.6)	2	0.5
Abdominal hernia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Abdominal pain lower	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Abdominal wall mass	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Ascites	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Barrett's oesophagus	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Chronic gastritis	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Colitis ulcerative	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Dental cyst	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Duodenal ulcer	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Enteritis	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Epigastric discomfort	0			0			1 (0.4)	2	0.8	1 (0.3)	2	0.5
Faeces discoloured	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Faeces soft	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Gastrointestinal disorder	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Haemorrhoids	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Inguinal hernia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Intestinal ischaemia	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Irritable bowel syndrome	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Mouth ulceration	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Oesophagitis	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Oesophagitis ulcerative	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Poor dental condition	0			0			1 (0.4)	2	0.8	1 (0.3)	2	0.5
Rectal polyp	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Reflux gastritis	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Retching	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Short-bowel syndrome	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Spigelian hernia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Musculoskeletal and connective tissue disorders	9 (22.0)	13	47.6	39 (32.2)	72	61.3	62 (27.0)	99	37.8	101 (31.8)	184	45.3

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Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Arthralgia	1 (2.4)	1	3.7	14 (11.6)	15	12.8	18 (7.8)	19	7.3	33 (10.4)	35	8.6
Back pain	2 (4.9)	2	7.3	6 (5.0)	8	6.8	19 (8.3)	21	8.0	27 (8.5)	31	7.6
Myalgia	2 (4.9)	2	7.3	7 (5.8)	7	6.0	6 (2.6)	8	3.1	15 (4.7)	17	4.2
Pain in extremity	1 (2.4)	1	3.7	6 (5.0)	8	6.8	4 (1.7)	4	1.5	11 (3.5)	13	3.2
Muscle spasms	1 (2.4)	2	7.3	0			7 (3.0)	7	2.7	8 (2.5)	9	2.2
Osteoarthritis	0			3 (2.5)	4	3.4	2 (0.9)	2	0.8	5 (1.6)	6	1.5
Joint stiffness	0			2 (1.7)	2	1.7	2 (0.9)	2	0.8	4 (1.3)	4	1.0
Joint swelling	0			4 (3.3)	5	4.3	0			4 (1.3)	5	1.2
Musculoskeletal pain	0			2 (1.7)	2	1.7	2 (0.9)	2	0.8	4 (1.3)	4	1.0
Musculoskeletal stiffness	0			1 (0.8)	1	0.9	3 (1.3)	3	1.1	4 (1.3)	4	1.0
Arthritis	0			1 (0.8)	1	0.9	2 (0.9)	2	0.8	3 (0.9)	3	0.7
Muscular weakness	0			1 (0.8)	1	0.9	2 (0.9)	4	1.5	3 (0.9)	5	1.2
Musculoskeletal chest pain	0			2 (1.7)	2	1.7	1 (0.4)	1	0.4	3 (0.9)	3	0.7
Neck pain	0			0			3 (1.3)	4	1.5	3 (0.9)	4	1.0
Tenosynovitis	1 (2.4)	1	3.7	1 (0.8)	2	1.7	1 (0.4)	1	0.4	3 (0.9)	4	1.0
Bursitis	1 (2.4)	2	7.3	0			2 (0.9)	3	1.1	2 (0.6)	5	1.2
Limb discomfort	0			1 (0.8)	1	0.9	1 (0.4)	2	0.8	2 (0.6)	3	0.7
Pain in jaw	0			1 (0.8)	1	0.9	1 (0.4)	2	0.8	2 (0.6)	3	0.7
Rotator cuff syndrome	0			2 (1.7)	3	2.6	0			2 (0.6)	3	0.7
Tendonitis	1 (2.4)	1	3.7	1 (0.8)	1	0.9	0			2 (0.6)	2	0.5
Costochondritis	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Exostosis	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Foot deformity	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Fracture pain	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Groin pain	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Intervertebral disc degeneration	0			0			1 (0.4)	2	0.8	1 (0.3)	2	0.5
Joint effusion	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Joint noise	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Lumbar spinal stenosis	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Muscle disorder	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Muscle tightness	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Muscle twitching	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Neck deformity	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Nodal osteoarthritis	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Periarthritis	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Rheumatoid arthritis	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Soft tissue disorder	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Soft tissue mass	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Spinal pain	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Tendon pain	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
General disorders and administration site conditions	7 (17.1)	10	36.6	34 (28.1)	51	43.4	57 (24.8)	94	35.9	88 (27.7)	155	38.1
Fatigue	2 (4.9)	2	7.3	9 (7.4)	9	7.7	14 (6.1)	18	6.9	25 (7.9)	29	7.1
Oedema peripheral	0			4 (3.3)	4	3.4	8 (3.5)	18	6.9	12 (3.8)	22	5.4
Pyrexia	0			1 (0.8)	2	1.7	10 (4.3)	11	4.2	11 (3.5)	13	3.2
Asthenia	1 (2.4)	1	3.7	3 (2.5)	3	2.6	5 (2.2)	5	1.9	9 (2.8)	9	2.2
Injection site bruising	2 (4.9)	3	11.0	6 (5.0)	6	5.1	1 (0.4)	1	0.4	9 (2.8)	10	2.5
Chest pain	1 (2.4)	1	3.7	3 (2.5)	3	2.6	3 (1.3)	3	1.1	7 (2.2)	7	1.7
Pain	0			3 (2.5)	3	2.6	4 (1.7)	5	1.9	7 (2.2)	8	2.0
Malaise	0			2 (1.7)	2	1.7	4 (1.7)	4	1.5	6 (1.9)	6	1.5
Peripheral swelling	1 (2.4)	1	3.7	2 (1.7)	2	1.7	2 (0.9)	2	0.8	5 (1.6)	5	1.2
Face oedema	0			1 (0.8)	1	0.9	3 (1.3)	3	1.1	3 (0.9)	4	1.0
Feeling hot	0			2 (1.7)	2	1.7	1 (0.4)	1	0.4	3 (0.9)	3	0.7
Injection site pain	1 (2.4)	1	3.7	1 (0.8)	1	0.9	1 (0.4)	1	0.4	3 (0.9)	3	0.7
Fat tissue decreased	0			1 (0.8)	1	0.9	1 (0.4)	3	1.1	2 (0.6)	4	1.0
Injection site reaction	0			1 (0.8)	1	0.9	1 (0.4)	3	1.1	2 (0.6)	4	1.0
Nodule	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Pre-existing condition improved	0			1 (0.8)	1	0.9	1 (0.4)	2	0.8	2 (0.6)	3	0.7
Thirst	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Axillary pain	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Chest discomfort	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Chills	0			1 (0.8)	2	1.7	0			1 (0.3)	2	0.5
Cyst	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Death	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Gait disturbance	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hunger	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Inflammatory pain	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Influenza like illness	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	1 (0.3)	2	0.5
Injection site atrophy	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Injection site haemorrhage	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Injection site hypertrophy	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Non-cardiac chest pain	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Oedema	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Oedema mucosal	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Retention cyst	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Swelling	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Vaccination site pain	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Vessel puncture site bruise	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Nervous system disorders	11 (26.8)	21	76.9	24 (19.8)	46	39.2	56 (24.3)	140	53.5	83 (26.1)	207	50.9
Headache	7 (17.1)	10	36.6	15 (12.4)	24	20.4	30 (13.0)	93	35.5	47 (14.8)	127	31.2
Dizziness	1 (2.4)	1	3.7	8 (6.6)	11	9.4	11 (4.8)	14	5.3	19 (6.0)	26	6.4
Hypoaesthesia	1 (2.4)	1	3.7	3 (2.5)	4	3.4	3 (1.3)	4	1.5	7 (2.2)	9	2.2
Paraesthesia	2 (4.9)	2	7.3	0			5 (2.2)	6	2.3	7 (2.2)	8	2.0
Sciatica	0			0			4 (1.7)	4	1.5	4 (1.3)	4	1.0
Migraine	1 (2.4)	3	11.0	0			3 (1.3)	4	1.5	3 (0.9)	7	1.7
Disturbance in attention	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Intercostal neuralgia	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Lethargy	1 (2.4)	1	3.7	0			1 (0.4)	1	0.4	2 (0.6)	2	0.5
Somnolence	0			1 (0.8)	1	0.9	1 (0.4)	2	0.8	2 (0.6)	3	0.7
Syncope	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Tremor	1 (2.4)	1	3.7	1 (0.8)	2	1.7	0			2 (0.6)	3	0.7
Burning sensation	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Carpal tunnel syndrome	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Depressed level of consciousness	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Dysgeusia	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Hydrocephalus	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Hypersomnia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hyposmia	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Memory impairment	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Meralgia paraesthetica	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Neuralgia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Parosmia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Vestibular migraine	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Skin and subcutaneous tissue disorders	8 (19.5)	10	36.6	22 (18.2)	31	26.4	28 (12.2)	38	14.5	55 (17.3)	79	19.4
Rash	1 (2.4)	1	3.7	8 (6.6)	9	7.7	3 (1.3)	3	1.1	12 (3.8)	13	3.2
Dry skin	1 (2.4)	1	3.7	0			5 (2.2)	5	1.9	6 (1.9)	6	1.5
Pruritus	0			3 (2.5)	3	2.6	3 (1.3)	4	1.5	6 (1.9)	7	1.7
Eczema	2 (4.9)	2	7.3	2 (1.7)	2	1.7	1 (0.4)	2	0.8	4 (1.3)	6	1.5
Urticaria	0			2 (1.7)	2	1.7	2 (0.9)	2	0.8	4 (1.3)	4	1.0
Miliaria	0			2 (1.7)	2	1.7	1 (0.4)	1	0.4	3 (0.9)	3	0.7
Dermatitis	1 (2.4)	1	3.7	0			1 (0.4)	1	0.4	2 (0.6)	2	0.5
Dermatitis atopic	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Dermatitis contact	1 (2.4)	1	3.7	0			1 (0.4)	1	0.4	2 (0.6)	2	0.5
Ecchymosis	1 (2.4)	1	3.7	1 (0.8)	1	0.9	0			2 (0.6)	2	0.5
Haemorrhage subcutaneous	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Hyperkeratosis	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Rash generalised	0			2 (1.7)	2	1.7	0			2 (0.6)	2	0.5
Acne	0			0			1 (0.4)	2	0.8	1 (0.3)	2	0.5
Alopecia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Asteatosis	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Blister	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Drug eruption	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Eczema asteatotic	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Erythema	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Exfoliative rash	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Hair disorder	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Lipodystrophy acquired	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Lipohypertrophy	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

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Onychoclasis	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Papule	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Pruritus generalised	1 (2.4)	2	7.3	0			0			1 (0.3)	2	0.5
Rash erythematous	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Rash macular	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Rash papular	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Skin burning sensation	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Skin discolouration	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Skin erosion	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Skin hyperpigmentation	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Skin mass	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Skin ulcer	0			1 (0.8)	2	1.7	0			1 (0.3)	2	0.5
Injury, poisoning and procedural complications	3 (7.3)	3	11.0	17 (14.0)	26	22.1	37 (16.1)	48	18.3	53 (16.7)	77	18.9
Fall	0			3 (2.5)	4	3.4	5 (2.2)	6	2.3	8 (2.5)	10	2.5
Contusion	1 (2.4)	1	3.7	5 (4.1)	7	6.0	1 (0.4)	1	0.4	7 (2.2)	9	2.2
Tooth fracture	1 (2.4)	1	3.7	2 (1.7)	2	1.7	3 (1.3)	3	1.1	6 (1.9)	6	1.5
Head injury	0			0			4 (1.7)	4	1.5	4 (1.3)	4	1.0
Foot fracture	0			2 (1.7)	2	1.7	1 (0.4)	1	0.4	3 (0.9)	3	0.7
Arthropod bite	0			1 (0.8)	1	0.9	2 (0.9)	2	0.8	2 (0.6)	3	0.7
Arthropod sting	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Chest injury	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Laceration	0			1 (0.8)	2	1.7	1 (0.4)	1	0.4	2 (0.6)	3	0.7
Ligament sprain	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Meniscus injury	0			2 (1.7)	2	1.7	0			2 (0.6)	2	0.5
Muscle strain	0			0			2 (0.9)	4	1.5	2 (0.6)	4	1.0
Post procedural complication	0			1 (0.8)	1	0.9	1 (0.4)	2	0.8	2 (0.6)	3	0.7
Procedural pain	1 (2.4)	1	3.7	0			1 (0.4)	2	0.8	2 (0.6)	3	0.7
Animal bite	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Bone contusion	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Concussion	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Corneal abrasion	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

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Drug dispensing error	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Hand fracture	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Heat illness	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Incorrect dose administered	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Muscle injury	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Patella fracture	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Post-traumatic pain	0			0			1 (0.4)	3	1.1	1 (0.3)	3	0.7
Procedural complication	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Procedural dizziness	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Radius fracture	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Scratch	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Spinal compression fracture	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Tibia fracture	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Wound	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Wrist fracture	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Investigations	6 (14.6)	9	32.9	20 (16.5)	40	34.1	26 (11.3)	57	21.8	47 (14.8)	106	26.1
Blood creatine phosphokinase increased	0			0			7 (3.0)	8	3.1	7 (2.2)	8	2.0
Weight increased	0			2 (1.7)	2	1.7	4 (1.7)	4	1.5	6 (1.9)	6	1.5
Alanine aminotransferase increased	1 (2.4)	1	3.7	2 (1.7)	2	1.7	2 (0.9)	2	0.8	4 (1.3)	5	1.2
Blood uric acid increased	0			2 (1.7)	2	1.7	2 (0.9)	2	0.8	4 (1.3)	4	1.0
Creatinine renal clearance decreased	0			1 (0.8)	1	0.9	3 (1.3)	3	1.1	4 (1.3)	4	1.0
Blood testosterone decreased	0			2 (1.7)	2	1.7	1 (0.4)	1	0.4	3 (0.9)	3	0.7
Cortisol decreased	0			0			3 (1.3)	3	1.1	3 (0.9)	3	0.7
Intraocular pressure increased	0			2 (1.7)	2	1.7	1 (0.4)	1	0.4	3 (0.9)	3	0.7
Thyroxine free decreased	1 (2.4)	1	3.7	0			2 (0.9)	3	1.1	3 (0.9)	4	1.0
Aspartate aminotransferase increased	1 (2.4)	1	3.7	0			2 (0.9)	2	0.8	2 (0.6)	3	0.7
Blood glucose increased	0			1 (0.8)	3	2.6	1 (0.4)	1	0.4	2 (0.6)	4	1.0
Blood potassium decreased	0			2 (1.7)	2	1.7	0			2 (0.6)	2	0.5

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Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Blood thyroid stimulating hormone decreased	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Gamma-glutamyltransferase increased	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Glycosylated haemoglobin increased	0			1 (0.8)	2	1.7	1 (0.4)	1	0.4	2 (0.6)	3	0.7
Haematocrit increased	1 (2.4)	1	3.7	0			1 (0.4)	1	0.4	2 (0.6)	2	0.5
Hepatic enzyme increased	2 (4.9)	2	7.3	0			0			2 (0.6)	2	0.5
Platelet count increased	0			1 (0.8)	2	1.7	1 (0.4)	1	0.4	2 (0.6)	3	0.7
White blood cell count increased	1 (2.4)	1	3.7	0			1 (0.4)	1	0.4	2 (0.6)	2	0.5
Blood alkaline phosphatase decreased	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Blood alkaline phosphatase increased	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Blood bilirubin increased	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Blood calcium decreased	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Blood cholesterol increased	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Blood corticotrophin decreased	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Blood creatinine increased	0			0			1 (0.4)	2	0.8	1 (0.3)	2	0.5
Blood insulin decreased	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Blood insulin increased	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Blood phosphorus increased	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Blood potassium increased	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Blood pressure increased	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Blood testosterone increased	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Cardiac murmur	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Cholangiogram	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Creatinine renal clearance increased	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Electrocardiogram PR prolongation	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Electrocardiogram QT prolonged	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Electrocardiogram T wave abnormal	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Electrocardiogram T wave inversion	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Glomerular filtration rate decreased	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Heart rate increased	0			1 (0.8)	3	2.6	0			1 (0.3)	3	0.7
Hormone level abnormal	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Liver function test abnormal	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Lymph node palpable	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Normetanephrine urine increased	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Platelet count decreased	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Pulmonary function test decreased	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Thyroid hormones decreased	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Thyroxine decreased	0			0			1 (0.4)	3	1.1	1 (0.3)	3	0.7
Thyroxine increased	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Tri-iodothyronine decreased	0			1 (0.8)	2	1.7	0			1 (0.3)	2	0.5
Urine analysis abnormal	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Vitamin D decreased	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Weight decreased	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Respiratory, thoracic and mediastinal disorders	3 (7.3)	4	14.6	17 (14.0)	30	25.5	25 (10.9)	42	16.0	44 (13.8)	76	18.7
Cough	2 (4.9)	2	7.3	6 (5.0)	7	6.0	7 (3.0)	9	3.4	15 (4.7)	18	4.4
Oropharyngeal pain	2 (4.9)	2	7.3	2 (1.7)	2	1.7	9 (3.9)	9	3.4	12 (3.8)	13	3.2
Epistaxis	0			4 (3.3)	9	7.7	1 (0.4)	1	0.4	5 (1.6)	10	2.5
Rhinitis allergic	0			3 (2.5)	4	3.4	1 (0.4)	1	0.4	4 (1.3)	5	1.2
Sleep apnoea syndrome	0			1 (0.8)	1	0.9	3 (1.3)	3	1.1	4 (1.3)	4	1.0
Dyspnoea	0			3 (2.5)	3	2.6	1 (0.4)	1	0.4	3 (0.9)	4	1.0
Nasal congestion	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Sinus congestion	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Upper respiratory tract congestion	0			1 (0.8)	1	0.9	1 (0.4)	2	0.8	2 (0.6)	3	0.7
Upper-airway cough syndrome	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Dyspnoea exertional	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Increased viscosity of upper respiratory secretion	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Paranasal sinus hypersecretion	0			0			1 (0.4)	2	0.8	1 (0.3)	2	0.5
Pharyngeal erythema	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Pneumonia aspiration	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Respiratory disorder	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Respiratory tract congestion	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Rhinorrhoea	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Sinus polyp	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Sneezing	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Snoring	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Upper respiratory tract inflammation	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Metabolism and nutrition disorders	4 (9.8)	5	18.3	8 (6.6)	9	7.7	16 (7.0)	20	7.6	28 (8.8)	34	8.4
Iron deficiency	0			0			4 (1.7)	4	1.5	4 (1.3)	4	1.0
Diabetes mellitus	0			3 (2.5)	3	2.6	0			3 (0.9)	3	0.7
Gout	0			1 (0.8)	1	0.9	2 (0.9)	4	1.5	3 (0.9)	5	1.2
Vitamin D deficiency	0			1 (0.8)	1	0.9	2 (0.9)	2	0.8	3 (0.9)	3	0.7
Dehydration	1 (2.4)	1	3.7	0			1 (0.4)	1	0.4	2 (0.6)	2	0.5
Dyslipidaemia	0			2 (1.7)	2	1.7	0			2 (0.6)	2	0.5
Hyperkalaemia	1 (2.4)	1	3.7	1 (0.8)	1	0.9	0			2 (0.6)	2	0.5
Hyperlipidaemia	1 (2.4)	1	3.7	0			1 (0.4)	1	0.4	2 (0.6)	2	0.5
Hypokalaemia	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Decreased appetite	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Fluid retention	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Hyperglycaemia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Hypocalcaemia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Hypoglycaemia	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Hyponatraemia	1 (2.4)	2	7.3	0			0			1 (0.3)	2	0.5
Polydipsia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Vitamin B complex deficiency	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Psychiatric disorders	2 (4.9)	2	7.3	6 (5.0)	7	6.0	17 (7.4)	20	7.6	24 (7.5)	29	7.1
Insomnia	0			1 (0.8)	1	0.9	6 (2.6)	8	3.1	7 (2.2)	9	2.2
Sleep disorder	1 (2.4)	1	3.7	1 (0.8)	1	0.9	4 (1.7)	4	1.5	6 (1.9)	6	1.5
Anxiety	1 (2.4)	1	3.7	0			3 (1.3)	3	1.1	4 (1.3)	4	1.0

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MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Attention deficit/hyperactivity disorder	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Depression	0			2 (1.7)	2	1.7	0			2 (0.6)	2	0.5
Adjustment disorder with depressed mood	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Emotional disorder	0			0			1 (0.4)	2	0.8	1 (0.3)	2	0.5
Initial insomnia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Mood swings	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Nervousness	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Vascular disorders	1 (2.4)	1	3.7	8 (6.6)	9	7.7	12 (5.2)	12	4.6	20 (6.3)	22	5.4
Hypertension	1 (2.4)	1	3.7	7 (5.8)	7	6.0	8 (3.5)	8	3.1	16 (5.0)	16	3.9
Hot flush	0			1 (0.8)	1	0.9	2 (0.9)	2	0.8	3 (0.9)	3	0.7
Hypotension	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Orthostatic hypotension	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Vascular fragility	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Ear and labyrinth disorders	0			7 (5.8)	9	7.7	14 (6.1)	15	5.7	19 (6.0)	24	5.9
Ear pain	0			5 (4.1)	6	5.1	3 (1.3)	3	1.1	7 (2.2)	9	2.2
Vertigo	0			1 (0.8)	1	0.9	4 (1.7)	4	1.5	5 (1.6)	5	1.2
Tinnitus	0			1 (0.8)	1	0.9	2 (0.9)	2	0.8	3 (0.9)	3	0.7
Cerumen impaction	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Ear discomfort	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Ear disorder	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Eustachian tube dysfunction	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
External ear pain	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Middle ear inflammation	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Vertigo positional	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Eye disorders	2 (4.9)	2	7.3	8 (6.6)	11	9.4	10 (4.3)	12	4.6	19 (6.0)	25	6.2
Cataract	0			3 (2.5)	3	2.6	0			3 (0.9)	3	0.7
Dry eye	0			0			3 (1.3)	3	1.1	3 (0.9)	3	0.7
Vision blurred	1 (2.4)	1	3.7	1 (0.8)	1	0.9	1 (0.4)	1	0.4	3 (0.9)	3	0.7

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Glaucoma	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Visual impairment	0			2 (1.7)	2	1.7	0			2 (0.6)	2	0.5
Age-related macular degeneration	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Conjunctival haemorrhage	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Diplopia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Eye irritation	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Eye pruritus	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Eyelid disorder	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Eyelid oedema	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Neovascular age-related macular degeneration	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Ocular hyperaemia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Scleral disorder	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Visual acuity reduced	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Xerophthalmia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Endocrine disorders	2 (4.9)	2	7.3	5 (4.1)	5	4.3	10 (4.3)	11	4.2	17 (5.3)	18	4.4
Adrenocortical insufficiency acute	1 (2.4)	1	3.7	0			4 (1.7)	4	1.5	5 (1.6)	5	1.2
Hypothyroidism	1 (2.4)	1	3.7	3 (2.5)	3	2.6	1 (0.4)	1	0.4	5 (1.6)	5	1.2
Adrenal insufficiency	0			0			3 (1.3)	3	1.1	3 (0.9)	3	0.7
Secondary hypothyroidism	0			2 (1.7)	2	1.7	0			2 (0.6)	2	0.5
Diabetes insipidus	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Thyroid disorder	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Thyroid mass	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Renal and urinary disorders	1 (2.4)	1	3.7	9 (7.4)	11	9.4	6 (2.6)	7	2.7	16 (5.0)	19	4.7
Pollakiuria	0			2 (1.7)	2	1.7	1 (0.4)	1	0.4	3 (0.9)	3	0.7
Haematuria	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Nephrolithiasis	0			2 (1.7)	2	1.7	0			2 (0.6)	2	0.5
Nocturia	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Renal cyst	0			1 (0.8)	1	0.9	1 (0.4)	1	0.4	2 (0.6)	2	0.5
Bladder pain	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Calculus urinary	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2

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Dysuria	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Micturition disorder	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Polyuria	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Ureterolithiasis	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Urinary incontinence	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Urinary tract obstruction	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Blood and lymphatic system disorders	0			5 (4.1)	7	6.0	10 (4.3)	13	5.0	15 (4.7)	20	4.9
Anaemia	0			2 (1.7)	2	1.7	5 (2.2)	5	1.9	7 (2.2)	7	1.7
Lymphadenopathy	0			0			3 (1.3)	6	2.3	3 (0.9)	6	1.5
Haemoconcentration	0			2 (1.7)	3	2.6	0			2 (0.6)	3	0.7
Iron deficiency anaemia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Polycythaemia	0			1 (0.8)	2	1.7	0			1 (0.3)	2	0.5
Thrombocytopenia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Reproductive system and breast disorders	1 (2.4)	1	3.7	4 (3.3)	4	3.4	7 (3.0)	8	3.1	12 (3.8)	13	3.2
Dysmenorrhoea	1 (2.4)	1	3.7	1 (0.8)	1	0.9	0			2 (0.6)	2	0.5
Gynaecomastia	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Cervical dysplasia	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Menstruation delayed	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Menstruation irregular	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Nipple pain	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Prostatitis	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Uterine polyp	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Vaginal discharge	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Vaginal haemorrhage	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Vulvovaginal pruritus	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Immune system disorders	2 (4.9)	2	7.3	3 (2.5)	3	2.6	6 (2.6)	7	2.7	11 (3.5)	12	3.0
Seasonal allergy	1 (2.4)	1	3.7	1 (0.8)	1	0.9	5 (2.2)	6	2.3	7 (2.2)	8	2.0
Allergy to plants	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Allergy to vaccine	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Food allergy	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Multiple allergies	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			3 (2.5)	3	2.6	6 (2.6)	6	2.3	9 (2.8)	9	2.2
Pituitary tumour benign	0			0			2 (0.9)	2	0.8	2 (0.6)	2	0.5
Angiomyolipoma	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Basal cell carcinoma	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Bladder transitional cell carcinoma	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Intraductal papillary mucinous neoplasm	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Melanocytic naevus	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Pituitary tumour	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Plasma cell myeloma	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Cardiac disorders	0			3 (2.5)	4	3.4	4 (1.7)	7	2.7	7 (2.2)	11	2.7
Angina unstable	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Atrial flutter	0			1 (0.8)	2	1.7	0			1 (0.3)	2	0.5
Atrioventricular block first degree	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Bundle branch block right	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Cardiogenic shock	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Cardiomyopathy	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Palpitations	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Tachycardia	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Ventricular extrasystoles	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Ventricular fibrillation	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Surgical and medical procedures	1 (2.4)	1	3.7	2 (1.7)	2	1.7	4 (1.7)	6	2.3	7 (2.2)	9	2.2
Tooth extraction	1 (2.4)	1	3.7	1 (0.8)	1	0.9	1 (0.4)	1	0.4	3 (0.9)	3	0.7
Arterial stent insertion	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Cholecystectomy	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Dental care	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Dental operation	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - Adulthood onset - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Skin operation	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Umbilical hernia repair	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Hepatobiliary disorders	0			2 (1.7)	3	2.6	3 (1.3)	3	1.1	5 (1.6)	6	1.5
Biliary colic	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Cholelithiasis	0			1 (0.8)	2	1.7	0			1 (0.3)	2	0.5
Hepatic cirrhosis	0			1 (0.8)	1	0.9	0			1 (0.3)	1	0.2
Hepatomegaly	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Liver disorder	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Congenital, familial and genetic disorders	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Rathke's cleft cyst	0			0			1 (0.4)	1	0.4	1 (0.3)	1	0.2
Product issues	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2
Device malfunction	1 (2.4)	1	3.7	0			0			1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
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MedDRA version 21.0.

60 Adverse Events - age <65 - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	51			138			281			380		
Total patient years	33.3			137.2			323.9			494.5		
All adverse events	37 (72.5)	139	417.3	110 (79.7)	589	429.2	229 (81.5)	1212	374.2	320 (84.2)	1940	392.3
Serious adverse events	4 (7.8)	6	18.0	10 (7.2)	13	9.5	24 (8.5)	40	12.3	35 (9.2)	59	11.9
Medical events of special interest	0			0			0			0		
Severity												
Mild	33 (64.7)	110	330.2	96 (69.6)	388	282.7	207 (73.7)	912	281.5	288 (75.8)	1410	285.2
Moderate	14 (27.5)	25	75.1	52 (37.7)	192	139.9	85 (30.2)	263	81.2	137 (36.1)	480	97.1
Severe	2 (3.9)	4	12.0	7 (5.1)	9	6.6	21 (7.5)	37	11.4	29 (7.6)	50	10.1
Causality												
Unlikely	36 (70.6)	122	366.3	105 (76.1)	510	371.6	214 (76.2)	990	305.6	303 (79.7)	1622	328.0
Possible	8 (15.7)	12	36.0	28 (20.3)	58	42.3	55 (19.6)	164	50.6	86 (22.6)	234	47.3
Probable	3 (5.9)	5	15.0	13 (9.4)	21	15.3	33 (11.7)	58	17.9	47 (12.4)	84	17.0
Outcome												
Recovered/Resolved	35 (68.6)	128	384.3	103 (74.6)	487	354.9	211 (75.1)	1000	308.7	302 (79.5)	1615	326.6
Recovering/Resolving	0			8 (5.8)	10	7.3	18 (6.4)	26	8.0	26 (6.8)	36	7.3
Recovered/Resolved With Sequelae	1 (2.0)	1	3.0	2 (1.4)	3	2.2	3 (1.1)	3	0.9	5 (1.3)	7	1.4
Not Recovered/Not Resolved	10 (19.6)	10	30.0	44 (31.9)	85	61.9	91 (32.4)	182	56.2	136 (35.8)	277	56.0
Fatal	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Unknown	0			1 (0.7)	3	2.2	1 (0.4)	1	0.3	2 (0.5)	4	0.8
Action												

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Adverse Events - age <65 - safety analysis set

	placebo				Norditropin				somapacitan				total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Drug Interrupted	2	(3.9)	2	6.0	4	(2.9)	7	5.1	2	(0.7)	3	0.9	8	(2.1)	12	2.4
Drug Withdrawn	0				6	(4.3)	9	6.6	5	(1.8)	7	2.2	11	(2.9)	16	3.2
Dose Reduced	0				5	(3.6)	7	5.1	9	(3.2)	13	4.0	14	(3.7)	20	4.0
Dose Not Changed	37	(72.5)	134	402.3	107	(77.5)	549	400.0	227	(80.8)	1126	347.6	316	(83.2)	1809	365.8
Not Applicable	2	(3.9)	3	9.0	11	(8.0)	17	12.4	36	(12.8)	63	19.4	49	(12.9)	83	16.8
Treatment discontinuations due to adverse events	0				6	(4.3)	9	6.6	5	(1.8)	7	2.2	11	(2.9)	16	3.2

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
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61 Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	51			138			281			380		
Total patient years	33.3			137.2			323.9			494.5		
All adverse events	37 (72.5)	139	417.3	110 (79.7)	589	429.2	229 (81.5)	1212	374.2	320 (84.2)	1940	392.3
Infections and infestations	28 (54.9)	36	108.1	68 (49.3)	125	91.1	142 (50.5)	305	94.2	209 (55.0)	466	94.2
Nasopharyngitis	7 (13.7)	10	30.0	33 (23.9)	45	32.8	70 (24.9)	112	34.6	102 (26.8)	167	33.8
Upper respiratory tract infection	4 (7.8)	4	12.0	11 (8.0)	17	12.4	19 (6.8)	22	6.8	30 (7.9)	43	8.7
Gastroenteritis	2 (3.9)	2	6.0	3 (2.2)	4	2.9	17 (6.0)	21	6.5	22 (5.8)	27	5.5
Influenza	2 (3.9)	3	9.0	3 (2.2)	4	2.9	15 (5.3)	18	5.6	19 (5.0)	25	5.1
Sinusitis	2 (3.9)	3	9.0	3 (2.2)	3	2.2	8 (2.8)	10	3.1	13 (3.4)	16	3.2
Tonsillitis	1 (2.0)	1	3.0	4 (2.9)	5	3.6	8 (2.8)	8	2.5	13 (3.4)	14	2.8
Bronchitis	2 (3.9)	2	6.0	4 (2.9)	4	2.9	7 (2.5)	7	2.2	12 (3.2)	13	2.6
Urinary tract infection	1 (2.0)	1	3.0	1 (0.7)	1	0.7	9 (3.2)	10	3.1	11 (2.9)	12	2.4
Respiratory tract infection	2 (3.9)	2	6.0	3 (2.2)	4	2.9	3 (1.1)	4	1.2	8 (2.1)	10	2.0
Ear infection	1 (2.0)	1	3.0	2 (1.4)	2	1.5	4 (1.4)	7	2.2	7 (1.8)	10	2.0
Pharyngitis	0			4 (2.9)	6	4.4	2 (0.7)	2	0.6	6 (1.6)	8	1.6
Viral infection	0			0			6 (2.1)	6	1.9	6 (1.6)	6	1.2
Cystitis	2 (3.9)	2	6.0	0			3 (1.1)	4	1.2	5 (1.3)	6	1.2
Herpes zoster	1 (2.0)	1	3.0	0			4 (1.4)	9	2.8	5 (1.3)	10	2.0
Respiratory tract infection viral	0			3 (2.2)	3	2.2	2 (0.7)	2	0.6	5 (1.3)	5	1.0
Rhinitis	0			2 (1.4)	2	1.5	3 (1.1)	3	0.9	5 (1.3)	5	1.0
Tooth abscess	0			2 (1.4)	2	1.5	3 (1.1)	3	0.9	5 (1.3)	5	1.0
Fungal infection	0			1 (0.7)	1	0.7	3 (1.1)	3	0.9	4 (1.1)	4	0.8
Gastroenteritis viral	1 (2.0)	1	3.0	2 (1.4)	2	1.5	1 (0.4)	1	0.3	4 (1.1)	4	0.8
Gingivitis	0			1 (0.7)	1	0.7	3 (1.1)	3	0.9	4 (1.1)	4	0.8
Lower respiratory tract infection	0			0			4 (1.4)	4	1.2	4 (1.1)	4	0.8
Pharyngitis streptococcal	0			0			4 (1.4)	5	1.5	4 (1.1)	5	1.0
Viral upper respiratory tract infection	0			1 (0.7)	1	0.7	3 (1.1)	3	0.9	4 (1.1)	4	0.8
Cellulitis	0			2 (1.4)	2	1.5	1 (0.4)	1	0.3	3 (0.8)	3	0.6

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Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Oral herpes	0			0			3 (1.1)	4	1.2	3 (0.8)	4	0.8
Otitis media	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Pulpitis dental	0			3 (2.2)	3	2.2	0			3 (0.8)	3	0.6
Appendicitis	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Bronchitis viral	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Laryngitis	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Parotitis	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Periodontitis	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Tinea infection	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Tooth infection	0			2 (1.4)	3	2.2	0			2 (0.5)	3	0.6
Acarodermatitis	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Candida infection	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Conjunctivitis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Escherichia infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Folliculitis	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Herpes simplex	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Herpes virus infection	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Hordeolum	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Lung infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Meningitis viral	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Molluscum contagiosum	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Onychomycosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Oral candidiasis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Otitis externa	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Paronychia	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Periporitis staphylogenes	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pilonidal cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pneumonia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pneumonia viral	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pulmonary tuberculosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pyoderma	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Rotavirus infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Sepsis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Tinea capitis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Tinea pedis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Upper respiratory tract infection bacterial	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Vaginal infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Vulvovaginal candidiasis	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Vulvovaginal mycotic infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Wound infection	0			1 (0.7)	2	1.5	0			1 (0.3)	2	0.4
Gastrointestinal disorders	11 (21.6)	19	57.0	29 (21.0)	53	38.6	73 (26.0)	145	44.8	107 (28.2)	217	43.9
Diarrhoea	5 (9.8)	8	24.0	5 (3.6)	5	3.6	19 (6.8)	28	8.6	28 (7.4)	41	8.3
Vomiting	1 (2.0)	2	6.0	5 (3.6)	6	4.4	14 (5.0)	16	4.9	20 (5.3)	24	4.9
Abdominal pain	1 (2.0)	1	3.0	3 (2.2)	4	2.9	8 (2.8)	10	3.1	12 (3.2)	15	3.0
Nausea	1 (2.0)	1	3.0	5 (3.6)	7	5.1	7 (2.5)	16	4.9	12 (3.2)	24	4.9
Toothache	1 (2.0)	1	3.0	4 (2.9)	4	2.9	4 (1.4)	6	1.9	9 (2.4)	11	2.2
Abdominal pain upper	1 (2.0)	1	3.0	2 (1.4)	2	1.5	5 (1.8)	8	2.5	8 (2.1)	11	2.2
Dyspepsia	1 (2.0)	2	6.0	4 (2.9)	4	2.9	3 (1.1)	3	0.9	8 (2.1)	9	1.8
Dental caries	0			2 (1.4)	3	2.2	5 (1.8)	5	1.5	7 (1.8)	8	1.6
Gastrooesophageal reflux disease	1 (2.0)	1	3.0	1 (0.7)	1	0.7	3 (1.1)	3	0.9	5 (1.3)	5	1.0
Abdominal tenderness	0			3 (2.2)	3	2.2	1 (0.4)	1	0.3	4 (1.1)	4	0.8
Gastritis	0			0			4 (1.4)	5	1.5	4 (1.1)	5	1.0
Large intestine polyp	0			0			4 (1.4)	4	1.2	4 (1.1)	4	0.8
Stomatitis	0			1 (0.7)	1	0.7	3 (1.1)	6	1.9	4 (1.1)	7	1.4
Abdominal distension	0			0			3 (1.1)	4	1.2	3 (0.8)	4	0.8
Constipation	0			2 (1.4)	2	1.5	2 (0.7)	3	0.9	3 (0.8)	5	1.0
Food poisoning	1 (2.0)	1	3.0	1 (0.7)	1	0.7	1 (0.4)	1	0.3	3 (0.8)	3	0.6
Colitis	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Enteritis	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Epigastric discomfort	0			0			2 (0.7)	5	1.5	2 (0.5)	5	1.0
Flatulence	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Inguinal hernia	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Irritable bowel syndrome	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Pancreatitis acute	1 (2.0)	1	3.0	1 (0.7)	1	0.7	0			2 (0.5)	2	0.4

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Abdominal hernia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Abdominal pain lower	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Abdominal wall mass	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Barrett's oesophagus	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Chronic gastritis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Colitis ulcerative	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Dental cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Dry mouth	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Duodenal ulcer	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Faeces soft	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Gastric polyps	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Gastrointestinal disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hiatus hernia	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Lip swelling	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Mouth ulceration	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Oesophagitis	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Poor dental condition	0			0			1 (0.4)	2	0.6	1 (0.3)	2	0.4
Rectal polyp	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Retching	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Musculoskeletal and connective tissue disorders	8 (15.7)	10	30.0	34 (24.6)	58	42.3	69 (24.6)	109	33.6	106 (27.9)	177	35.8
Arthralgia	1 (2.0)	1	3.0	12 (8.7)	13	9.5	17 (6.0)	18	5.6	29 (7.6)	32	6.5
Back pain	1 (2.0)	1	3.0	6 (4.3)	8	5.8	16 (5.7)	18	5.6	23 (6.1)	27	5.5
Myalgia	2 (3.9)	2	6.0	8 (5.8)	8	5.8	7 (2.5)	9	2.8	17 (4.5)	19	3.8
Pain in extremity	1 (2.0)	1	3.0	6 (4.3)	8	5.8	5 (1.8)	5	1.5	12 (3.2)	14	2.8
Musculoskeletal pain	0			2 (1.4)	2	1.5	5 (1.8)	5	1.5	7 (1.8)	7	1.4
Muscle spasms	0			0			5 (1.8)	5	1.5	5 (1.3)	5	1.0
Neck pain	0			1 (0.7)	1	0.7	4 (1.4)	5	1.5	5 (1.3)	6	1.2
Muscular weakness	0			1 (0.7)	1	0.7	3 (1.1)	6	1.9	4 (1.1)	7	1.4
Musculoskeletal stiffness	0			1 (0.7)	1	0.7	3 (1.1)	3	0.9	4 (1.1)	4	0.8
Joint stiffness	0			1 (0.7)	1	0.7	2 (0.7)	2	0.6	3 (0.8)	3	0.6
Joint swelling	0			3 (2.2)	4	2.9	0			3 (0.8)	4	0.8

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Pain in jaw	0			1 (0.7)	1	0.7	2 (0.7)	3	0.9	3 (0.8)	4	0.8
Tendonitis	1 (2.0)	1	3.0	1 (0.7)	1	0.7	1 (0.4)	1	0.3	3 (0.8)	3	0.6
Bursitis	1 (2.0)	2	6.0	0			2 (0.7)	3	0.9	2 (0.5)	5	1.0
Intervertebral disc degeneration	0			0			2 (0.7)	3	0.9	2 (0.5)	3	0.6
Intervertebral disc protrusion	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Limb discomfort	0			1 (0.7)	1	0.7	1 (0.4)	2	0.6	2 (0.5)	3	0.6
Muscle twitching	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Osteoarthritis	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Rotator cuff syndrome	0			2 (1.4)	3	2.2	0			2 (0.5)	3	0.6
Tenosynovitis	1 (2.0)	1	3.0	0			1 (0.4)	1	0.3	2 (0.5)	2	0.4
Coccydynia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Costochondritis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Exostosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Fracture pain	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Joint effusion	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Joint noise	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Limb deformity	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Muscle disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Muscle tightness	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Musculoskeletal chest pain	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Myositis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Neck deformity	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Nodal osteoarthritis	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Osteoporosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Periarthritis	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Plantar fasciitis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Soft tissue disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Soft tissue mass	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Tendon pain	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Trigger finger	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Nervous system disorders	12 (23.5)	21	63.0	31 (22.5)	114	83.1	69 (24.6)	157	48.5	103 (27.1)	292	59.1
Headache	10 (19.6)	15	45.0	22 (15.9)	85	61.9	38 (13.5)	103	31.8	64 (16.8)	203	41.1

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Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Dizziness	0			6 (4.3)	8	5.8	13 (4.6)	17	5.2	18 (4.7)	25	5.1
Hypoaesthesia	0			5 (3.6)	6	4.4	4 (1.4)	5	1.5	9 (2.4)	11	2.2
Paraesthesia	1 (2.0)	1	3.0	1 (0.7)	1	0.7	4 (1.4)	5	1.5	6 (1.6)	7	1.4
Migraine	1 (2.0)	3	9.0	1 (0.7)	1	0.7	3 (1.1)	4	1.2	4 (1.1)	8	1.6
Somnolence	0			2 (1.4)	2	1.5	2 (0.7)	3	0.9	4 (1.1)	5	1.0
Intercostal neuralgia	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Sciatica	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Carpal tunnel syndrome	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Disturbance in attention	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Hypersomnia	0			0			2 (0.7)	3	0.9	2 (0.5)	3	0.6
Lethargy	1 (2.0)	1	3.0	0			1 (0.4)	1	0.3	2 (0.5)	2	0.4
Ataxia	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Burning sensation	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Depressed level of consciousness	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Dysgeusia	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Hydrocephalus	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hyposmia	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Memory impairment	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Meralgia paraesthetica	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Neuralgia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Parosmia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Partial seizures	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Seizure	0			1 (0.7)	3	2.2	0			1 (0.3)	3	0.6
Syncope	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Tremor	0			1 (0.7)	2	1.5	0			1 (0.3)	2	0.4
Vestibular migraine	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
General disorders and administration site conditions	7 (13.7)	11	33.0	30 (21.7)	51	37.2	64 (22.8)	106	32.7	95 (25.0)	168	34.0
Fatigue	1 (2.0)	1	3.0	9 (6.5)	9	6.6	19 (6.8)	23	7.1	29 (7.6)	33	6.7
Oedema peripheral	0			5 (3.6)	8	5.8	11 (3.9)	23	7.1	16 (4.2)	31	6.3
Asthenia	1 (2.0)	1	3.0	3 (2.2)	4	2.9	8 (2.8)	10	3.1	12 (3.2)	15	3.0
Pyrexia	0			1 (0.7)	2	1.5	8 (2.8)	10	3.1	9 (2.4)	12	2.4

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MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Malaise	1 (2.0)	1	3.0	2 (1.4)	2	1.5	4 (1.4)	4	1.2	7 (1.8)	7	1.4
Pain	0			2 (1.4)	2	1.5	5 (1.8)	6	1.9	7 (1.8)	8	1.6
Peripheral swelling	1 (2.0)	1	3.0	2 (1.4)	2	1.5	4 (1.4)	4	1.2	7 (1.8)	7	1.4
Chest pain	1 (2.0)	1	3.0	2 (1.4)	2	1.5	3 (1.1)	3	0.9	6 (1.6)	6	1.2
Influenza like illness	0			3 (2.2)	3	2.2	2 (0.7)	4	1.2	4 (1.1)	7	1.4
Injection site bruising	2 (3.9)	3	9.0	2 (1.4)	2	1.5	0			4 (1.1)	5	1.0
Injection site pain	1 (2.0)	1	3.0	1 (0.7)	1	0.7	2 (0.7)	3	0.9	4 (1.1)	5	1.0
Face oedema	1 (2.0)	1	3.0	1 (0.7)	1	0.7	2 (0.7)	2	0.6	3 (0.8)	4	0.8
Feeling hot	0			2 (1.4)	2	1.5	1 (0.4)	1	0.3	3 (0.8)	3	0.6
Non-cardiac chest pain	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Pre-existing condition improved	0			1 (0.7)	1	0.7	1 (0.4)	2	0.6	2 (0.5)	3	0.6
Thirst	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Axillary pain	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Chest discomfort	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Chills	0			1 (0.7)	2	1.5	0			1 (0.3)	2	0.4
Cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Fat tissue decreased	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Inflammatory pain	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Injection site atrophy	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Injection site haematoma	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Injection site haemorrhage	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Injection site reaction	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Nodule	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Oedema mucosal	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Retention cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Swelling	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Vaccination site pain	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Vessel puncture site bruise	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Skin and subcutaneous tissue disorders	12 (23.5)	16	48.0	20 (14.5)	25	18.2	41 (14.6)	57	17.6	69 (18.2)	98	19.8
Rash	2 (3.9)	2	6.0	8 (5.8)	10	7.3	6 (2.1)	6	1.9	16 (4.2)	18	3.6
Dry skin	2 (3.9)	2	6.0	0			4 (1.4)	4	1.2	6 (1.6)	6	1.2

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Pruritus	0			3 (2.2)	3	2.2	3 (1.1)	4	1.2	6 (1.6)	7	1.4
Urticaria	0			0			5 (1.8)	6	1.9	5 (1.3)	6	1.2
Acne	0			0			3 (1.1)	4	1.2	3 (0.8)	4	0.8
Alopecia	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Dermatitis atopic	0			1 (0.7)	1	0.7	2 (0.7)	2	0.6	3 (0.8)	3	0.6
Eczema	2 (3.9)	2	6.0	1 (0.7)	1	0.7	1 (0.4)	2	0.6	3 (0.8)	5	1.0
Rash generalised	0			2 (1.4)	2	1.5	1 (0.4)	1	0.3	3 (0.8)	3	0.6
Acanthosis	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Dermatitis	2 (3.9)	2	6.0	0			1 (0.4)	1	0.3	2 (0.5)	3	0.6
Dermatitis contact	1 (2.0)	1	3.0	1 (0.7)	1	0.7	0			2 (0.5)	2	0.4
Lipodystrophy acquired	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Lipohypertrophy	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Skin discolouration	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Asteatosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blister	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Dermal cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Dermatitis allergic	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ecchymosis	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Erythema	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Haemorrhage subcutaneous	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hair disorder	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Hyperkeratosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ingrowing nail	1 (2.0)	1	3.0	0			1 (0.4)	1	0.3	1 (0.3)	2	0.4
Miliaria	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Onychoclasis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Papule	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Prurigo	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Pruritus generalised	1 (2.0)	2	6.0	0			0			1 (0.3)	2	0.4
Pustular psoriasis	0			0			1 (0.4)	2	0.6	1 (0.3)	2	0.4
Rash erythematous	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Rash macular	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Rash maculo-papular	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Rash papular	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Skin burning sensation	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Skin erosion	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Skin lesion	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Skin mass	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Skin warm	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Swelling face	0			0			1 (0.4)	2	0.6	1 (0.3)	2	0.4
Investigations	5 (9.8)	6	18.0	20 (14.5)	36	26.2	39 (13.9)	81	25.0	59 (15.5)	123	24.9
Blood creatine phosphokinase increased	0			0			12 (4.3)	14	4.3	12 (3.2)	14	2.8
Weight increased	0			1 (0.7)	1	0.7	9 (3.2)	10	3.1	10 (2.6)	11	2.2
Blood testosterone decreased	0			3 (2.2)	3	2.2	3 (1.1)	3	0.9	6 (1.6)	6	1.2
Cortisol decreased	0			0			4 (1.4)	4	1.2	4 (1.1)	4	0.8
Glycosylated haemoglobin increased	0			1 (0.7)	2	1.5	3 (1.1)	4	1.2	4 (1.1)	6	1.2
Thyroxine free decreased	0			1 (0.7)	1	0.7	3 (1.1)	4	1.2	4 (1.1)	5	1.0
Alanine aminotransferase increased	0			1 (0.7)	1	0.7	2 (0.7)	2	0.6	3 (0.8)	3	0.6
Aspartate aminotransferase increased	0			0			3 (1.1)	4	1.2	3 (0.8)	4	0.8
Blood insulin increased	0			1 (0.7)	1	0.7	2 (0.7)	2	0.6	3 (0.8)	3	0.6
Blood uric acid increased	0			1 (0.7)	1	0.7	2 (0.7)	2	0.6	3 (0.8)	3	0.6
Gamma-glutamyltransferase increased	0			1 (0.7)	1	0.7	2 (0.7)	2	0.6	3 (0.8)	3	0.6
Blood alkaline phosphatase increased	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Blood glucose increased	0			1 (0.7)	3	2.2	1 (0.4)	1	0.3	2 (0.5)	4	0.8
Blood potassium decreased	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Blood thyroid stimulating hormone decreased	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Creatinine renal clearance decreased	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Haematocrit increased	1 (2.0)	1	3.0	0			1 (0.4)	1	0.3	2 (0.5)	2	0.4
Hepatic enzyme increased	1 (2.0)	1	3.0	0			1 (0.4)	1	0.3	2 (0.5)	2	0.4
Intraocular pressure increased	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Platelet count increased	0			1 (0.7)	2	1.5	1 (0.4)	1	0.3	2 (0.5)	3	0.6

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Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
White blood cell count increased	1 (2.0)	1	3.0	0			1 (0.4)	1	0.3	2 (0.5)	2	0.4
Blood alkaline phosphatase decreased	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Blood bilirubin increased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blood cholesterol increased	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Blood corticotrophin decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blood creatinine decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blood insulin decreased	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Blood phosphorus increased	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Blood potassium increased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blood pressure decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blood pressure increased	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Blood testosterone increased	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Body temperature increased	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Cortisol increased	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Electrocardiogram QT prolonged	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Electrocardiogram T wave abnormal	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Electrocardiogram T wave inversion	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Electrocardiogram abnormal	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Glomerular filtration rate decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Glomerular filtration rate increased	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Heart rate increased	0			1 (0.7)	3	2.2	0			1 (0.3)	3	0.6
Hormone level abnormal	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Liver function test abnormal	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Lymph node palpable	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Normetanephrine urine increased	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Platelet count decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pulmonary function test decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Thyroid hormones decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Thyroxine decreased	0			0			1 (0.4)	3	0.9	1 (0.3)	3	0.6
Thyroxine increased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Tri-iodothyronine decreased	0			1 (0.7)	2	1.5	0			1 (0.3)	2	0.4
Urine analysis abnormal	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Vitamin D decreased	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Weight decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Injury, poisoning and procedural complications	3 (5.9)	3	9.0	15 (10.9)	23	16.8	35 (12.5)	44	13.6	52 (13.7)	70	14.2
Contusion	1 (2.0)	1	3.0	3 (2.2)	5	3.6	3 (1.1)	4	1.2	7 (1.8)	10	2.0
Tooth fracture	1 (2.0)	1	3.0	2 (1.4)	2	1.5	2 (0.7)	2	0.6	5 (1.3)	5	1.0
Fall	0			2 (1.4)	2	1.5	2 (0.7)	2	0.6	4 (1.1)	4	0.8
Ligament sprain	0			1 (0.7)	1	0.7	3 (1.1)	3	0.9	4 (1.1)	4	0.8
Foot fracture	0			2 (1.4)	2	1.5	1 (0.4)	1	0.3	3 (0.8)	3	0.6
Head injury	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Arthropod bite	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Laceration	0			1 (0.7)	2	1.5	1 (0.4)	1	0.3	2 (0.5)	3	0.6
Limb injury	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Muscle strain	0			1 (0.7)	1	0.7	1 (0.4)	2	0.6	2 (0.5)	3	0.6
Spinal compression fracture	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Arthropod sting	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Bone contusion	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Concussion	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Corneal abrasion	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hand fracture	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Heat illness	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Incorrect dose administered	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ligament rupture	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Meniscus injury	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Multiple fractures	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Muscle injury	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Patella fracture	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Post procedural complication	0			0			1 (0.4)	2	0.6	1 (0.3)	2	0.4
Post-traumatic pain	0			0			1 (0.4)	3	0.9	1 (0.3)	3	0.6

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Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Prescription drug used without a prescription	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Procedural complication	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Procedural dizziness	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Procedural pain	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Radius fracture	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Scratch	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Spinal column injury	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Thermal burn	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Tibia fracture	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Toxicity to various agents	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Wound	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Wrist fracture	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Respiratory, thoracic and mediastinal disorders	3 (5.9)	4	12.0	15 (10.9)	25	18.2	24 (8.5)	38	11.7	41 (10.8)	67	13.5
Oropharyngeal pain	2 (3.9)	2	6.0	3 (2.2)	3	2.2	10 (3.6)	10	3.1	14 (3.7)	15	3.0
Cough	2 (3.9)	2	6.0	5 (3.6)	6	4.4	6 (2.1)	6	1.9	13 (3.4)	14	2.8
Epistaxis	0			3 (2.2)	5	3.6	1 (0.4)	1	0.3	4 (1.1)	6	1.2
Rhinitis allergic	0			3 (2.2)	4	2.9	1 (0.4)	1	0.3	4 (1.1)	5	1.0
Sleep apnoea syndrome	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Asthma	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Dyspnoea	0			2 (1.4)	2	1.5	1 (0.4)	1	0.3	2 (0.5)	3	0.6
Nasal congestion	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Sinus congestion	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Upper respiratory tract congestion	0			1 (0.7)	1	0.7	1 (0.4)	2	0.6	2 (0.5)	3	0.6
Dyspnoea exertional	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Dyspnoea paroxysmal nocturnal	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Increased viscosity of upper respiratory secretion	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Paranasal sinus hypersecretion	0			0			1 (0.4)	2	0.6	1 (0.3)	2	0.4
Pharyngeal erythema	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Respiratory disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Respiratory tract congestion	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Rhinorrhoea	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Sinus polyp	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Snoring	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Upper-airway cough syndrome	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Metabolism and nutrition disorders	2 (3.9)	3	9.0	7 (5.1)	7	5.1	23 (8.2)	28	8.6	32 (8.4)	38	7.7
Hypokalaemia	0			0			5 (1.8)	5	1.5	5 (1.3)	5	1.0
Iron deficiency	0			0			4 (1.4)	4	1.2	4 (1.1)	4	0.8
Hyperphosphataemia	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Hypocalcaemia	1 (2.0)	1	3.0	0			2 (0.7)	2	0.6	3 (0.8)	3	0.6
Vitamin D deficiency	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Diabetes mellitus	0			2 (1.4)	2	1.5	0			2 (0.5)	2	0.4
Dyslipidaemia	0			2 (1.4)	2	1.5	0			2 (0.5)	2	0.4
Fluid retention	0			0			2 (0.7)	3	0.9	2 (0.5)	3	0.6
Hypercholesterolaemia	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Decreased appetite	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Fat redistribution	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Gout	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Hyperlipidaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hypertriglyceridaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hypoglycaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hyponatraemia	1 (2.0)	2	6.0	0			0			1 (0.3)	2	0.4
Increased appetite	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Obesity	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Vitamin B complex deficiency	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Psychiatric disorders	1 (2.0)	1	3.0	6 (4.3)	7	5.1	18 (6.4)	24	7.4	25 (6.6)	32	6.5
Insomnia	0			1 (0.7)	1	0.7	5 (1.8)	7	2.2	6 (1.6)	8	1.6
Sleep disorder	1 (2.0)	1	3.0	1 (0.7)	1	0.7	3 (1.1)	3	0.9	5 (1.3)	5	1.0
Anxiety	0			0			4 (1.4)	7	2.2	4 (1.1)	7	1.4
Depression	0			2 (1.4)	2	1.5	1 (0.4)	1	0.3	3 (0.8)	3	0.6

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Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Attention deficit/hyperactivity disorder	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Adjustment disorder with depressed mood	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Delirium	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Emotional disorder	0			0			1 (0.4)	2	0.6	1 (0.3)	2	0.4
Initial insomnia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Mood swings	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Nervousness	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Vascular disorders	1 (2.0)	1	3.0	6 (4.3)	6	4.4	15 (5.3)	15	4.6	22 (5.8)	22	4.4
Hypertension	1 (2.0)	1	3.0	5 (3.6)	5	3.6	9 (3.2)	9	2.8	15 (3.9)	15	3.0
Hot flush	0			1 (0.7)	1	0.7	3 (1.1)	3	0.9	4 (1.1)	4	0.8
Hypotension	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Arteriosclerosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eye disorders	1 (2.0)	1	3.0	8 (5.8)	9	6.6	11 (3.9)	11	3.4	20 (5.3)	21	4.2
Visual impairment	0			4 (2.9)	4	2.9	0			4 (1.1)	4	0.8
Dry eye	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Vision blurred	1 (2.0)	1	3.0	1 (0.7)	1	0.7	1 (0.4)	1	0.3	3 (0.8)	3	0.6
Conjunctival haemorrhage	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Conjunctivitis allergic	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Diplopia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eye irritation	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eye swelling	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Eyelid disorder	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Eyelid oedema	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Glaucoma	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Ocular hyperaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Xerophthalmia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Endocrine disorders	1 (2.0)	1	3.0	7 (5.1)	8	5.8	12 (4.3)	13	4.0	19 (5.0)	22	4.4
Hypothyroidism	1 (2.0)	1	3.0	3 (2.2)	3	2.2	2 (0.7)	2	0.6	6 (1.6)	6	1.2

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Adrenal insufficiency	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Adrenocortical insufficiency acute	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Secondary hypothyroidism	0			3 (2.2)	3	2.2	0			3 (0.8)	3	0.6
Diabetes insipidus	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Glucocorticoid deficiency	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Hyperthyroidism	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hypopituitarism	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Secondary adrenocortical insufficiency	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Thyroid disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Thyroid mass	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ear and labyrinth disorders	0			7 (5.1)	9	6.6	13 (4.6)	14	4.3	18 (4.7)	23	4.7
Ear pain	0			5 (3.6)	6	4.4	3 (1.1)	3	0.9	7 (1.8)	9	1.8
Vertigo	0			1 (0.7)	1	0.7	4 (1.4)	4	1.2	5 (1.3)	5	1.0
Tinnitus	0			1 (0.7)	1	0.7	2 (0.7)	2	0.6	3 (0.8)	3	0.6
Cerumen impaction	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ear discomfort	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Ear disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eustachian tube dysfunction	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
External ear pain	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Vertigo positional	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blood and lymphatic system disorders	0			6 (4.3)	8	5.8	11 (3.9)	14	4.3	17 (4.5)	22	4.4
Anaemia	0			3 (2.2)	3	2.2	6 (2.1)	6	1.9	9 (2.4)	9	1.8
Lymphadenopathy	0			0			3 (1.1)	6	1.9	3 (0.8)	6	1.2
Haemoconcentration	0			2 (1.4)	3	2.2	0			2 (0.5)	3	0.6
Iron deficiency anaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Polycythaemia	0			1 (0.7)	2	1.5	0			1 (0.3)	2	0.4
Thrombocytopenia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Reproductive system and breast disorders	2 (3.9)	2	6.0	4 (2.9)	4	2.9	11 (3.9)	12	3.7	17 (4.5)	18	3.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
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MedDRA version 21.0.

Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Dysmenorrhoea	2 (3.9)	2	6.0	1 (0.7)	1	0.7	2 (0.7)	2	0.6	5 (1.3)	5	1.0
Gynaecomastia	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Menstruation irregular	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Breast disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Cervical dysplasia	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Menstruation delayed	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Nipple pain	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Prostatitis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Uterine polyp	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Vaginal discharge	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Vaginal haemorrhage	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Vulvovaginal pruritus	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Cardiac disorders	1 (2.0)	1	3.0	3 (2.2)	3	2.2	9 (3.2)	14	4.3	13 (3.4)	18	3.6
Tachycardia	0			0			3 (1.1)	3	0.9	3 (0.8)	3	0.6
Atrioventricular block first degree	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Palpitations	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Aortic valve incompetence	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Bradycardia	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Bundle branch block right	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Cardiac discomfort	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Cardiomyopathy	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Cardiovascular disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Left ventricular dysfunction	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Mitral valve incompetence	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Myocardial ischaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Sinus arrhythmia	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Ventricular extrasystoles	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Renal and urinary disorders	0			8 (5.8)	9	6.6	5 (1.8)	6	1.9	13 (3.4)	15	3.0
Dysuria	0			1 (0.7)	1	0.7	1 (0.4)	2	0.6	2 (0.5)	3	0.6
Nephrolithiasis	0			2 (1.4)	2	1.5	0			2 (0.5)	2	0.4
Pollakiuria	0			2 (1.4)	2	1.5	0			2 (0.5)	2	0.4

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Calculus urinary	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Chronic kidney disease	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Haematuria	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Micturition disorder	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Nocturia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Renal cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ureterolithiasis	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Urinary incontinence	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Immune system disorders	1 (2.0)	1	3.0	3 (2.2)	3	2.2	7 (2.5)	8	2.5	11 (2.9)	12	2.4
Seasonal allergy	0			1 (0.7)	1	0.7	6 (2.1)	7	2.2	7 (1.8)	8	1.6
Allergy to plants	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Allergy to vaccine	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Food allergy	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Multiple allergies	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hepatobiliary disorders	0			1 (0.7)	2	1.5	4 (1.4)	4	1.2	5 (1.3)	6	1.2
Cholelithiasis	0			1 (0.7)	2	1.5	1 (0.4)	1	0.3	2 (0.5)	3	0.6
Biliary colic	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hepatic steatosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hepatomegaly	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			2 (1.4)	3	2.2	3 (1.1)	3	0.9	5 (1.3)	6	1.2
Lipoma	0			1 (0.7)	1	0.7	1 (0.4)	1	0.3	2 (0.5)	2	0.4
Intraductal papillary mucinous neoplasm	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Melanocytic naevus	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Pituitary tumour	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Soft tissue neoplasm	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Surgical and medical procedures	1 (2.0)	1	3.0	1 (0.7)	1	0.7	2 (0.7)	2	0.6	4 (1.1)	4	0.8
Tooth extraction	1 (2.0)	1	3.0	0			1 (0.4)	1	0.3	2 (0.5)	2	0.4

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
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MedDRA version 21.0.

Adverse events by system organ class and preferred term - age <65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Mammoplasty	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Skin operation	0			1 (0.7)	1	0.7	0			1 (0.3)	1	0.2
Congenital, familial and genetic disorders	0			0			2 (0.7)	2	0.6	2 (0.5)	2	0.4
Myotonia congenita	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Rathke's cleft cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Product issues	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2
Device malfunction	1 (2.0)	1	3.0	0			0			1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

62 Adverse Events - age >=65 - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	10			28			52			74		
Total patient years	6.5			23.8			53.9			84.2		
All adverse events	9 (90.0)	43	658.5	20 (71.4)	150	630.2	46 (88.5)	211	391.5	62 (83.8)	404	479.6
Serious adverse events	1 (10.0)	1	15.3	6 (21.4)	9	37.8	5 (9.6)	10	18.6	12 (16.2)	20	23.7
Medical events of special interest	0			0			0			0		
Severity												
Mild	8 (80.0)	34	520.7	19 (67.9)	111	466.3	43 (82.7)	169	313.5	59 (79.7)	314	372.8
Moderate	3 (30.0)	7	107.2	11 (39.3)	29	121.8	14 (26.9)	32	59.4	24 (32.4)	68	80.7
Severe	2 (20.0)	2	30.6	5 (17.9)	10	42.0	5 (9.6)	10	18.6	12 (16.2)	22	26.1
Causality												
Unlikely	9 (90.0)	41	627.9	20 (71.4)	119	499.9	43 (82.7)	186	345.1	59 (79.7)	346	410.8
Possible	1 (10.0)	1	15.3	6 (21.4)	10	42.0	10 (19.2)	16	29.7	15 (20.3)	27	32.1
Probable	1 (10.0)	1	15.3	7 (25.0)	21	88.2	4 (7.7)	9	16.7	10 (13.5)	31	36.8
Outcome												
Recovered/Resolved	8 (80.0)	32	490.1	18 (64.3)	107	449.5	43 (82.7)	169	313.5	57 (77.0)	308	365.7
Recovering/Resolving	1 (10.0)	2	30.6	5 (17.9)	9	37.8	7 (13.5)	8	14.8	13 (17.6)	19	22.6
Recovered/Resolved With Sequelae	0			2 (7.1)	2	8.4	0			2 (2.7)	2	2.4
Not Recovered/Not Resolved	3 (30.0)	8	122.5	14 (50.0)	31	130.2	17 (32.7)	30	55.7	29 (39.2)	69	81.9
Fatal	1 (10.0)	1	15.3	1 (3.6)	1	4.2	2 (3.8)	4	7.4	4 (5.4)	6	7.1

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Adverse Events - age >=65 - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Action												
Drug Interrupted	1	(10.0)	3 45.9	2	(7.1)	3 12.6	1	(1.9)	3 5.6	4	(5.4)	9 10.7
Drug Withdrawn	1	(10.0)	1 15.3	0			1	(1.9)	1 1.9	2	(2.7)	2 2.4
Dose Reduced	0			0			1	(1.9)	1 1.9	1	(1.4)	1 1.2
Dose Not Changed	8	(80.0)	36 551.3	19	(67.9)	140 588.2	46	(88.5)	201 372.9	60	(81.1)	377 447.6
Not Applicable	1	(10.0)	3 45.9	4	(14.3)	7 29.4	2	(3.8)	5 9.3	7	(9.5)	15 17.8
Treatment discontinuations due to adverse events*	1	(10.0)	1 15.3	1	(3.6)	1 4.2	1	(1.9)	1 1.9	3	(4.1)	3 3.6

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
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AE causality is based on judgement of investigators.
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*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

63 Adverse events by system organ class and preferred term - age >=65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	10			28			52			74		
Total patient years	6.5			23.8			53.9			84.2		
All adverse events	9 (90.0)	43	658.5	20 (71.4)	150	630.2	46 (88.5)	211	391.5	62 (83.8)	404	479.6
Infections and infestations	8 (80.0)	14	214.4	15 (53.6)	33	138.6	29 (55.8)	48	89.1	45 (60.8)	95	112.8
Nasopharyngitis	2 (20.0)	2	30.6	5 (17.9)	8	33.6	14 (26.9)	17	31.5	19 (25.7)	27	32.1
Upper respiratory tract infection	3 (30.0)	3	45.9	2 (7.1)	2	8.4	3 (5.8)	3	5.6	7 (9.5)	8	9.5
Urinary tract infection	0			2 (7.1)	3	12.6	5 (9.6)	10	18.6	6 (8.1)	13	15.4
Influenza	0			0			3 (5.8)	3	5.6	3 (4.1)	3	3.6
Bronchitis	1 (10.0)	1	15.3	0			1 (1.9)	1	1.9	2 (2.7)	2	2.4
Clostridium difficile infection	0			1 (3.6)	1	4.2	1 (1.9)	1	1.9	2 (2.7)	2	2.4
Gastroenteritis viral	1 (10.0)	1	15.3	0			1 (1.9)	1	1.9	2 (2.7)	2	2.4
Herpes zoster	0			2 (7.1)	2	8.4	0			2 (2.7)	2	2.4
Hordeolum	0			1 (3.6)	1	4.2	1 (1.9)	1	1.9	2 (2.7)	2	2.4
Lower respiratory tract infection	0			1 (3.6)	2	8.4	1 (1.9)	1	1.9	2 (2.7)	3	3.6
Pharyngitis	1 (10.0)	1	15.3	0			1 (1.9)	1	1.9	2 (2.7)	2	2.4
Sinusitis	1 (10.0)	3	45.9	1 (3.6)	1	4.2	1 (1.9)	1	1.9	2 (2.7)	5	5.9
Abscess	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Conjunctivitis	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Device related sepsis	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Diverticulitis	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Eye infection	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Fungal infection	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Gastrointestinal infection	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Helicobacter infection	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Ophthalmic herpes zoster	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Oral herpes	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Periodontitis	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Pneumonia	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Pneumonia bacterial	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2

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Adverse events by system organ class and preferred term - age >=65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Post procedural infection	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Respiratory tract infection viral	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Rhinitis	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Tinea cruris	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Tooth abscess	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Tooth infection	0			0			1 (1.9)	2	3.7	1 (1.4)	2	2.4
Urosepsis	0			1 (3.6)	2	8.4	0			1 (1.4)	2	2.4
Viral infection	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Viral upper respiratory tract infection	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Gastrointestinal disorders	2 (20.0)	5	76.6	9 (32.1)	14	58.8	17 (32.7)	26	48.2	26 (35.1)	45	53.4
Diarrhoea	0			3 (10.7)	3	12.6	2 (3.8)	3	5.6	5 (6.8)	6	7.1
Abdominal discomfort	1 (10.0)	1	15.3	1 (3.6)	1	4.2	1 (1.9)	1	1.9	3 (4.1)	3	3.6
Nausea	0			1 (3.6)	1	4.2	2 (3.8)	2	3.7	3 (4.1)	3	3.6
Abdominal pain	0			0			2 (3.8)	3	5.6	2 (2.7)	3	3.6
Constipation	0			1 (3.6)	1	4.2	1 (1.9)	1	1.9	2 (2.7)	2	2.4
Dental caries	0			1 (3.6)	1	4.2	1 (1.9)	1	1.9	2 (2.7)	2	2.4
Gastritis	1 (10.0)	1	15.3	0			1 (1.9)	1	1.9	2 (2.7)	2	2.4
Toothache	0			0			2 (3.8)	3	5.6	2 (2.7)	3	3.6
Vomiting	0			1 (3.6)	2	8.4	1 (1.9)	2	3.7	2 (2.7)	4	4.7
Abdominal pain upper	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Ascites	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Dry mouth	0			0			1 (1.9)	2	3.7	1 (1.4)	2	2.4
Dyspepsia	0			0			1 (1.9)	2	3.7	1 (1.4)	2	2.4
Faeces discoloured	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Gastric polyps	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Gastrooesophageal reflux disease	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Haemorrhoids	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Hiatus hernia	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Intestinal ischaemia	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Lip swelling	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Oesophagitis ulcerative	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - age >=65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Reflux gastritis	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Short-bowel syndrome	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Spigelian hernia	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Musculoskeletal and connective tissue disorders	2 (20.0)	4	61.3	11 (39.3)	20	84.0	16 (30.8)	23	42.7	24 (32.4)	47	55.8
Arthralgia	0			5 (17.9)	5	21.0	6 (11.5)	7	13.0	11 (14.9)	12	14.2
Back pain	1 (10.0)	1	15.3	0			5 (9.6)	5	9.3	6 (8.1)	6	7.1
Osteoarthritis	0			3 (10.7)	4	16.8	1 (1.9)	1	1.9	4 (5.4)	5	5.9
Arthritis	0			1 (3.6)	1	4.2	2 (3.8)	2	3.7	3 (4.1)	3	3.6
Muscle spasms	1 (10.0)	2	30.6	0			2 (3.8)	2	3.7	3 (4.1)	4	4.7
Joint stiffness	0			2 (7.1)	2	8.4	0			2 (2.7)	2	2.4
Musculoskeletal chest pain	0			2 (7.1)	2	8.4	0			2 (2.7)	2	2.4
Pain in extremity	0			0			2 (3.8)	2	3.7	2 (2.7)	2	2.4
Bursitis	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Foot deformity	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Groin pain	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Joint swelling	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Lumbar spinal stenosis	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Musculoskeletal stiffness	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Myalgia	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Rheumatoid arthritis	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Spinal pain	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Tenosynovitis	0			1 (3.6)	2	8.4	0			1 (1.4)	2	2.4
General disorders and administration site conditions	2 (20.0)	2	30.6	11 (39.3)	14	58.8	10 (19.2)	18	33.4	19 (25.7)	34	40.4
Fatigue	1 (10.0)	1	15.3	4 (14.3)	4	16.8	0			5 (6.8)	5	5.9
Injection site bruising	0			4 (14.3)	4	16.8	1 (1.9)	1	1.9	5 (6.8)	5	5.9
Pyrexia	0			0			3 (5.8)	3	5.6	3 (4.1)	3	3.6
Asthenia	0			1 (3.6)	1	4.2	1 (1.9)	1	1.9	2 (2.7)	2	2.4
Oedema peripheral	0			1 (3.6)	1	4.2	1 (1.9)	1	1.9	2 (2.7)	2	2.4
Chest pain	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2

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Adverse events by system organ class and preferred term - age >=65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Death	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Face oedema	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Fat tissue decreased	0			0			1 (1.9)	3	5.6	1 (1.4)	3	3.6
Gait disturbance	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Hunger	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Injection site hypertrophy	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Injection site reaction	0			0			1 (1.9)	3	5.6	1 (1.4)	3	3.6
Malaise	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Nodule	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Oedema	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Pain	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Peripheral swelling	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Nervous system disorders	2 (20.0)	5	76.6	4 (14.3)	5	21.0	10 (19.2)	12	22.3	16 (21.6)	22	26.1
Dizziness	1 (10.0)	1	15.3	3 (10.7)	4	16.8	1 (1.9)	1	1.9	5 (6.8)	6	7.1
Headache	0			0			5 (9.6)	6	11.1	5 (6.8)	6	7.1
Hypoaesthesia	1 (10.0)	1	15.3	0			2 (3.8)	2	3.7	3 (4.1)	3	3.6
Paraesthesia	1 (10.0)	1	15.3	0			1 (1.9)	1	1.9	2 (2.7)	2	2.4
Sciatica	0			0			2 (3.8)	2	3.7	2 (2.7)	2	2.4
Dysgeusia	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Syncope	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Tremor	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Injury, poisoning and procedural complications	0			7 (25.0)	8	33.6	10 (19.2)	15	27.8	14 (18.9)	23	27.3
Fall	0			1 (3.6)	2	8.4	3 (5.8)	4	7.4	4 (5.4)	6	7.1
Chest injury	0			0			2 (3.8)	2	3.7	2 (2.7)	2	2.4
Contusion	0			2 (7.1)	2	8.4	0			2 (2.7)	2	2.4
Animal bite	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Arthropod bite	0			1 (3.6)	1	4.2	1 (1.9)	1	1.9	1 (1.4)	2	2.4
Arthropod sting	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Drug dispensing error	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Head injury	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2

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Adverse events by system organ class and preferred term - age >=65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Meniscus injury	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Muscle strain	0			0			1 (1.9)	2	3.7	1 (1.4)	2	2.4
Post procedural complication	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Procedural pain	0			0			1 (1.9)	2	3.7	1 (1.4)	2	2.4
Tooth fracture	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Skin and subcutaneous tissue disorders	0			7 (25.0)	13	54.6	7 (13.5)	9	16.7	13 (17.6)	22	26.1
Dry skin	0			0			2 (3.8)	2	3.7	2 (2.7)	2	2.4
Miliaria	0			1 (3.6)	1	4.2	1 (1.9)	1	1.9	2 (2.7)	2	2.4
Rash	0			2 (7.1)	2	8.4	0			2 (2.7)	2	2.4
Urticaria	0			2 (7.1)	2	8.4	0			2 (2.7)	2	2.4
Dermatitis	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Dermatitis contact	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Drug eruption	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Ecchymosis	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Eczema	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Eczema asteatotic	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Exfoliative rash	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Haemorrhage subcutaneous	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Hyperkeratosis	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Onychoclasis	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Pruritus	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Skin hyperpigmentation	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Skin ulcer	0			1 (3.6)	2	8.4	0			1 (1.4)	2	2.4
Investigations	2 (20.0)	4	61.3	6 (21.4)	11	46.2	4 (7.7)	9	16.7	11 (14.9)	24	28.5
Alanine aminotransferase increased	1 (10.0)	1	15.3	1 (3.6)	1	4.2	1 (1.9)	1	1.9	2 (2.7)	3	3.6
Creatinine renal clearance decreased	0			1 (3.6)	1	4.2	1 (1.9)	1	1.9	2 (2.7)	2	2.4
Aspartate aminotransferase increased	1 (10.0)	1	15.3	0			1 (1.9)	1	1.9	1 (1.4)	2	2.4
Blood calcium decreased	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2

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Adverse events by system organ class and preferred term - age >=65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Blood creatinine increased	0			0			1 (1.9)	2	3.7	1 (1.4)	2	2.4
Blood potassium decreased	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Blood thyroid stimulating hormone decreased	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Blood uric acid increased	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Cardiac murmur	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Cholangiogram	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Creatinine renal clearance increased	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Electrocardiogram PR prolongation	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Gamma-glutamyltransferase increased	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Hepatic enzyme increased	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Intraocular pressure increased	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Liver function test abnormal	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Thyroxine free decreased	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Weight decreased	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Weight increased	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Respiratory, thoracic and mediastinal disorders	1 (10.0)	1	15.3	4 (14.3)	7	29.4	6 (11.5)	10	18.6	11 (14.9)	18	21.4
Cough	1 (10.0)	1	15.3	1 (3.6)	1	4.2	2 (3.8)	4	7.4	4 (5.4)	6	7.1
Dyspnoea	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Epistaxis	0			1 (3.6)	4	16.8	0			1 (1.4)	4	4.7
Oropharyngeal pain	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Pneumonia aspiration	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Rhinitis allergic	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Sleep apnoea syndrome	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Sneezing	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Upper respiratory tract inflammation	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Upper-airway cough syndrome	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Metabolism and nutrition disorders	3 (30.0)	3	45.9	3 (10.7)	4	16.8	4 (7.7)	7	13.0	10 (13.5)	14	16.6

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Adverse events by system organ class and preferred term - age >=65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Dehydration	1 (10.0)	1	15.3	0			1 (1.9)	1	1.9	2 (2.7)	2	2.4
Gout	0			0			2 (3.8)	4	7.4	2 (2.7)	4	4.7
Hyperkalaemia	1 (10.0)	1	15.3	1 (3.6)	1	4.2	0			2 (2.7)	2	2.4
Diabetes mellitus	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Hyperglycaemia	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Hyperlipidaemia	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Hypoglycaemia	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Polydipsia	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Vitamin D deficiency	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Eye disorders	1 (10.0)	1	15.3	3 (10.7)	5	21.0	3 (5.8)	5	9.3	6 (8.1)	11	13.1
Cataract	0			3 (10.7)	3	12.6	0			3 (4.1)	3	3.6
Age-related macular degeneration	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Dry eye	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Eye pruritus	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Glaucoma	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Neovascular age-related macular degeneration	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Scleral disorder	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Vision blurred	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Visual acuity reduced	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			2 (7.1)	2	8.4	4 (7.7)	4	7.4	6 (8.1)	6	7.1
Pituitary tumour benign	0			0			2 (3.8)	2	3.7	2 (2.7)	2	2.4
Angiomyolipoma	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Basal cell carcinoma	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Bladder transitional cell carcinoma	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Plasma cell myeloma	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Endocrine disorders	1 (10.0)	1	15.3	2 (7.1)	2	8.4	2 (3.8)	2	3.7	5 (6.8)	5	5.9
Adrenocortical insufficiency acute	1 (10.0)	1	15.3	0			1 (1.9)	1	1.9	2 (2.7)	2	2.4
Adrenal insufficiency	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2

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Adverse events by system organ class and preferred term - age >=65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hypothyroidism	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Secondary hypothyroidism	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Renal and urinary disorders	1 (10.0)	1	15.3	2 (7.1)	3	12.6	2 (3.8)	3	5.6	5 (6.8)	7	8.3
Bladder pain	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Haematuria	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Nocturia	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Pollakiuria	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Polyuria	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Renal cyst	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Urinary tract obstruction	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Hepatobiliary disorders	0			1 (3.6)	1	4.2	3 (5.8)	3	5.6	4 (5.4)	4	4.7
Biliary colic	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Cholelithiasis	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Hepatic cirrhosis	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Liver disorder	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Psychiatric disorders	1 (10.0)	1	15.3	0			4 (7.7)	4	7.4	4 (5.4)	5	5.9
Insomnia	0			0			2 (3.8)	2	3.7	2 (2.7)	2	2.4
Sleep disorder	0			0			2 (3.8)	2	3.7	2 (2.7)	2	2.4
Anxiety	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Surgical and medical procedures	0			1 (3.6)	1	4.2	3 (5.8)	5	9.3	4 (5.4)	6	7.1
Arterial stent insertion	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Cholecystectomy	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Dental care	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Dental operation	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Tooth extraction	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Umbilical hernia repair	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Cardiac disorders	0			2 (7.1)	3	12.6	1 (1.9)	3	5.6	3 (4.1)	6	7.1
Angina unstable	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - age >=65 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Atrial flutter	0			1 (3.6)	2	8.4	0			1 (1.4)	2	2.4
Cardiogenic shock	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Palpitations	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Ventricular fibrillation	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Ear and labyrinth disorders	0			1 (3.6)	1	4.2	2 (3.8)	2	3.7	3 (4.1)	3	3.6
Vertigo	0			1 (3.6)	1	4.2	1 (1.9)	1	1.9	2 (2.7)	2	2.4
Middle ear inflammation	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Vascular disorders	0			2 (7.1)	3	12.6	2 (3.8)	2	3.7	3 (4.1)	5	5.9
Hypertension	0			2 (7.1)	2	8.4	1 (1.9)	1	1.9	3 (4.1)	3	3.6
Orthostatic hypotension	0			1 (3.6)	1	4.2	0			1 (1.4)	1	1.2
Vascular fragility	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Blood and lymphatic system disorders	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Anaemia	0			0			1 (1.9)	1	1.9	1 (1.4)	1	1.2
Immune system disorders	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2
Seasonal allergy	1 (10.0)	1	15.3	0			0			1 (1.4)	1	1.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

64 Adverse events - Neoplasms benign, malignant and unspecified (including cysts and polyps) - 4043 - listing - safety analysis set

There is no data to display

65 Adverse events - Neoplasms benign, malignant and unspecified (including cysts and polyps) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
placebo/ somapacitan/ 204008	M/52/29.2	12	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Pituitary tumour/ ENLARGEMENT OF THE RESIDUAL PITUITARY TUMOR	2016-11-29	558/ extension/ -	N	N/N	MILD/ UNLIKELY/ UNLIKELY	DRUG WITHDRAWN
placebo/ somapacitan/ 251002	M/29/17.9	2	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Lipoma/ ABDOMINAL LIPOMA IN LEFT UMBILICAL REGION	2016-12-27 T10:20	334/ extension/ -	N	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
Norditropin/ Norditropin/ 101002	F/62/27.8	4	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Melanocytic naevus/ WORSENING OF MELANOCYTIC NEVI OF THE TRUNK	2016-02-18	109/ main/ 1	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
Norditropin/ Norditropin/ 128001	F/46/36.4	10	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Soft tissue neoplasm/ SOFT TISSUE NODULE OVER LEFT SUPRACLAVICULAR REGION	2016-11-23 T16:00	451/ extension/ -	N	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

Adverse events - Neoplasms benign, malignant and unspecified (including cysts and polyps) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ Norditropin/ 128001	F/46/36.4	8	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Lipoma/ INCREASED SIZE OF LIPOMA	2016-06-25 T11:00	300/ extension/ -	N	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
Norditropin/ Norditropin/ 605009	F/76/30.8	5	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Angiomyolipoma/ ANGIOMYOLIPOMA NOTED ON CT ABDOMEN	2016-11-14	197/ main/ -	N	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
Norditropin/ somapacitan/ 116006	M/73/39.9	10	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Pituitary tumour benign/ INTERVAL INCREASE 78% IN SIZE OF RESIDUAL PITUITARY ADENOMA	2016-08-18	298/ extension/ 64	Y	N/N	MODERATE/ UNLIKELY/ POSSIBLE	DRUG WITHDRAWN
Norditropin/ somapacitan/ 211004	M/68/23.3	2	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Plasma cell myeloma/ MULTIPLE MYELOMA	2016-04-27 T10:30	146/ main/ -	N	Y/N	SEVERE/ UNLIKELY/ UNLIKELY	DRUG WITHDRAWN

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

Adverse events - Neoplasms benign, malignant and unspecified (including cysts and polyps) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ somapacitan/ 603005	M/72/27.8	5	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Bladder transitional cell carcinoma/ BLADDER TUMOUR - HIGH GRADE PAPILLARY UROTHELIAL CARCINOMA	2016-12-23	564/ extension/ -	N	Y/N	SEVERE/ POSSIBLE/ POSSIBLE	DOSE NOT CHANGED
Norditropin/ somapacitan/ 853002	F/66/28.3	13	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Basal cell carcinoma/ BASALIOMA GRADE IA ACCORDING TO BIOPSY	2017-03-27	405/ extension/ 212	Y	N/N	MODERATE/ POSSIBLE/ POSSIBLE	DOSE NOT CHANGED

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

66 Adverse events - Neoplasms benign, malignant and unspecified (including cysts and polyps) - 4244 - listing - safety analysis set

Treatment group/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	Syatem Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality	Action Taken
somapacitan/ 101001	M/67.4/23.6	3	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Pituitary tumour benign/ REGROUTH OF PITUITARY ADENOMA	2017-11-08	195/-	N	N/	MODERATE/ UNLIKELY	DOSE NOT CHANGED
somapacitan/ 106004	F/62.4/21.3	3	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Intraductal papillary mucinous neoplasm/ INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM	2018-08-17	362/-	N	N/	MILD/ UNLIKELY	NOT APPLICABLE

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

67 Adverse events - Cardiac and vascular investigations incl. arrhythmia - 4043 - listing - safety analysis set

Treatment group/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	Syatem Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality	Action Taken
Norditropin/ 103007	M/72/27.7	3	Cardiac disorders/ Atrial flutter/ ATRIAL FLUTTER	2015-07-23	63/3	Y	N/N	MODERATE/ UNLIKELY	DOSE NOT CHANGED
		8	Cardiac disorders/ Atrial flutter/ ATRIAL FLUTTER	2015-10-06	138/4	Y	N/N	MODERATE/ UNLIKELY	DOSE NOT CHANGED

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

68 Adverse events - Cardiac and vascular investigations incl. arrhythmia - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
placebo/ somapacitan/ 110003	F/26/21.6	3	Cardiac disorders/ Atrioventricular block first degree/ PROLONGED PR INTERVAL ON ECG INTERPRETED AS FIRST DEGREE AV BLOCK	2017-04-12 T10:32	619/ extension/ 14	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
placebo/ somapacitan/ 126018	F/38/43.6	6	Cardiac disorders/ Tachycardia/ TACHYCARDIA HR 100	2016-09-19	274/ extension/ 191	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
placebo/ somapacitan/ 204008	M/52/29.2	1	Investigations/ Electrocardiogram T wave abnormal/ ELECTROCARDIOGRAM T WAVE ABNORMAL	2015-11-13	176/ main/ 63	Y	Y/N	MILD/ UNLIKELY/ -	DRUG INTERRUPTED
placebo/ somapacitan/ 351005	M/38/21.0	2	Cardiac disorders/ Sinus arrhythmia/ SINUS ARRTHMIA	2016-01-17 T08:51	191/ main/ 56	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
placebo/ somapacitan/ 601003	M/66/32.4	6	Cardiac disorders/ Ventricular fibrillation/ VENTRICULAR FIBRILLATION	2016-03-13 T21:00	363/ extension/ 12	N	Y/N	SEVERE/ UNLIKELY/ UNLIKELY	DRUG INTERRUPTED
somapacitan/ somapacitan/ 106003	M/50/26.0	16	Cardiac disorders/ Ventricular extrasystoles/ PREMATURE VENTRICULAR CONTRACTIONS	2016-12-23	331/ extension/ 12	Y	Y/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED

AE no.: Adverse event number, BMI: Body mass index, Ext: Extension, F: Female, M: Male, N: No, Y: Yes, yrs: Years
*BMI at baseline.
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

Adverse events - Cardiac and vascular investigations incl. arrhythmia - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
somapacitan/ somapacitan/ 106003	M/50/26.0	24	Cardiac disorders/ Atrioventricular block first degree/ SINUS BRADYCARDIA WITH FIRST DEGREE AV BLOCK	2017-07-13 T09:35	533/ extension/ -	N	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
somapacitan/ somapacitan/ 109003	F/24/26.8	6	Cardiac disorders/ Tachycardia/ TACHYCARDIA	2016-01-24 T08:00	301/ extension/ 2	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
somapacitan/ somapacitan/ 119004	F/23/36.6	8	Investigations/ Electrocardiogram abnormal/ ABNORMAL ECG	2016-11-22	184/ main/ 63	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
somapacitan/ somapacitan/ 209001	F/35/20.8	21	Investigations/ Electrocardiogram QT prolonged/ LONG QT INTERVAL	2016-11-09 T09:19	615/ extension/ 7	Y	N/N	MILD/ POSSIBLE/ POSSIBLE	NOT APPLICABLE
somapacitan/ somapacitan/ 350004	F/32/23.0	47	Investigations/ Blood pressure decreased/ LOW ARTERIAL PRESSURE	2017-01-20	355/ extension/ 2	Y	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		49	Cardiac disorders/ Tachycardia/ TACHYCARDIA	2017-01-20	355/ extension/ 2	Y	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
Norditropin/ Norditropin/ 104002	M/38/18.4	3	Cardiac disorders/ Bundle branch block right/ INCOMPLETE RIGHT BUNDLE BRANCH BLOCK	2015-07-21 T07:25	85/ main/ -	N	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED

AE no.: Adverse event number, BMI: Body mass index, Ext: Extension, F: Female, M: Male, N: No, Y: Yes, yrs: Years
*BMI at baseline.
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

Adverse events - Cardiac and vascular investigations incl. arrhythmia - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ Norditropin/ 303002	F/26/30.4	4	Cardiac disorders/ Bradycardia/ BRADYCARDIA	2017-02-03 T10:54	621/ extension/ 56	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	NOT APPLICABLE
Norditropin/ Norditropin/ 303007	F/52/18.7	1	Investigations/ Electrocardiogram T wave inversion/ T INVERSION II, III, V4, V5, V6	2017-10-06 T11:16	617/ extension/ 166	Y	N/N	MODERATE/ POSSIBLE/ POSSIBLE	NOT APPLICABLE
Norditropin/ somapacitan/ 133001	F/61/33.2	12	Investigations/ Heart rate increased/ INCREASED HEART RATE	2016-06-10 T05:30	36/ main/ 1	Y	N/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED
		20	Investigations/ Heart rate increased/ INCREASED HEART RATE	2016-10-23	171/ main/ 1	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		5	Investigations/ Heart rate increased/ INCREASED HEART RATE	2016-05-09	4/ main/ 1	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
Norditropin/ somapacitan/ 211002	M/60/23.2	3	Investigations/ Blood pressure increased/ BLOOD PRESSURE INCREASING	2015-07-08 T09:30	57/ main/ 561	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
Norditropin/ somapacitan/ 605004	F/73/19.6	13	Investigations/ Electrocardiogram PR prolongation/ NEW MILD PROLONGATION OF PR INTERVAL (NCS) NOTED ON ECG	2015-09-18 T09:44	187/ main/ 49	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED

AE no.: Adverse event number, BMI: Body mass index, Ext: Extension, F: Female, M: Male, N: No, Y: Yes, yrs: Years
*BMI at baseline.
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

Adverse events - Cardiac and vascular investigations incl. arrhythmia - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ somapacitan/ 853002	F/66/28.3	9	Investigations/ Cardiac murmur/ SYSTOLIC CARDIAC MURMUR	2016-12-13	301/ extension/ -	N	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED

AE no.: Adverse event number, BMI: Body mass index, Ext: Extension, F: Female, M: Male, N: No, Y: Yes, yrs: Years
*BMI at baseline.
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

69 Adverse events - Cardiac and vascular investigations incl. arrhythmia - 4244 - listing - safety analysis set

There is no data to display

70 Adverse events for patients with diabetes (diagnosis present at baseline) - 4043 - listing - safety analysis set

Treatment group/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	Syatem Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality	Action Taken
Norditropin/ 608001	M/62/31.2	1	General disorders and administration site conditions/ Malaise/ GENERAL MALAISE	2015-03-30	1/5	Y	N/N	MILD/ POSSIBLE	DOSE NOT CHANGED
		2	Infections and infestations/ Nasopharyngitis/ COMMON COLD	2015-05-24	56/6	Y	N/N	MILD/ UNLIKELY	DOSE NOT CHANGED

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
*AE causality is based on judgement of investigators.
MedDRA version 21.0.

71 Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
placebo/ somapacitan/ 304011	F/47/18.3	1	Infections and infestations/ Urinary tract infection/ URINARY TRACT INFECTION.	2016-02-10	153/ main/ 10	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
placebo/ somapacitan/ 506003	F/26/33.8	2	Skin and subcutaneous tissue di sorders/ Skin erosion/ SMALL SEROUS - PURULENT EROSIONS ON LOWER LEGS.	2016-05-09	15/ main/ 43	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		3	Gastrointestinal disorders/ Diarrhoea/ DIARRHEA	2016-06-14	51/ main/ 1	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		4	Gastrointestinal disorders/ Diarrhoea/ DIARRHEA	2016-06-18	55/ main/ 1	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		5	Gastrointestinal disorders/ Diarrhoea/ DIARRHEA	2016-07-01	68/ main/ 57	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		6	Nervous system disorders/ Headache/ HEADACHE	2016-08-01	99/ main/ 15	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		7	Infections and infestations/ Pyoderma/ PURULENT SKIN CHANGES ON THE LOWER LEGS	2016-08-27	125/ main/ 18	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
*AE causality is based on judgement of investigators.
MedDRA version 21.0.

Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
placebo/ somapacitan/ 601003	M/66/32.4	1	Renal and urinary disorders/ Urinary tract obstruction/ URINARY OBSTRUCTION	2015-05-06	51/ main/ -	N	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		2	Immune system disorders/ Seasonal allergy/ HAYFEVER	2015-09-02	170/ main/ 61	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		3	Injury, poisoning and procedural complications/ Chest injury/ CHEST INJURY DUE TO MOTOR VEHICLE ACCIDENT	2016-01-09	299/ extension/ -	N	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		4	Cardiac disorders/ Angina unstable/ UNSTABLE ANGINA	2015-12-31 T05:30	290/ extension/ 1	Y	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		5	Gastrointestinal disorders/ Constipation/ CONSTIPATION	2015-12-22	281/ extension/ -	N	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		6	Cardiac disorders/ Ventricular fibrillation/ VENTRICULAR FIBRILLATION	2016-03-13 T21:00	363/ extension/ 12	N	Y/N	SEVERE/ UNLIKELY/ UNLIKELY	DRUG INTERRUPTED
		7	Cardiac disorders/ Cardiogenic shock/ CARDIOGENIC SHOCK	2016-03-13 T21:00	363/ extension/ 12	N	Y/N	SEVERE/ UNLIKELY/ UNLIKELY	DRUG INTERRUPTED

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
*AE causality is based on judgement of investigators.
MedDRA version 21.0.

Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
placebo/ somapacitan/ 601003	M/66/32.4	8	Respiratory, thoracic and media stinal disorders/ Pneumonia aspiration/ ASPIRATION PNEUMONIA	2016-03-13	363/ extension/ 12	N	Y/N	SEVERE/ UNLIKELY/ UNLIKELY	DRUG INTERRUPTED
		9	Infections and infestations/ Viral upper respiratory tract i nfection/ VIRAL UPPER RESPIRATORY INFECTION	2015-05-01	46/ main/ 5	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
somapacitan/ somapacitan/ 122007	M/48/42.5	1	Infections and infestations/ Ear infection/ EAR INFECTION	2016-03-19	44/ main/ 7	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		2	Respiratory, thoracic and media stinal disorders/ Cough/ COUGH	2016-03-29	54/ main/ 18	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		3	Infections and infestations/ Ear infection/ EAR INFECTION	2016-06-29	146/ main/ 8	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		4	Musculoskeletal and connective tissue disorders/ Arthralgia/ WRIST PAIN	2016-10-04	243/ main/ 393	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
somapacitan/ somapacitan/ 123002	M/75/30.6	1	Gastrointestinal disorders/ Dry mouth/ DRY MOUTH	2015-08-17 T11:00	1/ main/ 1	Y	N/N	MILD/ POSSIBLE/ -	DOSE NOT CHANGED

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
*AE causality is based on judgement of investigators.
MedDRA version 21.0.

Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
somapacitan/ somapacitan/ 123002	M/75/30.6	2	Gastrointestinal disorders/ Dry mouth/ DRY MOUTH	2015-08-24 T10:00	8/ main/ 1	Y	N/N	MILD/ POSSIBLE/ -	DOSE NOT CHANGED
somapacitan/ somapacitan/ 506002	F/44/42.1	1	Psychiatric disorders/ Sleep disorder/ SLEEP DISORDER	2016-01-16	6/ main/ 2	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		10	Infections and infestations/ Ear infection/ OTITIS	2016-09-01	235/ main/ 6	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		11	Musculoskeletal and connective tissue disorders/ Myalgia/ MUSCLE PAIN	2016-07-11	183/ main/ 52	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		12	Infections and infestations/ Gastroenteritis/ ACUTE GASTROENTERITIS	2016-10-13	277/ extension/ 8	Y	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		13	Infections and infestations/ Nasopharyngitis/ COMMON COLD	2016-10-10	274/ extension/ 3	Y	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		14	Blood and lymphatic system diso rders/ Lymphadenopathy/ ENLARGED LYMPH NODES IN THE LEFT ARMPIT	2016-10-21	285/ extension/ -	N	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED

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MedDRA version 21.0.

Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
somapacitan/ somapacitan/ 506002	F/44/42.1	15	Infections and infestations/ Ear infection/ OTITIS	2016-12-16	341/ extension/ 16	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		16	Infections and infestations/ Ear infection/ OTITIS	2017-01-27	383/ extension/ 15	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		17	Injury, poisoning and procedural complications/ Scratch/ SCRATCH OF EPIDERMIS ON THE RIGHT FOREARM	2017-06-22	529/ extension/ 8	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		18	Blood and lymphatic system disorders/ Lymphadenopathy/ ENLARGED LYMPH NODE ON THE RIGHT SIDE OF NECK	2017-09-19	618/ extension/ -	N	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		2	Infections and infestations/ Gastroenteritis/ ACUTE GASTROENTERITIS	2016-03-01	51/ main/ 3	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		3	Infections and infestations/ Gastroenteritis/ ACUTE GASTROENTERITIS	2016-05-02	113/ main/ 7	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED

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Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
somapacitan/ somapacitan/ 506002	F/44/42.1	4	Infections and infestations/ Upper respiratory tract infecti on/ UPPER RESPIRATORY TRACT INFECTION	2016-05-09	120/ main/ 8	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		5	Musculoskeletal and connective tissue disorders/ Intervertebral disc degeneratio n/ EXACERBATION OF DEGENERATIVE DISEASE OF THE SPINE.	2016-04-18	99/ main/ 13	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		6	Musculoskeletal and connective tissue disorders/ Intervertebral disc degeneratio n/ EXACERBATION OF DEGENERATIVE DISEASE OF THE SPINE.	2016-05-16	127/ main/ 5	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		7	Blood and lymphatic system diso rders/ Lymphadenopathy/ ENLARGED LYMPH NODES	2016-05-23	134/ main/ 43	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		8	Infections and infestations/ Upper respiratory tract infecti on bacterial/ BACTERIAL UPPER RESPIRATORY TRACT INFECTION	2016-06-24	166/ main/ 19	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED

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Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
somapacitan/ somapacitan/ 506002	F/44/42.1	9	Musculoskeletal and connective tissue disorders/ Exostosis/ HEEL SPURS	2016-07-05	177/ main/ -	N	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
somapacitan/ somapacitan/ 552002	F/41/38.6	1	Musculoskeletal and connective tissue disorders/ Intervertebral disc protrusion/ WORSENING OF DISCAL HERNIA	2016-04-23	48/ main/ -	N	N/N	SEVERE/ POSSIBLE/ -	DOSE NOT CHANGED
		2	Gastrointestinal disorders/ Vomiting/ VOMITING	2017-10-31	604/ extension/ 2	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
somapacitan/ somapacitan/ 702002	F/53/47.2	1	Infections and infestations/ Tonsillitis/ TONSILLITIS	2015-08-31	15/ main/ 7	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		2	Infections and infestations/ Urinary tract infection/ URINARY TRACT INFECTION	2015-12-02	108/ main/ 5	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		3	Musculoskeletal and connective tissue disorders/ Costochondritis/ MUSCULO-SCELETAL PAIN - COSTO-CHONDRITIS	2015-12-15	121/ main/ 29	Y	N/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED
		4	Musculoskeletal and connective tissue disorders/ Muscle spasms/ CRAMPS	2016-02-02	170/ main/ 28	Y	N/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED

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Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
somapacitan/ somapacitan/ 702002	F/53/47.2	5	Nervous system disorders/ Sciatica/ ISCHIALGIA	2016-02-02	170/ main/ -	N	N/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED
		6	Musculoskeletal and connective tissue disorders/ Osteoarthritis/ OSTEOARTHRITIS	2016-02-02	170/ main/ -	N	N/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED
		7	Vascular disorders/ Hypertension/ HYPERTENSION	2016-06-13	302/ extension/ -	N	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
Norditropin/ Norditropin/ 101002	F/62/27.8	1	Infections and infestations/ Sinusitis/ SINUS INFECTION	2015-12-18	47/ main/ 10	Y	N/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED
		10	Injury, poisoning and procedural complications/ Fall/ SHOULDER INJURY DUE TO FALL	2016-03-23	143/ main/ 5	Y	N/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED
		11	Injury, poisoning and procedural complications/ Tooth fracture/ BROKEN TOOTH	2016-03-16	136/ main/ 1	Y	N/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED
		12	Injury, poisoning and procedural complications/ Laceration/ LEFT FOREARM LACERATION	2016-06-15	227/ main/ 209	Y	N/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED

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Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ Norditropin/ 101002	F/62/27.8	13	Investigations/ Blood glucose increased/ ELEVATED GLUCOSE	2016-06-23	235/ main/ 173	Y	N/N	MODERATE/ POSSIBLE/ -	DRUG INTERRUPTED
		14	Investigations/ Glycosylated haemoglobin increased/ ELEVATED HEMOGLOBIN A1C	2016-06-23	235/ main/ -	N	N/N	MODERATE/ POSSIBLE/ -	DRUG INTERRUPTED
		15	Infections and infestations/ Nasopharyngitis/ COLD SYMPTOMS	2016-12-28	423/ extension/ 30	Y	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		16	Investigations/ Platelet count increased/ ELEVATED PLATELETS	2016-12-12	407/ extension/ 136	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		17	Musculoskeletal and connective tissue disorders/ Arthralgia/ JOINT PAIN LEFT INDEX FINGER	2016-11-01	366/ extension/ 70	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		18	Gastrointestinal disorders/ Constipation/ CONSTIPATION	2016-08-10	283/ extension/ 11	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		19	Injury, poisoning and procedural complications/ Foot fracture/ LEFT METATARSAL FOOT FRACTURE	2017-06-24	601/ extension/ 81	Y	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED

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Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ Norditropin/ 101002	F/62/27.8	2	Investigations/ Blood glucose increased/ ELEVATED GLUCOSE	2016-01-11	71/ main/ 164	Y	N/N	MILD/ POSSIBLE/ -	DOSE NOT CHANGED
		20	Infections and infestations/ Wound infection/ INFECTION FROM PUNCTURE WOUND	2017-05-29	575/ extension/ 40	Y	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		21	Musculoskeletal and connective tissue disorders/ Fracture pain/ PAIN FROM FOOT FRACTURE	2017-06-24	601/ extension/ 167	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		22	Investigations/ Blood glucose increased/ ELEVATED GLUCOSE	2017-09-22	691/ extension/ -	N	N/N	MILD/ POSSIBLE/ POSSIBLE	DOSE NOT CHANGED
		23	Infections and infestations/ Wound infection/ INFECTION FROM PUNCTURE WOUN	2017-05-29	575/ extension/ 11	Y	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		24	General disorders and administration site conditions/ Vaccination site pain/ PAIN FROM FLU SHOT	2017-11-21	751/ extension/ 2	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		25	Injury, poisoning and procedural complications/ Laceration/ SKIN LACERATION RIGHT SHIN	2017-12-07	767/ extension/ -	N	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED

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Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ Norditropin/ 101002	F/62/27.8	3	Investigations/ Glycosylated haemoglobin increased/ ELEVATED HBA1C	2016-01-11	71/ main/ 164	Y	N/N	MILD/ POSSIBLE/ -	DOSE NOT CHANGED
		4	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Melanocytic naevus/ WORSENING OF MELANOCYTIC NEVI OF THE TRUNK	2016-02-18	109/ main/ 1	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		5	Investigations/ Blood uric acid increased/ ELEVATED URIC ACID	2016-01-21	81/ main/ 97	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		8	Investigations/ Platelet count increased/ ELEVATION IN PLATELETS	2016-03-04	124/ main/ 54	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		9	Surgical and medical procedures/ Skin operation/ WIDE SKIN EXCISION	2016-03-07	127/ main/ 1	Y	N/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED
Norditropin/ Norditropin/ 111019	F/69/39.9	1	Investigations/ Blood uric acid increased/ INCREASE IN URIC ACID	2016-07-30	110/ main/ 207	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED

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Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ Norditropin/ 111019	F/69/39.9	2	General disorders and administration site conditions/ Chest pain/ CHEST PAIN	2017-04-11	365/ extension/ 5	N	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
Norditropin/ Norditropin/ 902003	M/77/27.0	1	Infections and infestations/ Nasopharyngitis/ COMMON COLD	2015-05-24 T20:00	6/ main/ 2	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		10	Injury, poisoning and procedural complications/ Fall/ SACRAL PAIN AFTER A FALL	2017-01-20	613/ extension/ 5	Y	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		11	Gastrointestinal disorders/ Diarrhoea/ ACUTE DIARRHEA	2017-01-23	616/ extension/ 2	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		3	Musculoskeletal and connective tissue disorders/ Spinal pain/ CERVICAL SPINE PAIN	2015-09-22	127/ main/ 22	Y	N/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED
		4	General disorders and administration site conditions/ Injection site bruising/ BRUISING AT ABDOMINAL INJECTION SITE	2015-06-15	28/ main/ 12	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED

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Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ Norditropin/ 902003	M/77/27.0	5	Infections and infestations/ Upper respiratory tract infecti on/ UPPER RESPIROTARY TRACT INFECTION	2016-01-03	230/ main/ 7	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		6	Infections and infestations/ Fungal infection/ FUNGAL INFECTION	2015-06	14/ main/ -	N	N/N	MILD/ POSSIBLE/ -	DOSE NOT CHANGED
		7	Metabolism and nutrition disord ers/ Hypoglycaemia/ POSSIBLE HYPOGLYCAEMIA	2016-05-01	349/ extension/ 8	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		8	Gastrointestinal disorders/ Haemorrhoids/ HAEMORRHOIDS	2016-09-26	497/ extension/ 23	Y	N/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		9	Injury, poisoning and procedura l complications/ Fall/ RIGHT HIP PAIN SECONDARY TO FALL	2016-11-06	538/ extension/ 80	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
Norditropin/ somapacitan/ 104003	M/68/40.7	1	Gastrointestinal disorders/ Abdominal discomfort/ GI UPSET	2015-09-08	1/ main/ 4	Y	N/N	MILD/ POSSIBLE/ -	DOSE NOT CHANGED

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Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ somapacitan/ 104003	M/68/40.7	10	Skin and subcutaneous tissue di sorders/ Rash/ RASH	2016-01-09	124/ main/ 23	Y	N/N	MILD/ UNLIKELY/ -	DRUG INTERRUPTED
		11	Musculoskeletal and connective tissue disorders/ Osteoarthritis/ OSTEOARTHRITIS IN THE RIGHT KNEE	2016-09-06	365/ extension/ -	N	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		12	Infections and infestations/ Upper respiratory tract infecti on/ UPPER RESPIRATORY INFECTION	2016-12-10	460/ extension/ 11	Y	N/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
		2	Musculoskeletal and connective tissue disorders/ Musculoskeletal chest pain/ RIB PAIN	2015-09-13	6/ main/ 18	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		3	Injury, poisoning and procedura l complications/ Contusion/ 2 CM BRUISE ON ABDOMEN	2015-09-19	12/ main/ 12	Y	N/N	MILD/ POSSIBLE/ -	DOSE NOT CHANGED
		4	Infections and infestations/ Herpes zoster/ SHINGLES	2015-12-08	92/ main/ 54	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED

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Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ somapacitan/ 104003	M/68/40.7	5	Skin and subcutaneous tissue di sorders/ Urticaria/ HIVES	2016-01-09	124/ main/ 22	Y	N/N	MILD/ UNLIKELY/ -	DRUG INTERRUPTED
		6	Hepatobiliary disorders/ Hepatic cirrhosis/ CIRRHOSIS OF THE LIVER	2016-02-03	149/ main/ -	N	N/N	MILD/ UNLIKELY/ -	NOT APPLICABLE
		7	Investigations/ Weight decreased/ WEIGHT LOSS	2016-01-18	133/ main/ 199	Y	N/N	MILD/ POSSIBLE/ -	DOSE NOT CHANGED
		8	Metabolism and nutrition disord ers/ Hyperkalaemia/ HYPERKALEMIA	2016-02-16	162/ main/ 49	Y	N/N	MILD/ UNLIKELY/ -	NOT APPLICABLE
		9	Gastrointestinal disorders/ Ascites/ ASCITIES	2016-02-01	147/ main/ 59	Y	N/N	MILD/ UNLIKELY/ -	NOT APPLICABLE
Norditropin/ somapacitan/ 901001	F/34/27.2	1	Respiratory, thoracic and media stinal disorders/ Asthma/ ACUTE EXACERBATION OF PRE EXISTING ASTHMA	2015-05-27	38/ main/ 10	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		2	Musculoskeletal and connective tissue disorders/ Arthralgia/ BILATERAL ANKLE PAIN	2015-12-16	241/ main/ 16	Y	N/N	MODERATE/ PROBABLE/ -	DOSE NOT CHANGED

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Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ somapacitan/ 901001	F/34/27.2	3	Injury, poisoning and procedural complications/ Thermal burn/ RIGHT WRIST BURN	2016-01-15	271/ main/ 14	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		4	Nervous system disorders/ Headache/ HEADACHE	2016-03-14	330/ extension/ 79	Y	N/N	MODERATE/ UNLIKELY/ PROBABLE	DOSE REDUCED
		5	Musculoskeletal and connective tissue disorders/ Arthralgia/ EPISODIC JOINT PAIN MAINLY INVOLVING ANKLES AND KNEES. NO FEVER.	2016-09-12	512/ extension/ 10	Y	N/N	MODERATE/ UNLIKELY/ PROBABLE	DOSE NOT CHANGED
		6	Musculoskeletal and connective tissue disorders/ Arthralgia/ ALTHRALGIA (JOINT PAIN MAINLY ANKLE AND SHOULDER AS WELL AS BACKACHE ON AND OFF ASSOCAITED WITH NON TENDER ANKLE SWELLING. NO REDNESSS ON JOINT AND NOT INTERFERING WITH MOVEMENT)	2016-10-10	540/ extension/ -	N	N/N	MODERATE/ UNLIKELY/ PROBABLE	DOSE REDUCED
Norditropin/ no treatment/ 410004	M/77/25.5	2	Infections and infestations/ Clostridium difficile infection / CLOSTRIDIUM DIFFICILE INFECTION	2016-05-28	24/ main/ 11	Y	Y/N	SEVERE/ UNLIKELY/ -	NOT APPLICABLE

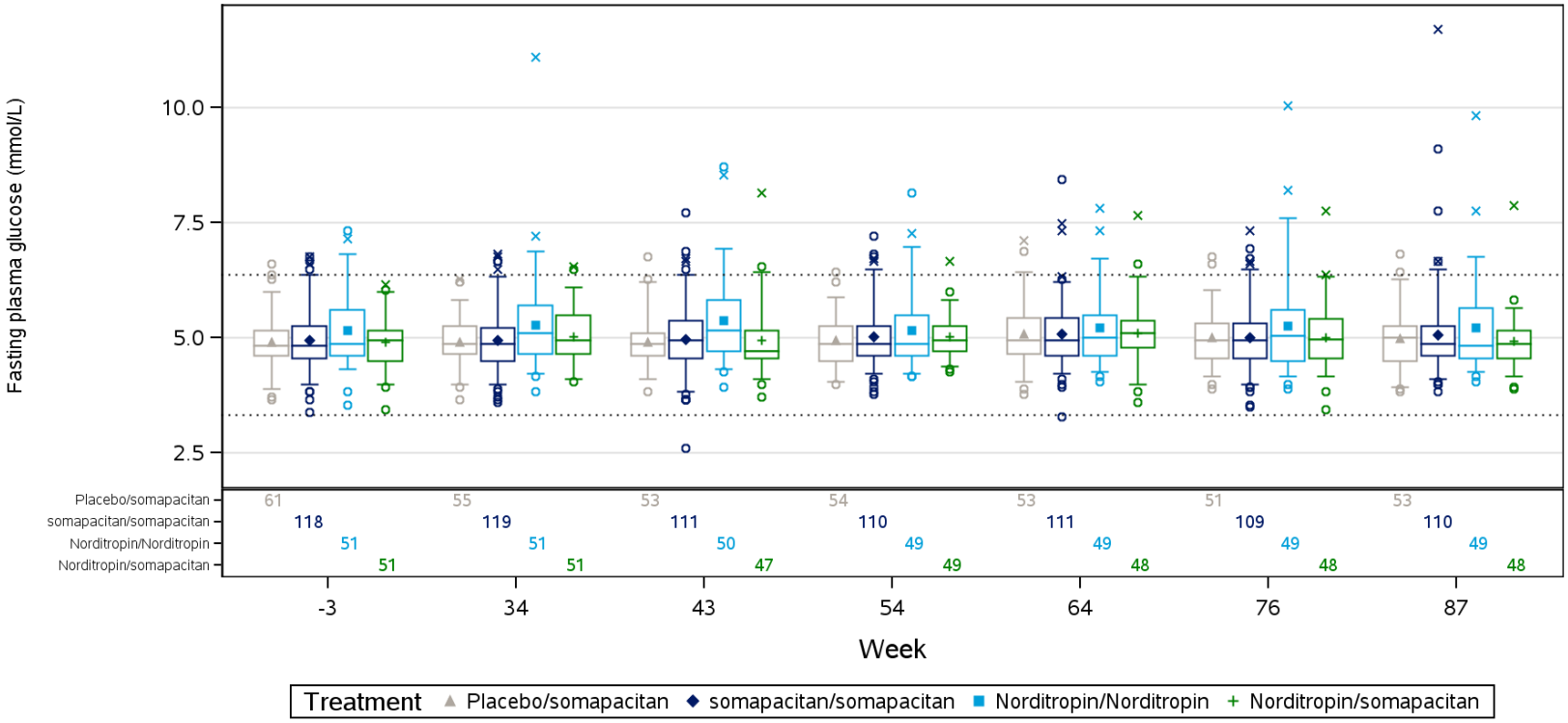
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Adverse events for patients with diabetes (diagnosis present at baseline) - 4054 - listing - safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ no treatment/ 410004	M/77/25.5	3	Gastrointestinal disorders/ Diarrhoea/ LOOSE STOOL	2016-05-31	27/ main/ 3	Y	N/N	MILD/ UNLIKELY/ -	NOT APPLICABLE
		4	Renal and urinary disorders/ Nocturia/ NYCTURIA	2016-05-05	1/ main/ -	N	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		5	Respiratory, thoracic and mediastinal disorders/ Dyspnoea/ SHORTNESS OF BREATH	2016-05-05	1/ main/ -	N	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		6	Cardiac disorders/ Palpitations/ PALPITATIONS	2016-05-05	1/ main/ -	N	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		7	Nervous system disorders/ Dizziness/ DIZZINESS	2016-05-05	1/ main/ 29	Y	N/N	MILD/ UNLIKELY/ -	DOSE NOT CHANGED
		8	General disorders and administration site conditions/ Pain/ BODILY PAIN	2016-05-05	1/ main/ -	N	N/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
*AE causality is based on judgement of investigators.
MedDRA version 21.0.

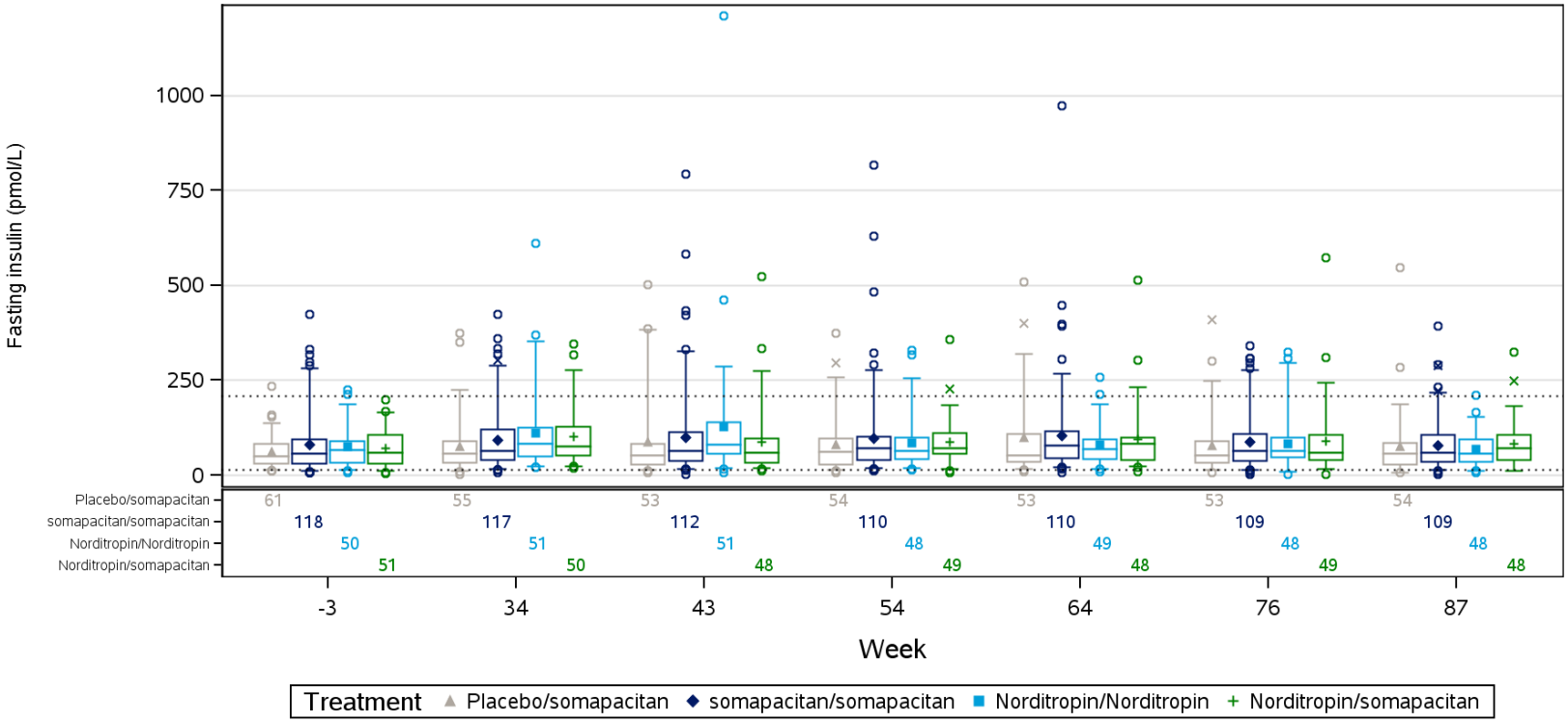
72 Box plot for fasting subjects of fasting plasma glucose (mmol/L) by visit - 4054 extension – safety analysis set



Observed data.
Mean (triangle, square, plus and diamond), median (centre line), 25th and 75th percentiles (box), outliers: non-diabetic at baseline (circles) and diabetic at baseline (X). 5th and 95th percentiles (whiskers).
Number of subjects contributing to the data points appear in the bottom panel.
Normal range (mmol/L): F age 18-125 [3.33 ; 6.38], M age 18-125 [3.33 ; 6.38].

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:14:28 - f_sum_box_diab.sas/f_f_fpg_abs_box_diab_4054_sas.png

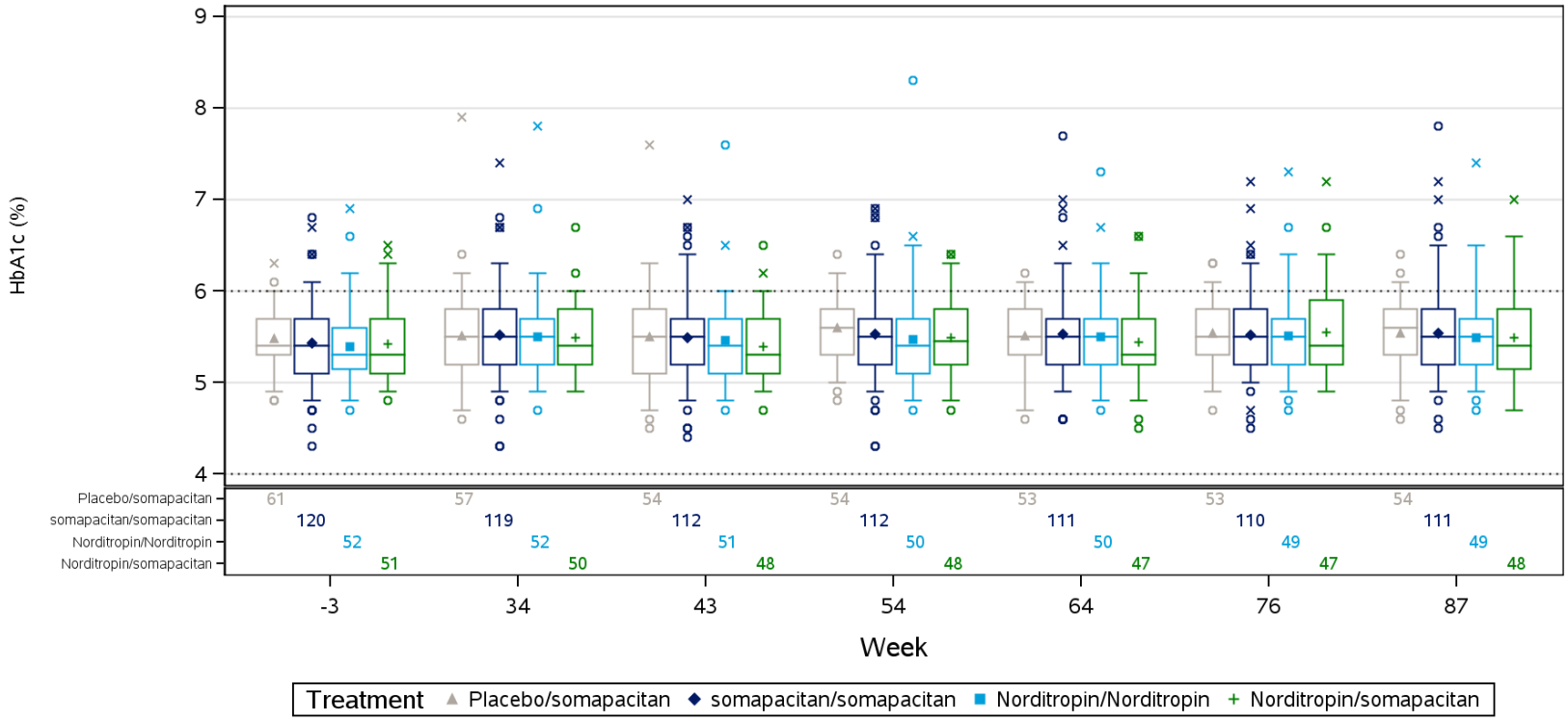
73 Box plot for fasting subjects of fasting insulin (pmol/L) by visit - 4054 extension – safety analysis set



Observed data.
Mean (triangle, square, plus and diamond), median (centre line), 25th and 75th percentiles (box), outliers: non-diabetic at baseline (circles) and diabetic at baseline (X). 5th and 95th percentiles (whiskers).
Number of subjects contributing to the data points appear in the bottom panel.
Normal range (pmol/L): F age 18-125 [14 ; 208], M age 18-125 [14 ; 208].

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:14:37 - f_sum_box_diab.sas/f_f_fsi_abs_box_diab_4054_sas.png

74 Box plot of HbA1c (%) by visit - 4054 extension – safety analysis set



Observed data.
Mean (triangle, square, plus and diamond), median (centre line), 25th and 75th percentiles (box), outliers: non-diabetic at baseline (circles) and diabetic at baseline (X). 5th and 95th percentiles (whiskers).
Number of subjects contributing to the data points appear in the bottom panel.
Normal range (%): F age 18-125 [4 ; 6], M age 18-125 [4 ; 6].

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:14:41 - f_sum_box_diab.sas/f_hba1c_abs_box_diab_4054_sas.png

75 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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Norditropin/ NN8640-4043/ 300004	M/43/35.3	Visit 2 (Week -2)	6.49	H	Y	251.0	H	Y	5.50		Y
		Visit 11 (Week 8)	6.27		Y	310.0	H	Y	5.50		Y
		Visit 11 (Week 8)	6.44*	H	Y	317.0*	H	Y	5.50*		Y
		Visit 12 (Week 16)	5.27		Y	1182.0	H	Y	5.60		Y
		Visit 13 (Week 25)	7.11	H	Y	788.0	H	Y	5.50		Y
Norditropin/ NN8640-4043/ 401003	F/63/25.0	Visit 2 (Week -2)	6.00		Y	69.0		Y	6.50	H	Y
		Visit 11 (Week 8)	6.00		Y	49.0		Y	6.20	H	Y
		Visit 12 (Week 16)	5.55		Y	65.0		Y	6.30	H	Y
		Visit 13 (Week 25)	6.05		Y	56.0		Y	6.40	H	Y
Norditropin/ NN8640-4043/ 608001**	M/62/31.2	Visit 2 (Week -2)	7.60	H	Y	197.0		Y	6.50	H	Y
		Visit 11 (Week 8)	7.38	H	Y	81.0		Y	6.00		Y
		Visit 12 (Week 16)	6.61	H	Y	151.0		Y	6.50	H	Y
		Visit 13 (Week 25)	6.72	H	Y	126.0		Y	6.20	H	Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Norditropin/ NN8640-4244/ 101008	M/71/29.6	Visit 1 (Week -3)	6.30			251.4	H		6.60	H	
		Visit 5 (Week 7)	6.10			114.6			6.40		
		Visit 11 (Week 19)	6.70	H		88.9			6.10		
		Visit 13 (Week 33)	6.20			125.7			6.30		
		Visit 15 (Week 52)	6.70	H		128.5			6.40		
		End of trial	6.70	H		128.5			6.40		
Norditropin/ NN8640-4244/ 111006	F/63/32.8	Visit 1 (Week -3)	6.40			182.7	H		6.40		
		Visit 5 (Week 7)	6.40			157.0			6.40		
		Visit 11 (Week 19)	6.60	H		145.2			6.30		
		Visit 13 (Week 33)	7.40	H		332.7	H		6.80	H	
		Visit 15 (Week 52)	8.00	H		204.9	H		7.10	H	
		Visit 15a	7.00	H		152.1			7.00	H	
		End of trial	8.00	H		204.9	H		7.10	H	
Somapacitan/ NN8640-4043/ 101006	M/32/26.7	Visit 2 (Week -2)	6.72	H	Y	288.0	H	Y	5.90		Y
		Visit 11 (Week 8)	5.88		Y	279.0	H	Y	6.10	H	Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Somapacitan/ NN8640-4043/ 101006	M/32/26.7	Visit 12 (Week 16)	5.88		Y	164.0		Y	6.20	H	Y
		Visit 13 (Week 25)	7.16	H	Y	208.0		Y	6.30	H	Y
Somapacitan/ NN8640-4043/ 102002	M/60/28.5	Visit 2 (Week -2)	7.44	H	Y	70.0		Y	6.20	H	Y
		Visit 11 (Week 8)	6.44	H	Y	28.0		Y	5.90		Y
		Visit 12 (Week 16)	6.44	H	Y	29.0		Y	5.90		Y
		Visit 13 (Week 25)	6.22		Y	29.0		Y	6.00		Y
Somapacitan/ NN8640-4043/ 301001	M/73/32.5	Visit 2 (Week -2)	6.88	H	Y	76.0		Y	5.20		Y
		Visit 11 (Week 8)	6.99	H	Y	60.0		Y	5.50		Y
		Visit 12 (Week 16)	6.72	H	Y	64.0		Y	5.80		Y
		Visit 13 (Week 25)	7.33	H	Y	63.0		Y	5.50		Y
Somapacitan/ NN8640-4043/ 405001	F/72/36.0	Visit 2 (Week -2)	5.44		Y	113.0		Y	6.20	H	Y
		Visit 11 (Week 8)	5.44		Y	129.0		Y	6.30	H	Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Somapacitan/ NN8640-4043/ 405001	F/72/36.0	Visit 12 (Week 16)	5.61		Y	149.0		Y	6.70	H	Y
		Visit 13 (Week 25)	5.33		Y	137.0		Y	6.40	H	Y
Somapacitan/ NN8640-4043/ 602001	M/74/33.3	Visit 2 (Week -2)	6.99	H	Y	51.0		Y	6.50	H	Y
		Visit 11 (Week 8)	5.77		Y	18.0		Y	6.30	H	Y
		Visit 12 (Week 16)	5.27		Y	25.0		Y	6.10	H	Y
		Visit 13 (Week 25)	5.11		Y	22.0		Y	5.90		Y
Somapacitan/ NN8640-4244/ 103006	F/66/23.1	Visit 1 (Week -3)	5.80			41.0			6.50	H	
		Visit 5 (Week 7)	5.60			48.6			6.10		
		Visit 11 (Week 19)	6.00			50.0			6.40		
		Visit 13 (Week 33)	6.10			42.4			6.50	H	
		Visit 15 (Week 52)	6.50	H		73.6			6.60	H	
		End of trial	6.50	H		73.6			6.60	H	

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Somapacitan/ NN8640-4244/ 111003	M/67/24.7	Visit 1 (Week -3)	5.30			34.0			6.30		
		Visit 5 (Week 7)	5.40			63.2			6.50	H	
		Visit 11 (Week 19)	5.60			43.8			6.30		
		Visit 13 (Week 33)	5.60			32.6			6.30		
		Visit 15 (Week 52)	5.20			34.0			6.30		
		End of trial	5.20			34.0			6.30		
Placebo/Somapacitan/ NN8640-4054-EXT/ 304011**	F/47/18.3	VISIT 1B (WEEK -3)	5.27		Y	51.0		Y	5.60		Y
		VISIT 10 (WEEK 8)	4.27		Y	35.0		Y	5.50		Y
		VISIT 12 (WEEK 17)	3.72		Y	5.0	L	Y	5.60		Y
		VISIT 13 (WEEK 25)	7.33	H	Y	244.0	H	Y	5.30		Y
		VISIT 14 (WEEK 34)	4.83		Y	74.0		Y	5.10		Y
		VISIT 23 (WEEK 43)	4.88		Y	52.0		Y	5.50		Y
		VISIT 25 (WEEK 54)	5.83		Y	297.0	H	Y	5.80		Y
		VISIT 26 (WEEK 64)	7.11	H	Y	400.0	H	Y	5.90		Y
		VISIT 27 (WEEK 76)	5.61		Y	409.0	H	Y	5.90		Y
		VISIT 28 (WEEK 87)	4.33		Y	139.0		Y	5.80		Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Placebo/Somapacitan/ NN8640-4054-EXT/ 601003**	M/66/32.4	VISIT 1B (WEEK -3)	5.83		Y	48.0		Y	6.30	H	Y
		VISIT 10 (WEEK 8)	7.99	H	Y	66.0		Y	6.70	H	Y
		VISIT 12 (WEEK 17)	7.49	H	Y	36.0		Y	8.00	H	Y
		VISIT 13 (WEEK 25)	8.94	H	Y	65.0		Y	7.80	H	Y
		VISIT 14 (WEEK 34)	6.27		Y	51.0		Y	7.90	H	Y
		VISIT 23 (WEEK 43)	6.22		Y	46.0		Y	7.60	H	Y
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 109004	F/29/41.2	VISIT 1B (WEEK -3)	5.11		Y	289.0	H	Y	5.80		Y
		VISIT 10 (WEEK 8)	6.33		Y	120.0		Y	6.30	H	Y
		VISIT 12 (WEEK 17)	5.33		Y	306.0	H	Y	6.60	H	Y
		VISIT 13 (WEEK 25)	5.27		Y	174.0		Y	6.30	H	Y
		VISIT 14 (WEEK 34)	6.00		Y	290.0	H	Y	6.30	H	Y
		VISIT 23 (WEEK 43)	5.61		Y	434.0	H	Y	6.50	H	Y
		VISIT 25 (WEEK 54)	6.77	H	Y	817.0	H	Y	6.90	H	Y
		VISIT 26 (WEEK 64)	8.44	H	Y	972.0	H	Y	7.70	H	Y
		VISIT 28 (WEEK 87)	6.66	H	Y	135.0		Y	7.80	H	Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 123002**	M/75/30.6	VISIT 1B (WEEK -3)	6.27		Y	248.0	H	Y	6.00		Y
		VISIT 10 (WEEK 8)	6.44	H	Y	183.0		Y	5.90		Y
		VISIT 12 (WEEK 17)	6.72	H	Y	168.0		Y	6.10	H	Y
		VISIT 13 (WEEK 25)	8.05	H	Y	235.0	H	Y	6.10	H	Y
		VISIT 14 (WEEK 34)	6.49	H	Y	156.0		Y	6.00		Y
		VISIT 23 (WEEK 43)	6.72	H	Y	183.0		Y	5.90		Y
		VISIT 25 (WEEK 54)	6.72	H	Y	182.0		Y	6.10	H	Y
		VISIT 26 (WEEK 64)	6.33		Y	192.0		Y	5.90		Y
		VISIT 27 (WEEK 76)	6.66	H	Y	205.0		Y	6.40	H	Y
		VISIT 28 (WEEK 87)	6.16		Y	222.0	H	Y	5.80		Y
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 123003	M/55/38.7	VISIT 1B (WEEK -3)	6.77	H	Y	215.0	H	Y	6.40	H	Y
		VISIT 10 (WEEK 8)	6.77	H	Y	278.0	H	Y	6.00		Y
		VISIT 12 (WEEK 17)	7.49	H	Y	374.0	H	Y	6.10	H	Y
		VISIT 13 (WEEK 25)	8.05	H	Y	494.0	H	Y	6.00		Y
		VISIT 14 (WEEK 34)	6.33		Y	360.0	H	Y	5.90		Y
		VISIT 23 (WEEK 43)	6.88	H	Y	263.0	H	Y	6.10	H	Y
		VISIT 25 (WEEK 54)	6.83	H	Y	194.0		Y	6.00		Y
		VISIT 26 (WEEK 64)	5.94		Y	213.0	H	Y	6.20	H	Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 123003	M/55/38.7	VISIT 27 (WEEK 76)	6.33		Y	238.0	H	Y	6.00		Y
		VISIT 28 (WEEK 87)	9.10	H	Y	126.0		Y	6.60	H	Y
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 123004**	M/61/26.3	VISIT 1B (WEEK -3)	6.61	H	Y	67.0		Y	6.70	H	Y
		VISIT 10 (WEEK 8)	9.10	H	Y	332.0	H	Y	6.90	H	Y
		VISIT 12 (WEEK 17)	6.83	H	Y	126.0		Y	7.10	H	Y
		VISIT 13 (WEEK 25)	7.05	H	Y	87.0		Y	7.00	H	Y
		VISIT 14 (WEEK 34)	6.83	H	Y	127.0		Y	7.40	H	Y
		VISIT 23 (WEEK 43)	6.66	H	Y	109.0		Y	7.00	H	Y
		VISIT 25 (WEEK 54)	6.27		Y	109.0		Y	6.90	H	Y
		VISIT 26 (WEEK 64)	7.49	H	Y	119.0		Y	7.00	H	Y
		VISIT 27 (WEEK 76)	7.33	H	Y	162.0		Y	7.20	H	Y
		VISIT 28 (WEEK 87)	11.7	H	Y	290.0	H	Y	7.20	H	Y
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 126019	F/69/40.7	VISIT 1B (WEEK -3)	5.55		Y	79.0		Y	5.40		Y
		VISIT 10 (WEEK 8)	5.05		Y	174.0		Y	5.30		Y
		VISIT 12 (WEEK 17)	5.33		Y	119.0		Y	5.30		Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 126019	F/69/40.7	VISIT 13 (WEEK 25)	5.44		Y	105.0		Y	5.20		Y
		VISIT 14 (WEEK 34)	4.77		Y	131.0		Y	5.00		Y
		VISIT 25 (WEEK 54)	4.94		Y	97.0		Y	5.60		Y
		VISIT 26 (WEEK 64)	4.72		Y	129.0		Y	5.50		Y
		VISIT 27 (WEEK 76)	4.77		Y	103.0		Y	5.10		Y
		VISIT 28 (WEEK 87)	7.77	H	Y	97.0		Y	5.70		Y
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 204013	M/64/30.3	VISIT 1B (WEEK -3)	6.11		Y	126.0		Y	6.80	H	Y
		VISIT 10 (WEEK 8)	5.61		Y	78.0		Y	5.90		Y
		VISIT 12 (WEEK 17)	5.27		Y	81.0		Y	6.10	H	Y
		VISIT 13 (WEEK 25)	5.66		Y	118.0		Y	6.00		Y
		VISIT 14 (WEEK 34)	5.83		Y	114.0		Y	6.30	H	Y
		VISIT 23 (WEEK 43)	6.38		Y	87.0		Y	6.60	H	Y
		VISIT 25 (WEEK 54)	5.94		Y	86.0		Y	6.50	H	Y
		VISIT 26 (WEEK 64)	6.27		Y	88.0		Y	6.00		Y
		VISIT 27 (WEEK 76)	6.94	H	Y	137.0		Y	6.20	H	Y
		VISIT 28 (WEEK 87)	5.88		Y	54.0		Y	6.20	H	Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 206003	M/69/23.3	VISIT 1B (WEEK -3)	4.22		Y	14.0		Y	5.60		Y
		VISIT 10 (WEEK 8)	4.44		Y	28.0		Y	6.50	H	Y
		VISIT 12 (WEEK 17)	4.44		Y	23.0		Y	6.20	H	Y
		VISIT 13 (WEEK 25)	3.94		Y	30.0		Y	5.80		Y
		VISIT 14 (WEEK 34)	4.27		Y	34.0		Y	6.70	H	Y
		VISIT 23 (WEEK 43)	4.55		Y	33.0		Y	5.70		Y
		VISIT 25 (WEEK 54)	4.88		Y	15.0		Y	6.10	H	Y
		VISIT 26 (WEEK 64)	4.50		Y	58.0		Y	6.10	H	Y
		VISIT 27 (WEEK 76)	4.55		Y	15.0		Y	6.30	H	Y
		VISIT 28 (WEEK 87)	4.27		Y	24.0		Y	6.10	H	Y
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 206005	M/58/25.4	VISIT 1B (WEEK -3)	5.22		Y	46.0		Y	6.40	H	Y
		VISIT 10 (WEEK 8)	5.05		Y	48.0		Y	6.30	H	Y
		VISIT 12 (WEEK 17)	5.22		Y	88.0		Y	6.60	H	Y
		VISIT 13 (WEEK 25)	5.16		Y	35.0		Y	6.50	H	Y
		VISIT 14 (WEEK 34)	5.00		Y	39.0		Y	6.80	H	Y
		VISIT 23 (WEEK 43)	5.05		Y	35.0		Y	6.70	H	Y
		VISIT 25 (WEEK 54)	4.94		Y	29.0		Y	6.80	H	Y
		VISIT 26 (WEEK 64)	5.50		Y	21.0		Y	6.80	H	Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 206005	M/58/25.4	VISIT 27 (WEEK 76)	5.38		Y	38.0		Y	6.10	H	Y
		VISIT 28 (WEEK 87)	5.05		Y	28.0		Y	6.70	H	Y
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 308001	M/23/38.7	VISIT 1B (WEEK -3)	5.77		Y	332.0	H	Y	6.00		Y
		VISIT 10 (WEEK 8)	4.33		Y	335.0	H	Y	6.10	H	Y
		VISIT 12 (WEEK 17)	4.55		Y	183.0		Y	6.70	H	Y
		VISIT 13 (WEEK 25)	5.38		Y	371.0	H	Y	6.60	H	Y
		VISIT 14 (WEEK 34)	4.16		Y	285.0	H	Y	5.90		Y
		VISIT 23 (WEEK 43)	4.05		Y	278.0	H	Y	6.40	H	Y
		VISIT 25 (WEEK 54)	5.72		Y	482.0	H	Y	5.80		Y
		VISIT 26 (WEEK 64)	4.88		Y	305.0	H	Y	6.00		Y
		VISIT 27 (WEEK 76)	4.33		Y	276.0	H	Y	6.00		Y
		VISIT 28 (WEEK 87)	4.55		Y	232.0	H	Y	5.70		Y
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 503003	F/24/17.9	VISIT 1B (WEEK -3)	4.77		Y	19.0		Y	5.10		Y
		VISIT 10 (WEEK 8)	4.66		Y	67.0		Y	5.00		Y
		VISIT 12 (WEEK 17)	7.22	H	Y	165.0		Y	5.20		Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 503003	F/24/17.9	VISIT 13 (WEEK 25)	6.66	H	Y	124.0		Y	5.20		Y
		VISIT 14 (WEEK 34)	5.11		Y	38.0		Y	5.00		Y
		VISIT 23 (WEEK 43)	5.44		Y	97.0		Y	5.10		Y
		VISIT 25 (WEEK 54)	7.22	H	Y	151.0		Y	5.00		Y
		VISIT 26 (WEEK 64)	4.72		Y	57.0		Y	5.20		Y
		VISIT 27 (WEEK 76)	4.61		Y	340.0	H	Y	5.20		Y
		VISIT 28 (WEEK 87)	5.33		Y	65.0		Y	5.20		Y
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 506002**	F/44/42.1	VISIT 1B (WEEK -3)	6.77	H	Y	109.0		Y	6.00		Y
		VISIT 10 (WEEK 8)	7.27	H	Y	169.0		Y	6.30	H	Y
		VISIT 12 (WEEK 17)	7.55	H	Y	156.0		Y	6.20	H	Y
		VISIT 13 (WEEK 25)	6.00		Y	101.0		Y	6.00		Y
		VISIT 14 (WEEK 34)	6.22		Y	81.0		Y	5.60		Y
		VISIT 23 (WEEK 43)	5.94		Y	85.0		Y	5.10		Y
		VISIT 25 (WEEK 54)	6.66	H	Y	125.0		Y	5.20		Y
		VISIT 26 (WEEK 64)	4.55		Y	51.0		Y	5.50		Y
		VISIT 27 (WEEK 76)	5.00		Y	40.0		Y	4.70		Y
		VISIT 28 (WEEK 87)	4.77		Y	32.0		Y	4.90		Y

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@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 552002**	F/41/38.6	VISIT 1B (WEEK -3)	6.33		Y	58.0		Y	5.90		Y
		VISIT 10 (WEEK 8)	6.22		Y	60.0		Y	6.50	H	Y
		VISIT 12 (WEEK 17)	6.44	H	Y	56.0		Y	6.40	H	Y
		VISIT 13 (WEEK 25)	6.72	H	Y	39.0		Y	6.50	H	Y
		VISIT 14 (WEEK 34)	6.77	H	Y	65.0		Y	6.70	H	Y
		VISIT 23 (WEEK 43)	5.55		Y	53.0		Y	6.70	H	Y
		VISIT 25 (WEEK 54)	6.49	H	Y	44.0		Y	6.80	H	Y
		VISIT 26 (WEEK 64)	7.33	H	Y	55.0		Y	6.90	H	Y
		VISIT 27 (WEEK 76)	6.61	H	Y	38.0		Y	6.90	H	Y
		VISIT 28 (WEEK 87)	6.66	H	Y	51.0		Y	7.00	H	Y
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 702002**	F/53/47.2	VISIT 1B (WEEK -3)	4.72		Y	117.0		Y	6.40	H	Y
		VISIT 10 (WEEK 8)	5.16		Y	227.0	H	Y	6.50	H	Y
		VISIT 12 (WEEK 17)	4.94		Y	230.0	H	Y	6.40	H	Y
		VISIT 13 (WEEK 25)	5.00		Y	165.0		Y	6.70	H	Y
		VISIT 14 (WEEK 34)	6.11		Y	303.0	H	Y	6.70	H	Y
		VISIT 23 (WEEK 43)	5.22		Y	163.0		Y	6.30	H	Y
		VISIT 25 (WEEK 54)	5.22		Y	113.0		Y	6.30	H	Y
		VISIT 26 (WEEK 64)	4.55		Y	215.0	H	Y	6.50	H	Y

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@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 702002**	F/53/47.2	VISIT 27 (WEEK 76)	5.16		Y	140.0		Y	6.50	H	Y
		VISIT 28 (WEEK 87)	.		Y	126.0*			.		Y
		VISIT 28 (WEEK 87)	4.61			212.0	H	Y	6.50	H	
Somapacitan/Somapacitan/ NN8640-4054-EXT/ 804004	M/66/31.3	VISIT 1B (WEEK -3)	6.22		Y	141.0		Y	5.60		Y
		VISIT 10 (WEEK 8)	6.83	H	Y	195.0		Y	5.30		Y
		VISIT 12 (WEEK 17)	5.94		Y	130.0		Y	5.70		Y
		VISIT 13 (WEEK 25)	6.94	H	Y	215.0	H	Y	5.60		Y
		VISIT 14 (WEEK 34)	6.66	H	Y	162.0		Y	5.20		Y
		VISIT 23 (WEEK 43)	7.72	H	Y	188.0		Y	5.90		Y
		VISIT 25 (WEEK 54)	6.27		Y	147.0		Y	5.40		Y
		VISIT 26 (WEEK 64)	6.22		Y	140.0		Y	5.50		Y
		VISIT 27 (WEEK 76)	6.72	H	Y	138.0		Y	5.30		Y
		VISIT 28 (WEEK 87)	5.72		Y	110.0		Y	5.00		Y
Norditropin/Norditropin/ NN8640-4054-EXT/ 101002**	F/62/27.8	VISIT 1B (WEEK -3)	7.16	H	Y	33.0		Y	6.90	H	Y
		VISIT 10 (WEEK 8)	9.83*	H	Y	74.0*		Y	.		

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@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Norditropin/Norditropin/ NN8640-4054-EXT/ 101002**	F/62/27.8	VISIT 10 (WEEK 8)	10.9	H		256.0	H		7.40	H	Y
		VISIT 12 (WEEK 17)	10.5	H	Y	74.0		Y	7.60	H	Y
		VISIT 13 (WEEK 25)	8.55	H	Y	58.0		Y	7.70	H	Y
		VISIT 14 (WEEK 34)	7.72*	H		39.0*			6.40*	H	
		VISIT 14 (WEEK 34)	11.1		Y	105.0		Y	7.80		Y
		VISIT 23 (WEEK 43)	8.55	H	Y	48.0		Y	6.50	H	Y
		VISIT 25 (WEEK 54)	7.27	H	Y	73.0		Y	6.60	H	Y
		VISIT 26 (WEEK 64)	7.33	H	Y	69.0		Y	6.70	H	Y
		VISIT 27 (WEEK 76)	8.22	H	Y	68.0		Y	7.30	H	Y
		VISIT 28 (WEEK 87)	9.83	H	Y	65.0		Y	7.40	H	Y
Norditropin/Norditropin/ NN8640-4054-EXT/ 111019**	F/69/39.9	VISIT 1B (WEEK -3)	6.83	H	Y	83.0		Y	5.70		Y
		VISIT 10 (WEEK 8)	8.05	H	Y	147.0		Y	5.70		Y
		VISIT 12 (WEEK 17)	7.94	H	Y	84.0		Y	5.80		Y
		VISIT 13 (WEEK 25)	7.55	H	Y	77.0		Y	5.70		Y
		VISIT 14 (WEEK 34)	7.22	H	Y	67.0		Y	5.70		Y
		VISIT 23 (WEEK 43)	6.94	H	Y	76.0		Y	5.70		Y
		VISIT 25 (WEEK 54)	6.99	H	Y	109.0		Y	5.60		Y
		VISIT 26 (WEEK 64)	7.83	H	Y	71.0		Y	5.70		Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
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@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Norditropin/Norditropin/ NN8640-4054-EXT/ 111019**	F/69/39.9	VISIT 27 (WEEK 76)	7.60	H	Y	73.0		Y	5.80		Y
		VISIT 28 (WEEK 87)	6.77	H	Y	70.0		Y	6.10	H	Y
Norditropin/Norditropin/ NN8640-4054-EXT/ 207003	M/26/27.5	VISIT 1B (WEEK -3)	5.50		Y	182.0		Y	5.60		Y
		VISIT 10 (WEEK 8)	5.55		Y	237.0	H	Y	5.80		Y
		VISIT 12 (WEEK 17)	7.05	H	Y	488.0	H	Y	5.90		Y
		VISIT 13 (WEEK 25)	5.61		Y	146.0		Y	5.80		Y
		VISIT 14 (WEEK 34)	6.27		Y	610.0	H	Y	6.00		Y
		VISIT 23 (WEEK 43)	5.50		Y	138.0		Y	5.80		Y
		VISIT 25 (WEEK 54)	5.50		Y	95.0		Y	5.80		Y
		VISIT 26 (WEEK 64)	6.16		Y	123.0		Y	5.90		Y
		VISIT 27 (WEEK 76)	5.83		Y	176.0		Y	5.70		Y
		VISIT 28 (WEEK 87)	5.55		Y	165.0		Y	5.80		Y
Norditropin/Norditropin/ NN8640-4054-EXT/ 216002	M/55/31.3	VISIT 1B (WEEK -3)	6.61	H	Y	146.0		Y	5.60		Y
		VISIT 10 (WEEK 8)	6.22		Y	90.0		Y	5.70		Y
		VISIT 12 (WEEK 17)	6.88	H	Y	100.0		Y	5.90		Y

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@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Norditropin/Norditropin/ NN8640-4054-EXT/ 216002	M/55/31.3	VISIT 13 (WEEK 25)	6.61	H	Y	95.0		Y	6.00		Y
		VISIT 14 (WEEK 34)	6.88	H	Y	213.0	H	Y	6.20	H	Y
		VISIT 23 (WEEK 43)	6.49	H	Y	71.0		Y	6.00		Y
		VISIT 25 (WEEK 54)	6.44	H	Y	74.0		Y	6.30	H	Y
		VISIT 26 (WEEK 64)	6.61	H	Y	91.0		Y	6.00		Y
		VISIT 27 (WEEK 76)	6.99	H	Y	67.0		Y	6.40	H	Y
		VISIT 28 (WEEK 87)	6.33		Y	75.0		Y	6.50	H	Y
Norditropin/Norditropin/ NN8640-4054-EXT/ 410002	M/65/38.7	VISIT 1B (WEEK -3)	7.33	H	Y	188.0		Y	6.60	H	Y
		VISIT 10 (WEEK 8)	6.49	H	Y	156.0		Y	7.20	H	Y
		VISIT 12 (WEEK 17)	7.33	H	Y	253.0	H	Y	7.20	H	Y
		VISIT 13 (WEEK 25)	6.94	H	Y	227.0	H	Y	7.00	H	Y
		VISIT 14 (WEEK 34)	6.11		Y	137.0		Y	6.90	H	Y
		VISIT 23 (WEEK 43)	8.72	H	Y	193.0		Y	7.60	H	Y
		VISIT 25 (WEEK 54)	8.16	H	Y	158.0		Y	8.30	H	Y
		VISIT 26 (WEEK 64)	6.72	H	Y	188.0		Y	7.30	H	Y
		VISIT 27 (WEEK 76)	6.99	H	Y	183.0		Y	6.70	H	Y
		VISIT 28 (WEEK 87)	5.77		Y	.		Y	6.50	H	Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Norditropin/Norditropin/ NN8640-4054-EXT/ 902003**	M/77/27.0	VISIT 1B (WEEK -3)	6.11		Y	60.0		Y	6.20	H	Y
		VISIT 10 (WEEK 8)	6.27		Y	65.0		Y	6.10	H	Y
		VISIT 12 (WEEK 17)	5.22		Y	56.0		Y	6.30	H	Y
		VISIT 13 (WEEK 25)	5.38		Y	70.0		Y	6.30	H	Y
		VISIT 14 (WEEK 34)	5.38		Y	82.0		Y	6.20	H	Y
		VISIT 23 (WEEK 43)	5.22		Y	56.0		Y	6.00		Y
		VISIT 25 (WEEK 54)	5.50		Y	53.0		Y	6.50	H	Y
		VISIT 26 (WEEK 64)	4.94		Y	26.0		Y	6.30	H	Y
		VISIT 27 (WEEK 76)	10.1	H	Y	295.0	H	Y	6.30	H	Y
		VISIT 28 (WEEK 87)	7.77	H	Y	94.0		Y	6.40	H	Y
Norditropin/Somapacitan/ NN8640-4054-EXT/ 104003**	M/68/40.7	VISIT 1B (WEEK -3)	6.16		Y	143.0		Y	6.50	H	Y
		VISIT 10 (WEEK 8)	8.10	H	Y	268.0	H	Y	6.40	H	Y
		VISIT 12 (WEEK 17)	7.66	H	Y	238.0	H	Y	6.50	H	Y
		VISIT 13 (WEEK 25)	7.11	H	Y	194.0		Y	6.50	H	Y
		VISIT 14 (WEEK 34)	6.55	H	Y	139.0		Y	5.80		Y
		VISIT 23 (WEEK 43)	8.16	H	Y	275.0	H	Y	6.20	H	Y
		VISIT 25 (WEEK 54)	6.66	H	Y	228.0	H	Y	6.40	H	Y
		VISIT 26 (WEEK 64)	7.66	H	Y	174.0		Y	6.20	H	Y

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@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Norditropin/Somapacitan/ NN8640-4054-EXT/ 104003**	M/68/40.7	VISIT 27 (WEEK 76)	7.77	H	Y	182.0		Y	6.40	H	Y
		VISIT 28 (WEEK 87)	7.88	H	Y	249.0	H	Y	6.60	H	Y
Norditropin/Somapacitan/ NN8640-4054-EXT/ 108007	F/44/24.6	VISIT 1B (WEEK -3)	4.72		Y	49.0		Y	6.30	H	Y
		VISIT 10 (WEEK 8)	5.38		Y	55.0		Y	6.30	H	Y
		VISIT 12 (WEEK 17)	5.33		Y	80.0		Y	6.80	H	Y
		VISIT 13 (WEEK 25)	6.16		Y	80.0		Y	7.00	H	Y
		VISIT 14 (WEEK 34)	5.88		Y	76.0		Y	6.70	H	Y
		VISIT 23 (WEEK 43)	5.44		Y	56.0		Y	6.50	H	Y
		VISIT 25 (WEEK 54)	5.50		Y	60.0		Y	6.40	H	Y
		VISIT 26 (WEEK 64)	5.44		Y	89.0		Y	6.60	H	Y
		VISIT 27 (WEEK 76)	5.38		Y	60.0		Y	6.70	H	Y
		VISIT 28 (WEEK 87)	5.44		Y	74.0		Y	6.60	H	Y
Norditropin/Somapacitan/ NN8640-4054-EXT/ 901001**	F/34/27.2	VISIT 1B (WEEK -3)	4.77		Y	110.0		Y	6.40	H	Y
		VISIT 10 (WEEK 8)	8.72	H	Y	245.0	H	Y	6.50	H	Y
		VISIT 12 (WEEK 17)	7.33	H	Y	187.0		Y	6.10	H	Y

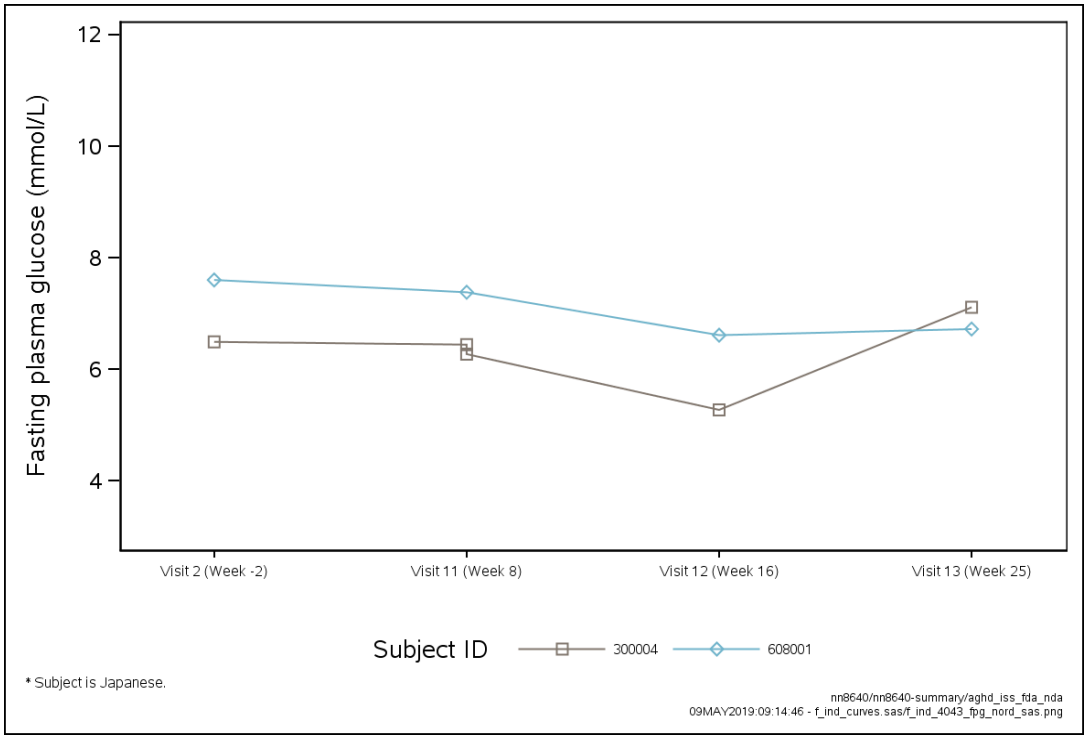
BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

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

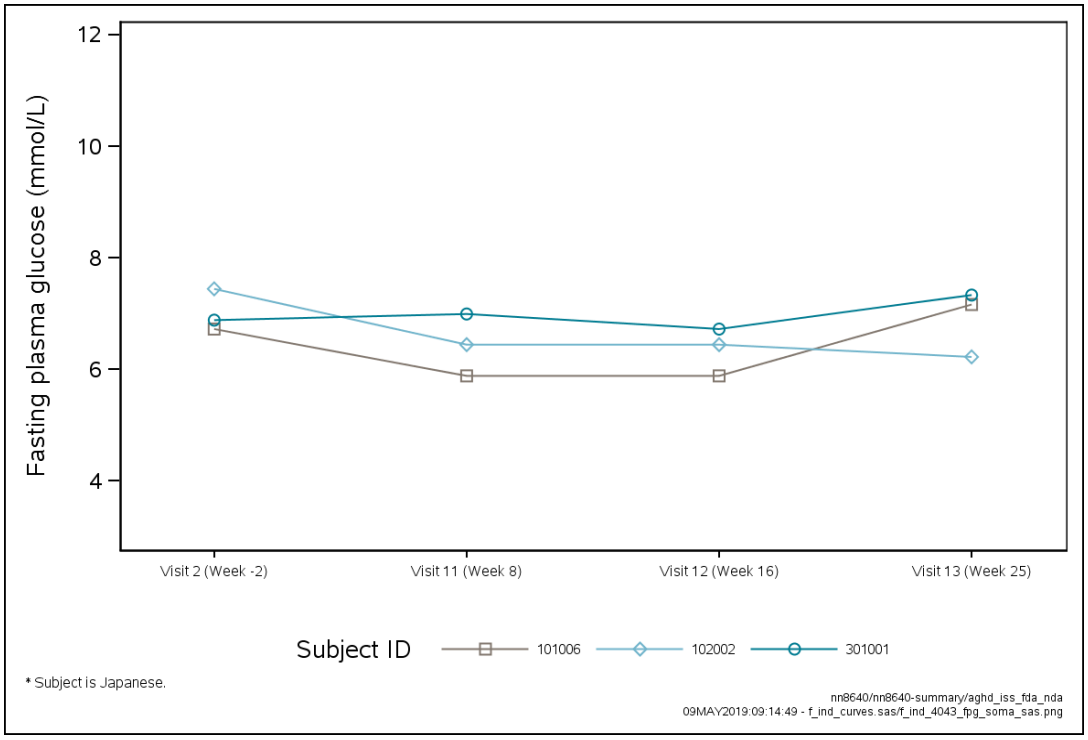
Treatment/ trial id/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	Visit	Fasting plasma glucose (mmol/L)	@	@@	Fasting insulin (pmol/L)	@	@@	HbA1c (%)	@	@@
Norditropin/Somapacitan/ NN8640-4054-EXT/ 901001**	F/34/27.2	VISIT 13 (WEEK 25)	6.16		Y	290.0	H	Y	.		Y
		VISIT 14 (WEEK 34)	5.88		Y	175.0		Y	.		Y
		VISIT 23 (WEEK 43)	4.66		Y	117.0		Y	6.00		Y
		VISIT 25 (WEEK 54)	5.66		Y	147.0		Y	6.30	H	Y
		VISIT 26 (WEEK 64)	4.94		Y	92.0		Y	6.60	H	Y
		VISIT 27 (WEEK 76)	6.38		Y	117.0		Y	7.20	H	Y
		VISIT 28 (WEEK 87)	5.16		Y	52.0		Y	7.00	H	Y
Norditropin/No Treatment / NN8640-4054-EXT/ 216003	M/60/28.0	VISIT 1B (WEEK -3)	5.94		Y	226.0	H	Y	6.10	H	Y
		VISIT 10 (WEEK 8)	6.61	H	Y	367.0	H	Y	5.90		Y
		VISIT 12 (WEEK 17)	6.83	H	Y	358.0	H	Y	6.00		Y
		VISIT 13 (WEEK 25)	7.33	H	Y	560.0	H	Y	6.50	H	Y
		VISIT 14 (WEEK 34)	5.88		Y	119.0		Y	6.20	H	Y
		VISIT 25 (WEEK 54)	5.55		Y	106.0		Y	5.70		Y
		VISIT 26 (WEEK 64)	6.16		Y	209.0	H	Y	5.90		Y

BMI: Body mass index, F: Female, M: Male, yrs: Years
@ compared to reference ranges: L (low) = below reference range, H (high) = above reference range.
@@ Fasting (Y/N).
* This value was not included in descriptive statistics for this visit due to rescheduling.
**Diabetes mellitus diagnosis present at randomisation.

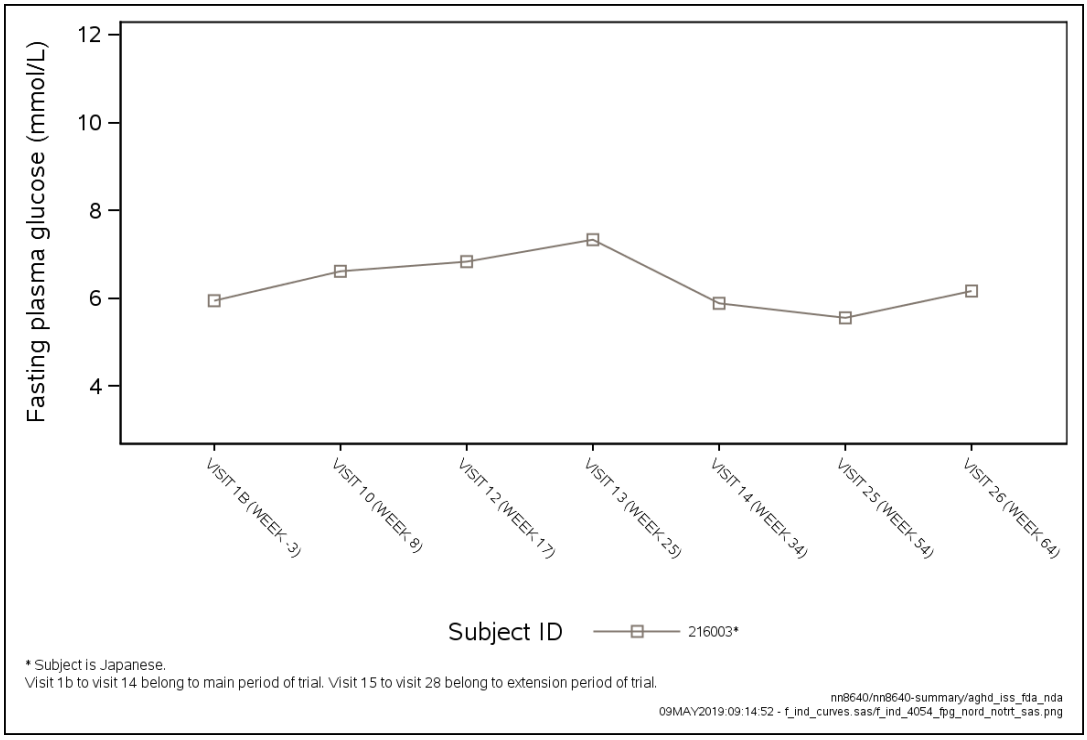
76 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4043 - Norditropin - safety analysis set



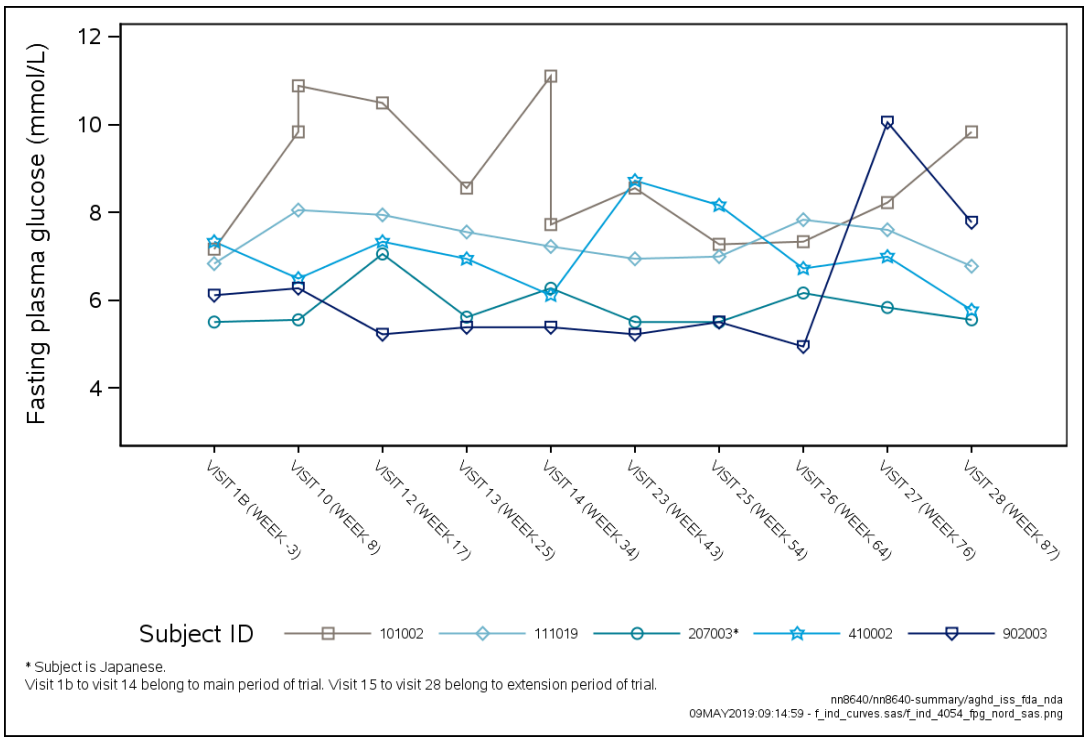
77 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4043 - somapacitan - safety analysis set



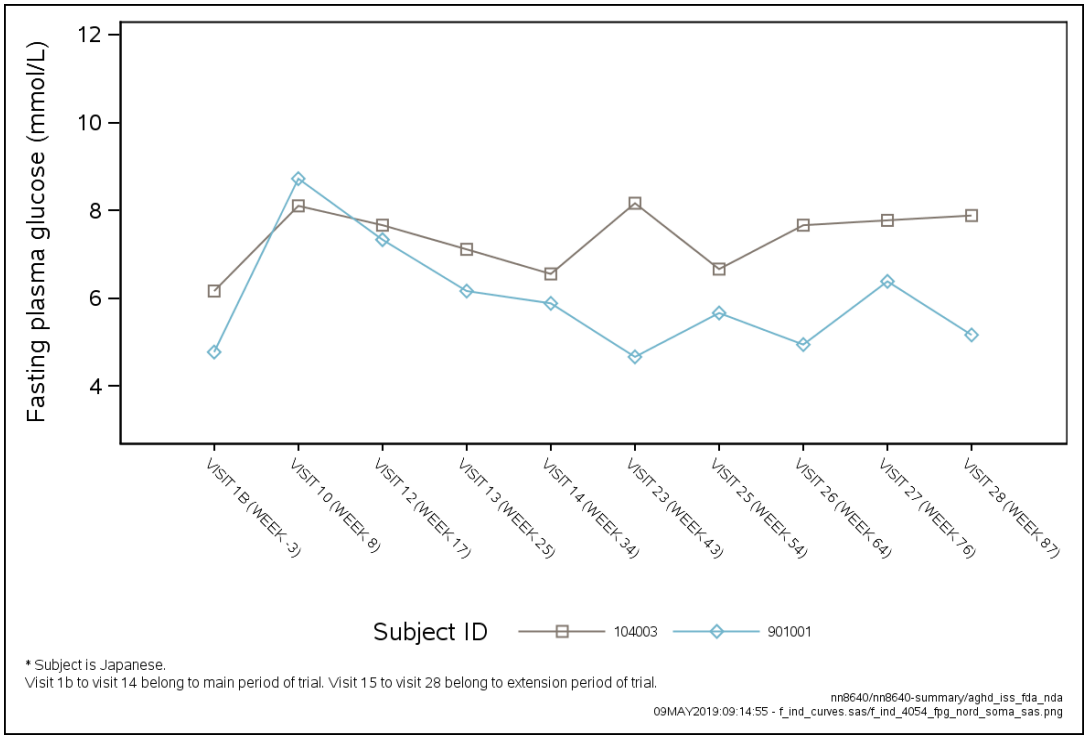
78 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4054 - Norditropin/no treatment - safety analysis set



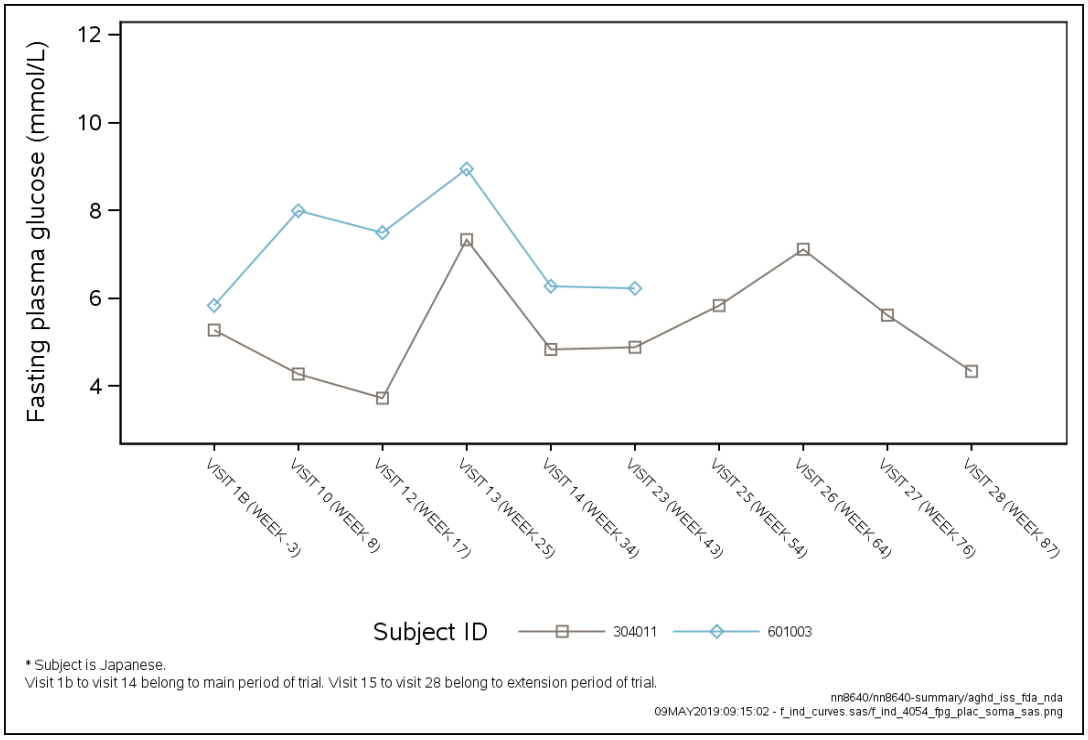
79 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4054 - Norditropin/Norditropin - safety analysis set



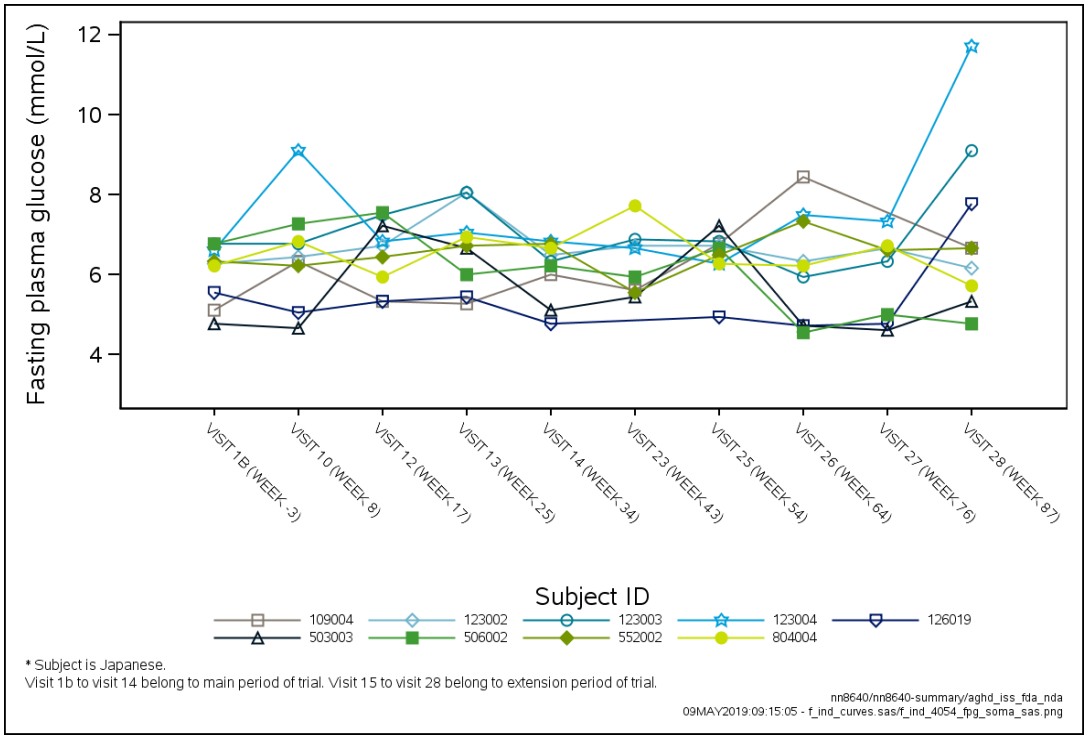
80 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4054 - Norditropin/somapacitan - safety analysis set



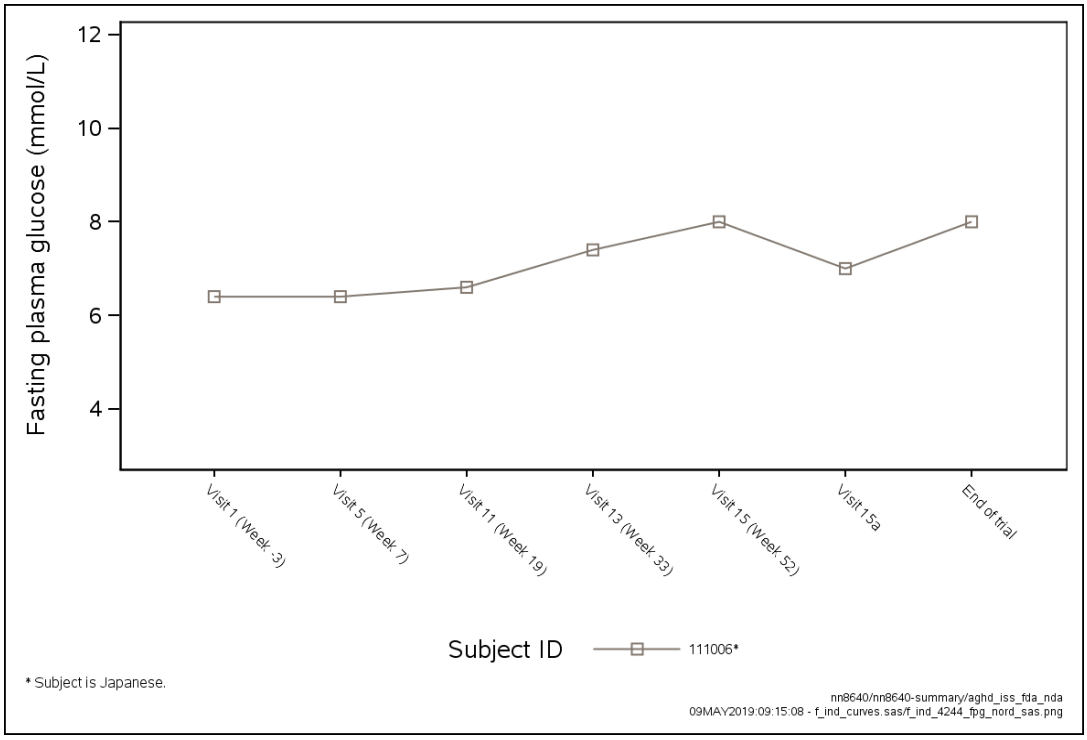
81 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4054 - placebo/somapacitan - safety analysis set



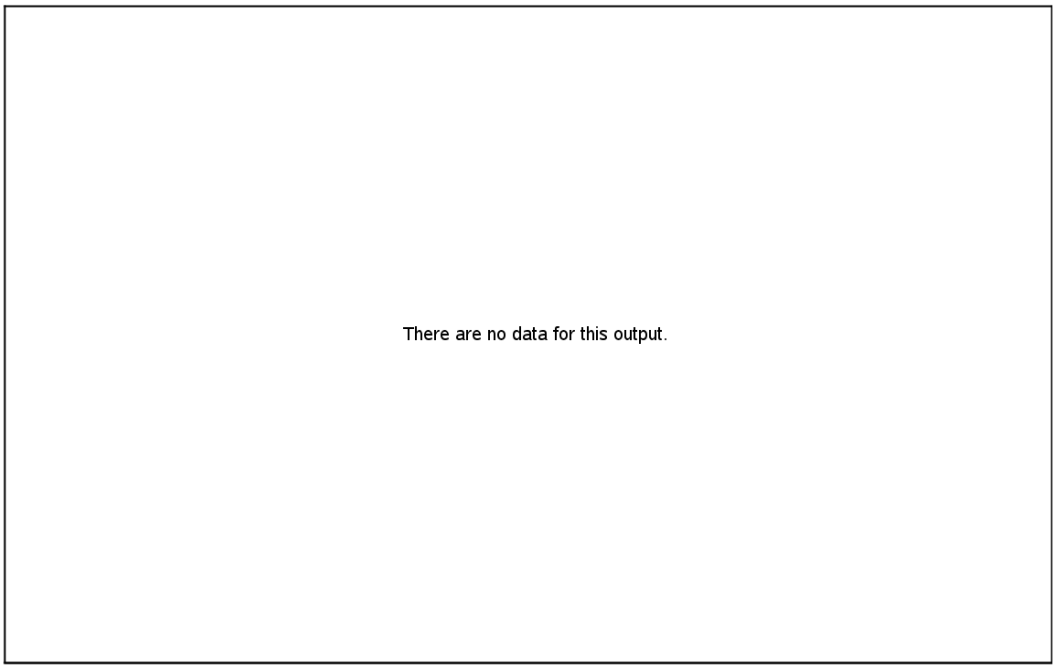
82 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4054 - somapacitan/somapacitan - safety analysis set



83 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4244 - Norditropin - safety analysis set

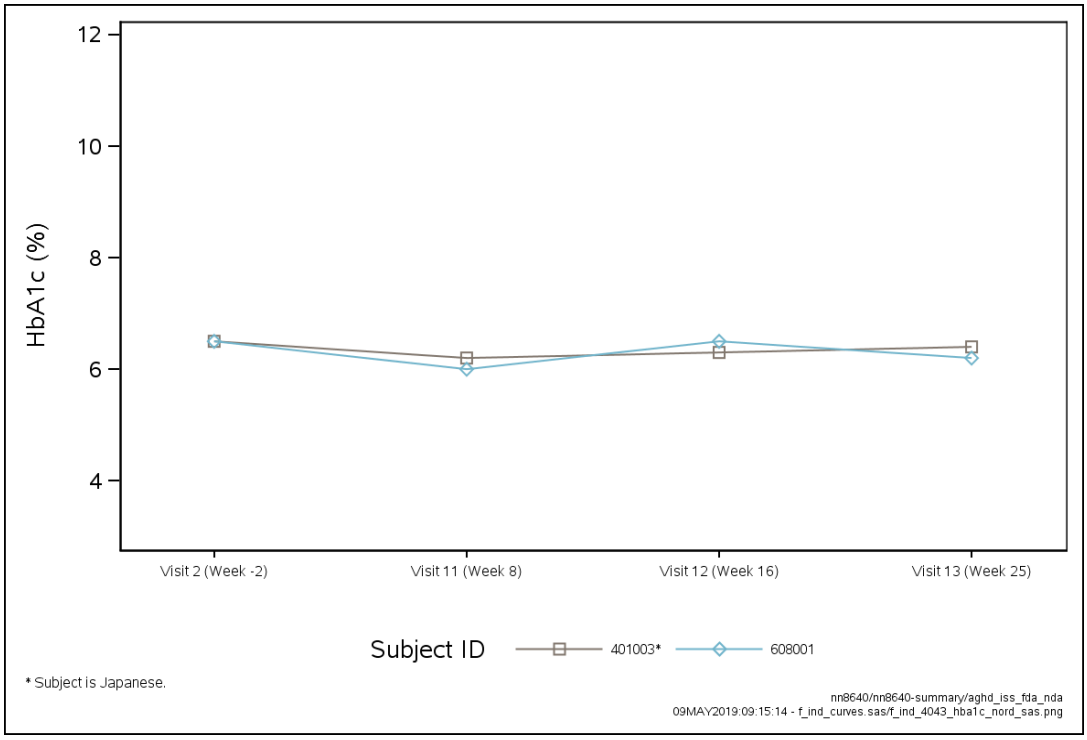


84 Fasting plasma glucose (mmol/L) - Individual curves - subjects who have FPG>=7 mmol/L during trial - 4244 - somapacitan - safety analysis set

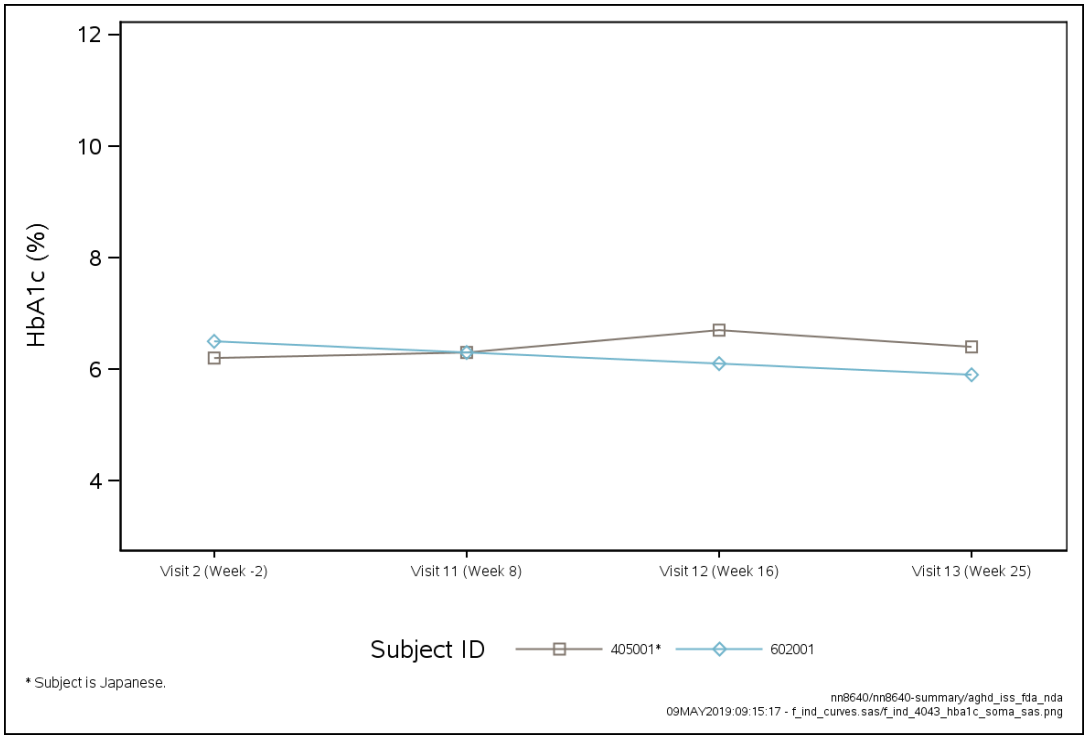


nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:15:11 - f_ind_curves.sas/f_ind_4244_fpg_soma_sas.png

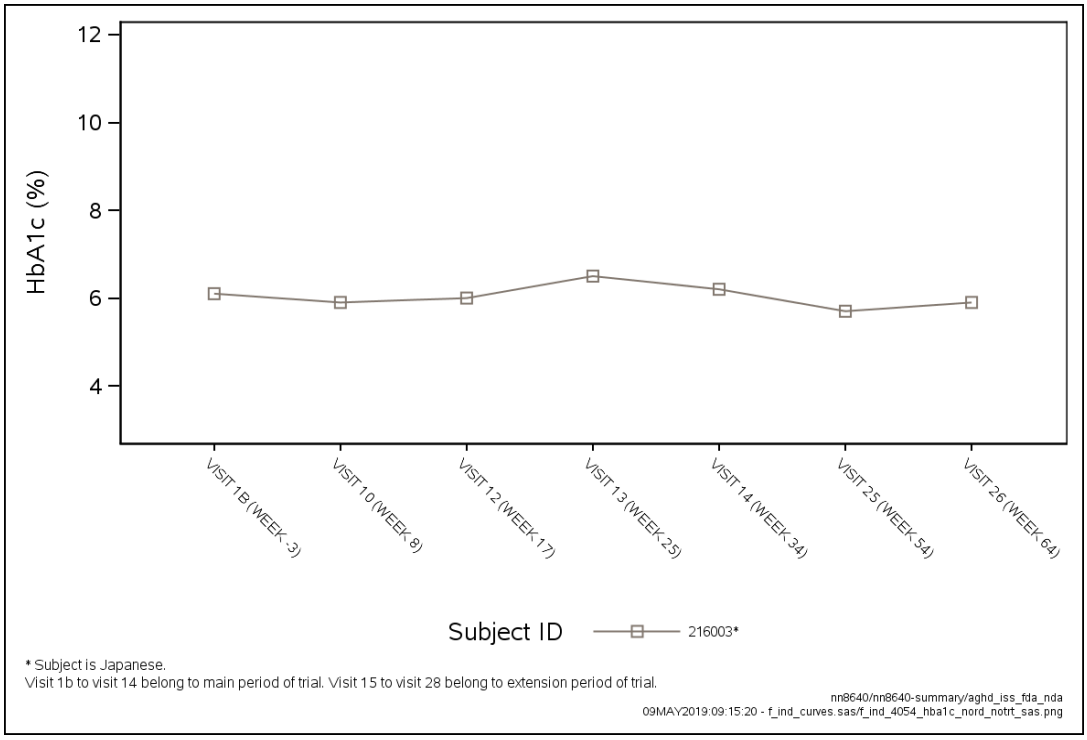
85 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4043 - Norditropin - safety analysis set



86 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4043 - somapacitan - safety analysis set



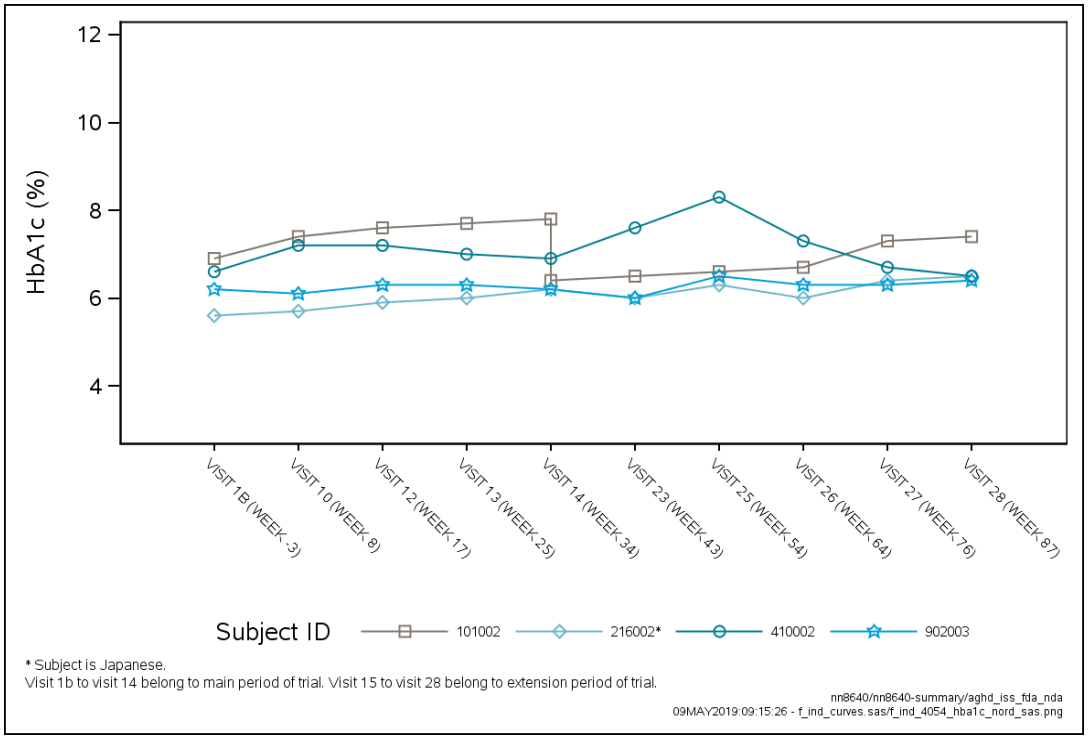
87 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4054 - Norditropin/no treatment - safety analysis set



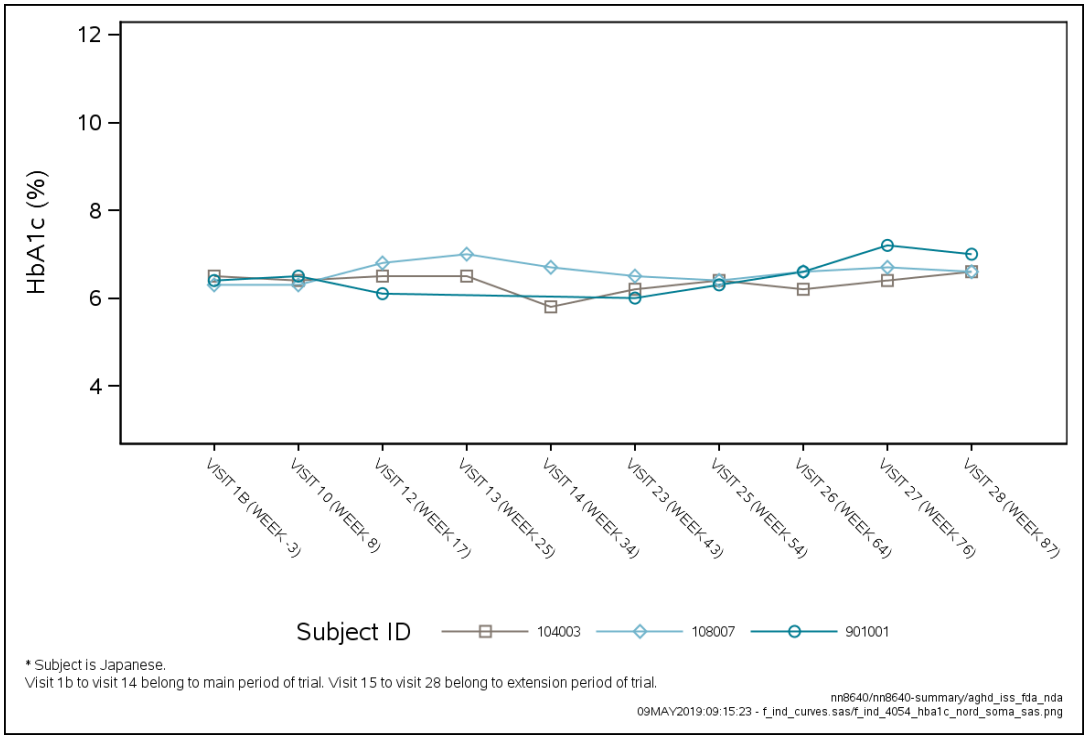
* Subject is Japanese.
Visit 1b to visit 14 belong to main period of trial. Visit 15 to visit 28 belong to extension period of trial.

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:15:20 - f_ind_curves.sas/f_ind_4054_hba1c_nord_notrt_sas.png

88 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4054 - Norditropin/Norditropin - safety analysis set



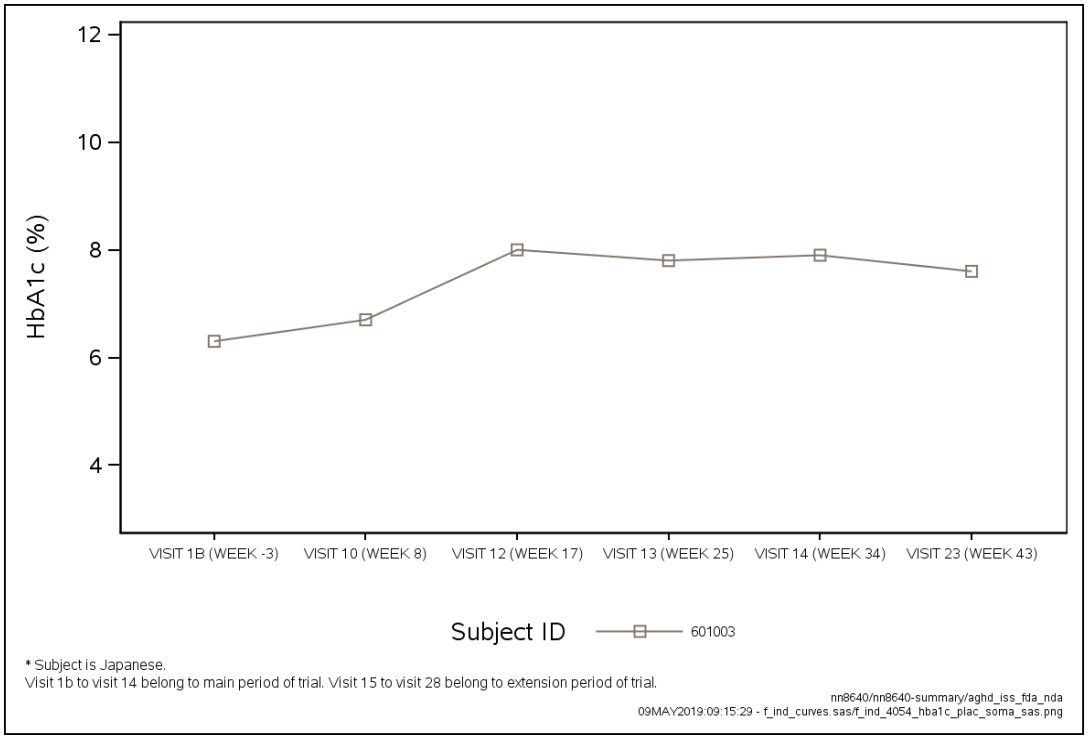
89 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4054 - Norditropin/somapacitan - safety analysis set



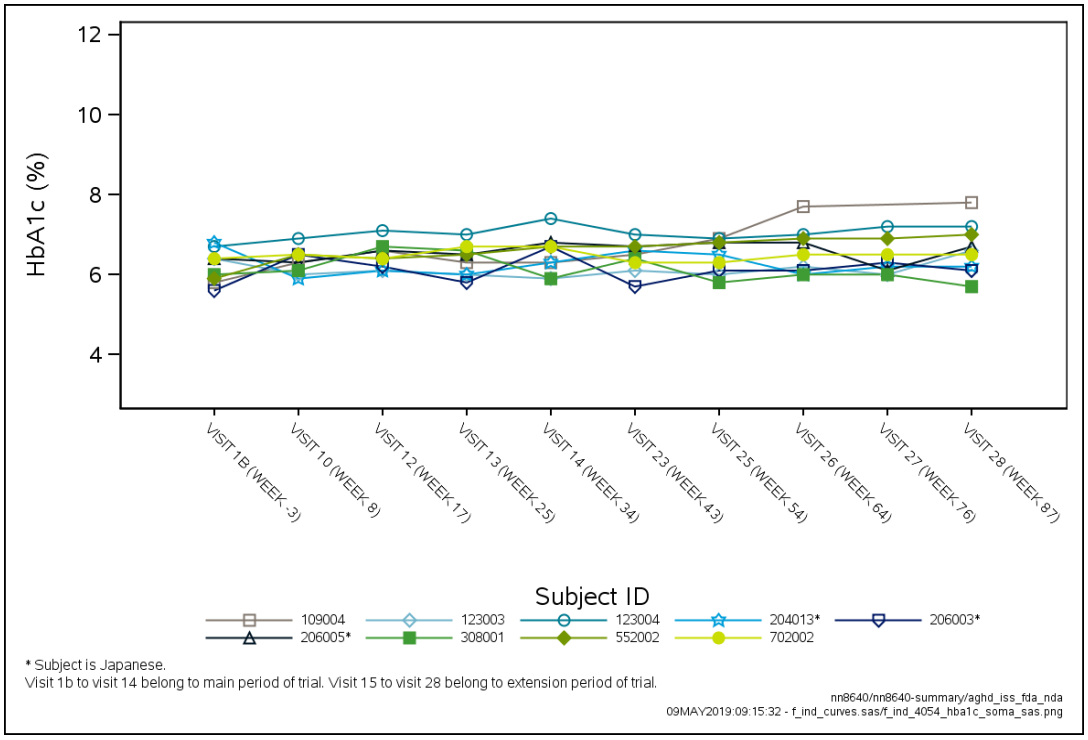
* Subject is Japanese.
Visit 1b to visit 14 belong to main period of trial. Visit 15 to visit 28 belong to extension period of trial.

nn8640/nn8640-summary/aghd_iss_fda_nda
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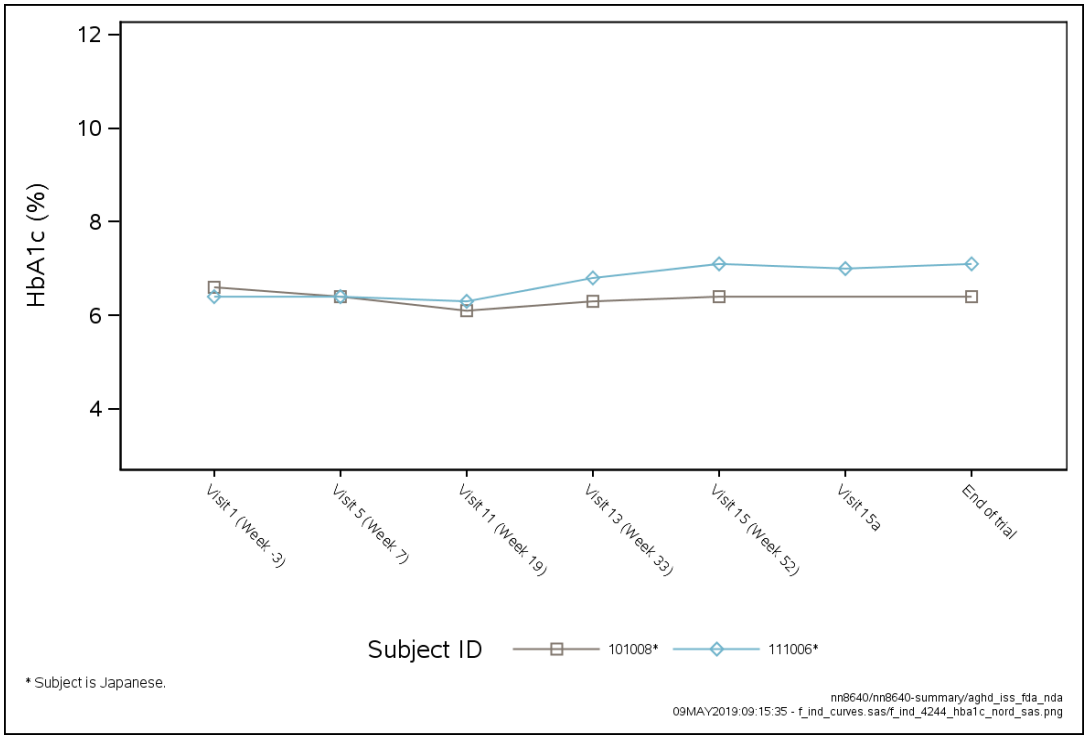
90 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4054 - placebo/somapacitan - safety analysis set



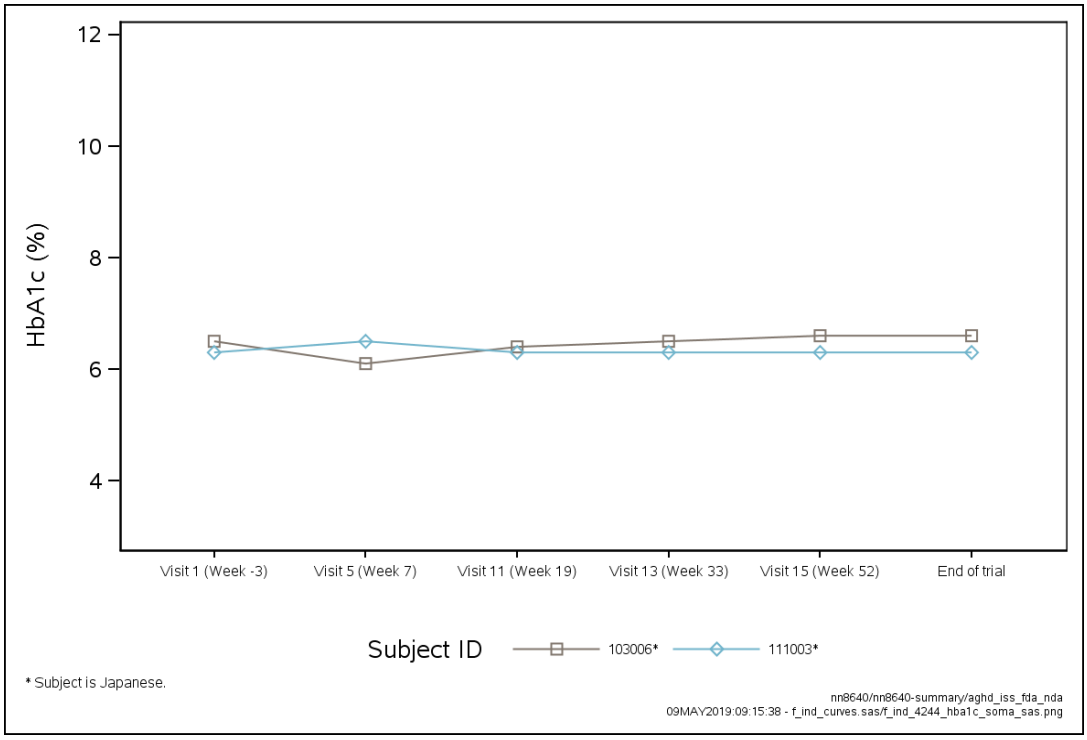
91 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4054 - somapacitan/somapacitan - safety analysis set



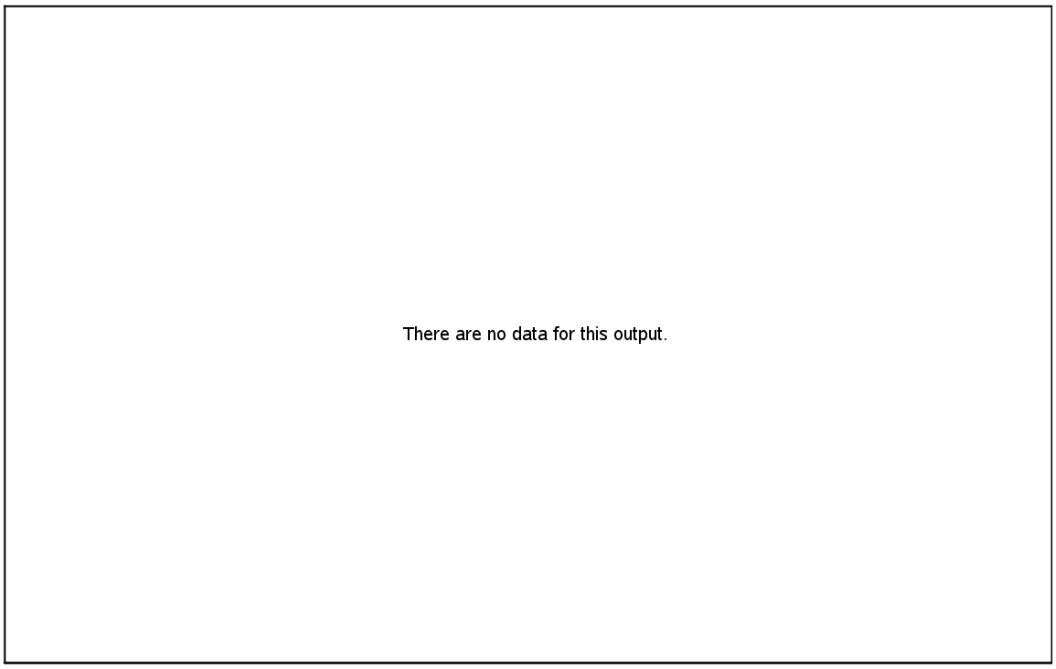
92 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4244 - Norditropin - safety analysis set



93 HbA1c (%) - Individual curves - subjects who have HBA1C>=6.5% during trial - 4244 - somapacitan - safety analysis set

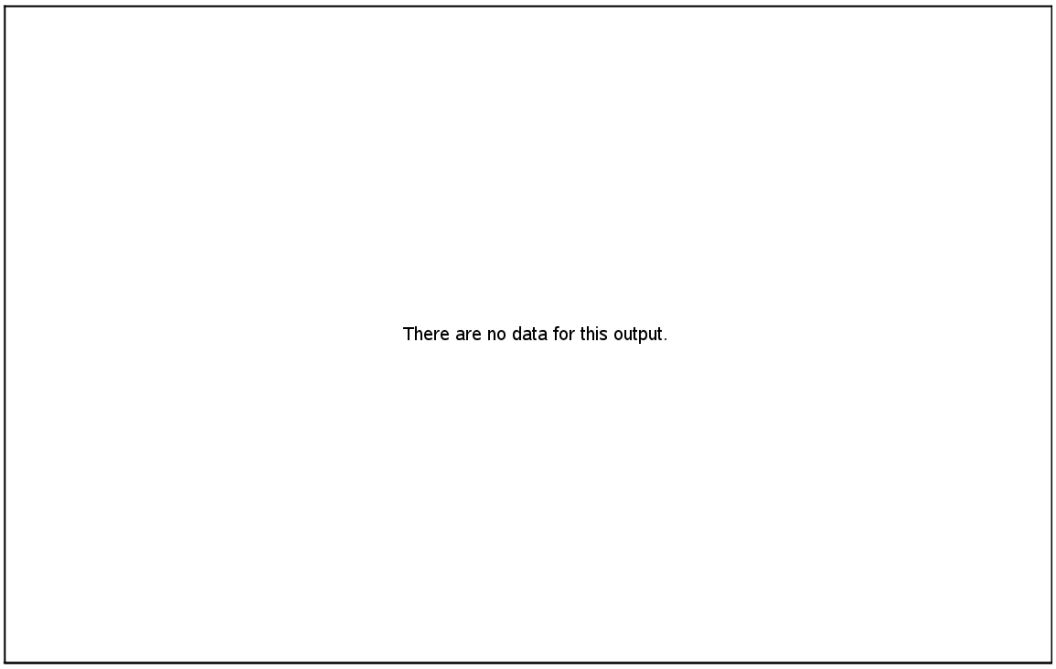


94 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4043 - Norditropin - safety analysis set



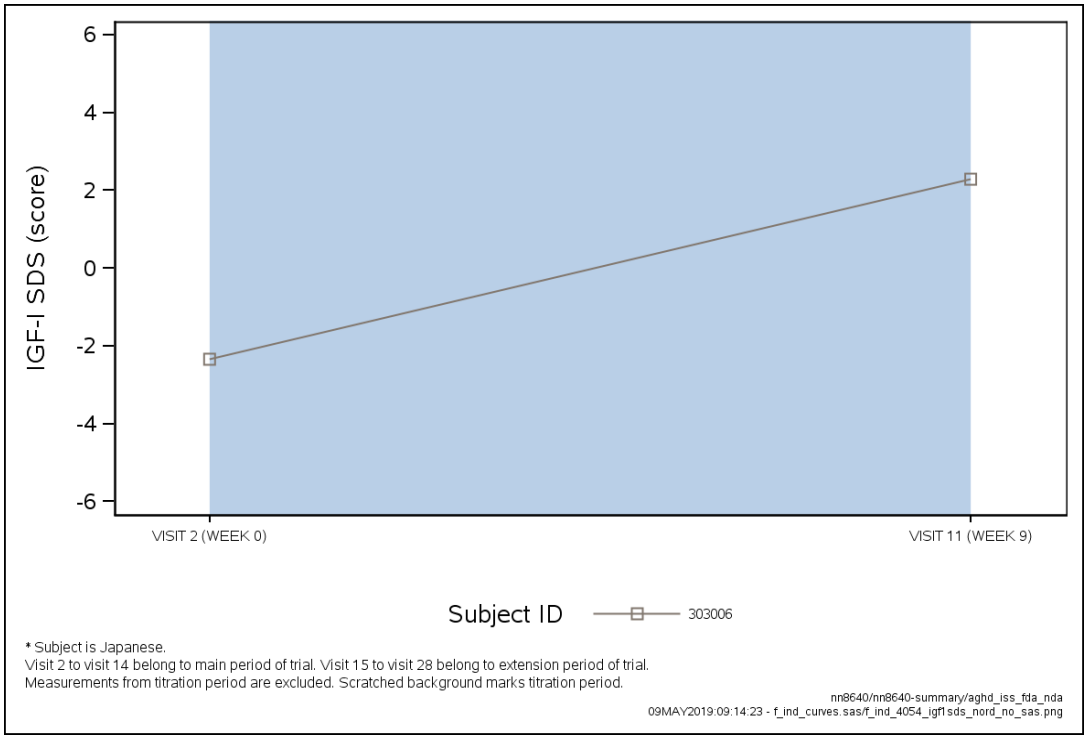
nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:14:14 - f_ind_curves.sas/f_ind_4043_igf1sds_nord_sas.png

95 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4043 - somapacitan - safety analysis set

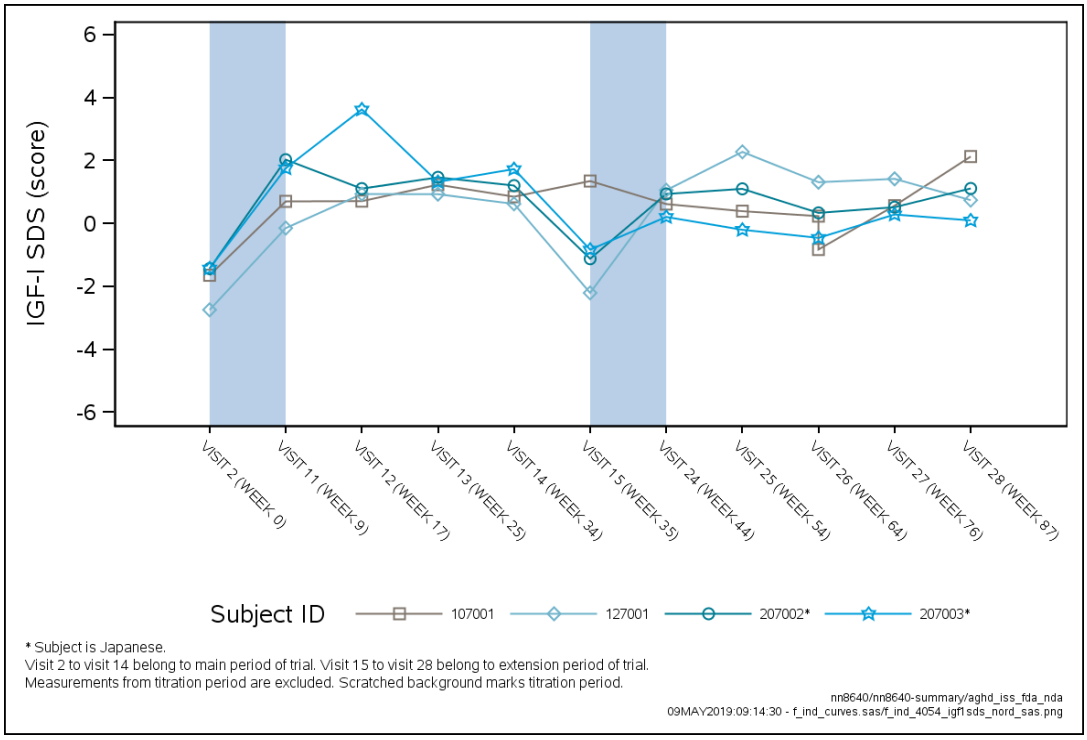


nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:14:20 - f_ind_curves.sas/f_ind_4043_igf1sds_soma_sas.png

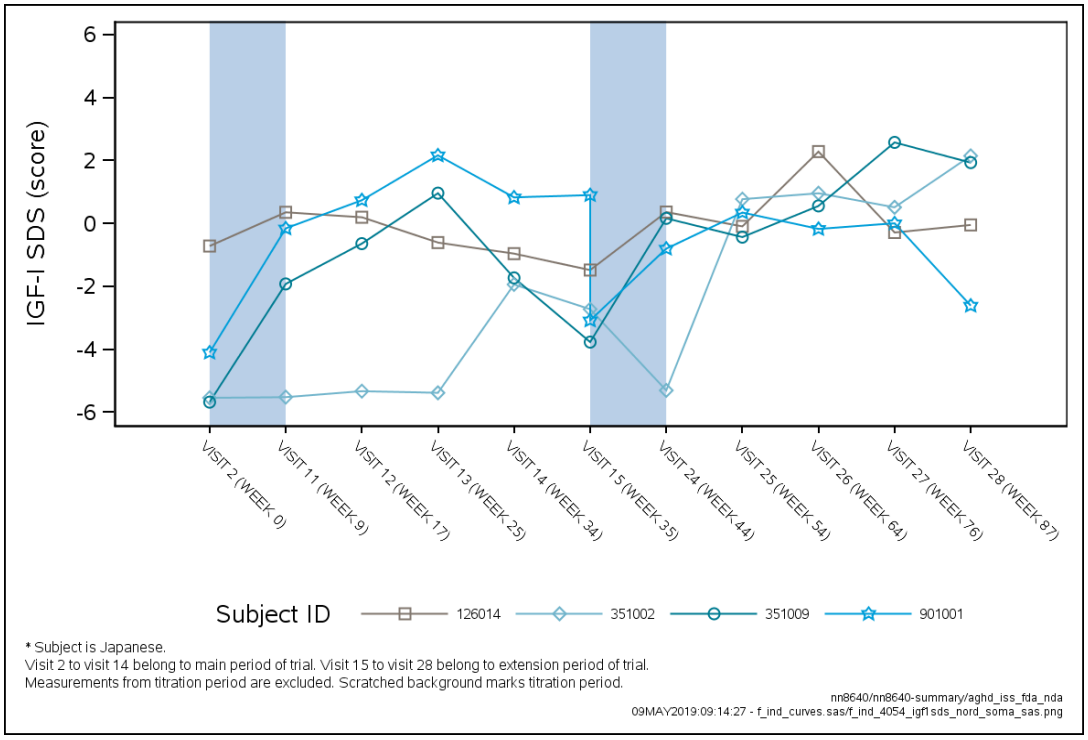
96 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4054 - Norditropin/no treatment - safety analysis set



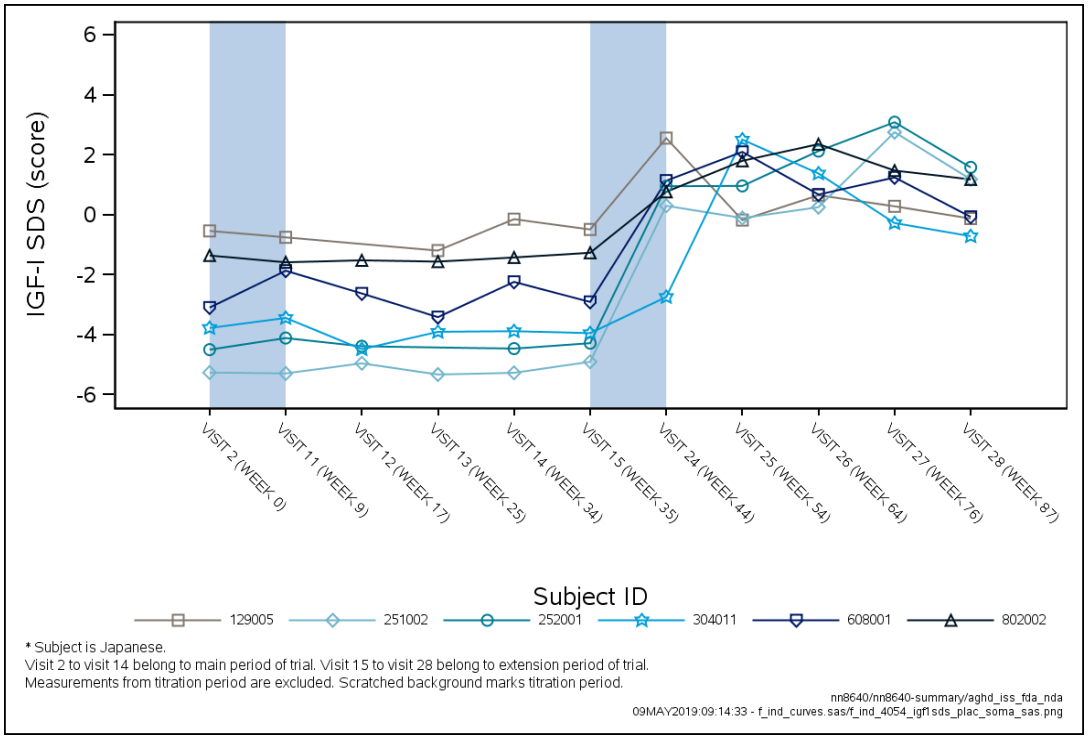
97 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4054 - Norditropin/Norditropin - safety analysis set



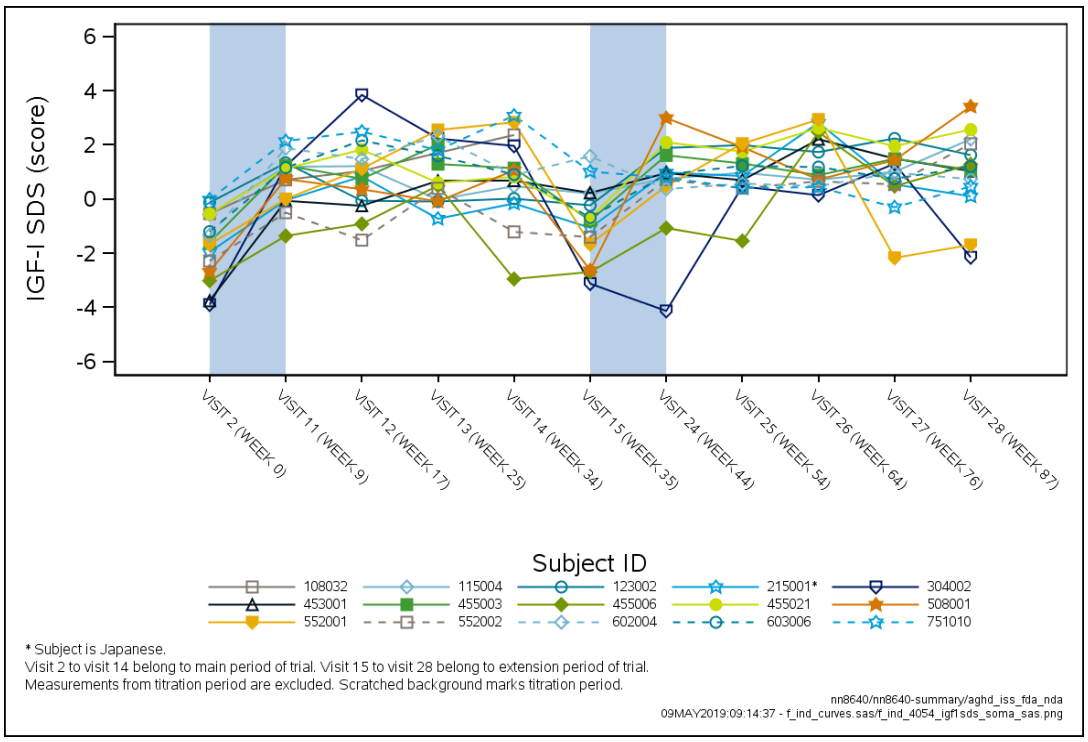
98 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4054 - Norditropin/somapacitan - safety analysis set



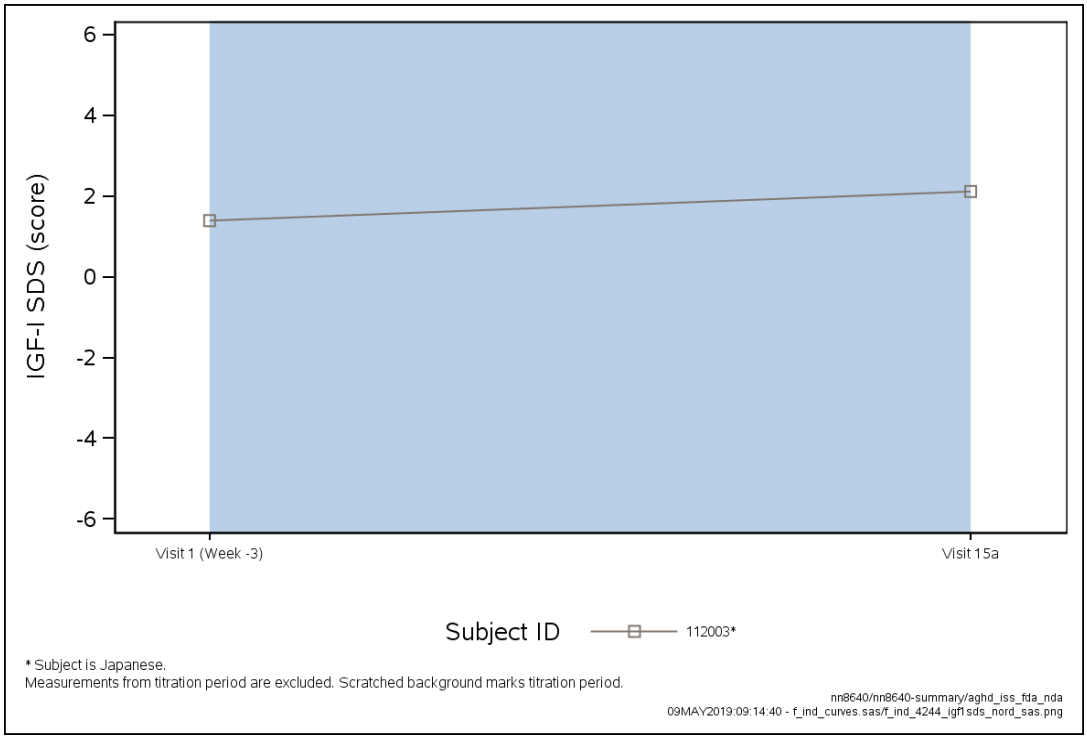
99 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4054 - placebo/somapacitan - safety analysis set



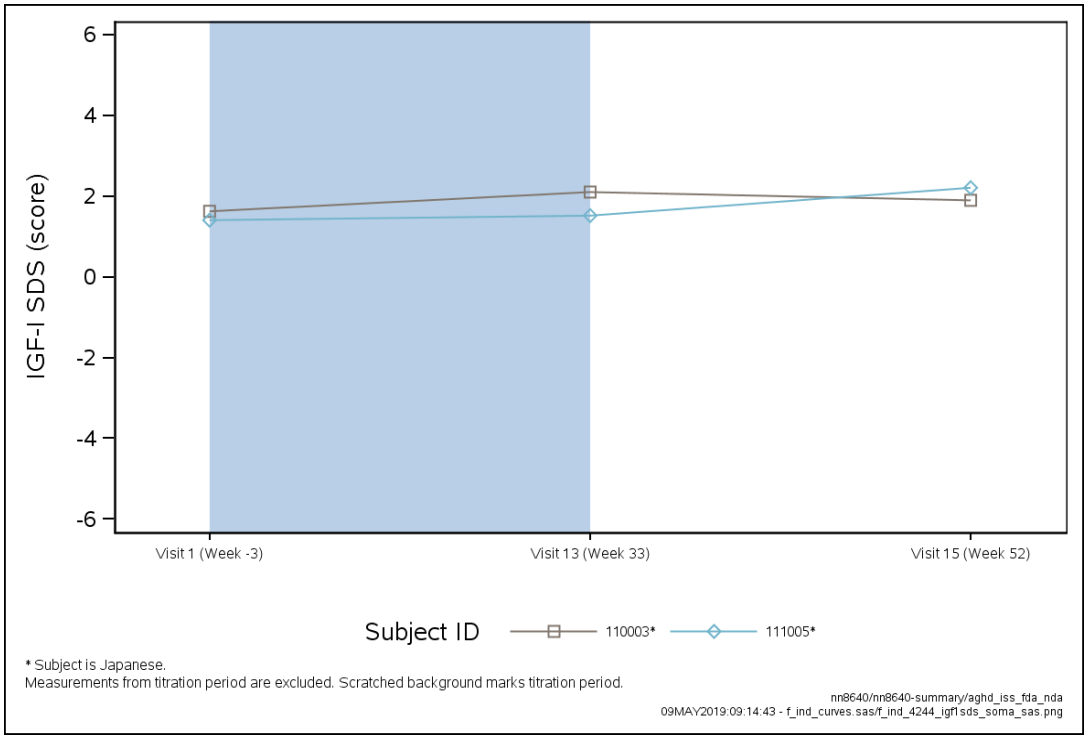
100 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4054 - somapacitan/somapacitan - safety analysis set



101 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4244 - Norditropin - safety analysis set



102 IGF-I SDS (score) - Individual curves - subjects who have IGF-I SDS>2 during maintenance period - 4244 - somapacitan - safety analysis set



103 Summary of exposure - Norditropin/somapacitan pool - safety analysis set

	Norditropin	somapacitan
	once daily	once weekly
Number of exposed subjects	166	227
Days of exposure*		
Mean (SD)	226 (64.5)	243 (71.3)
Median	237	238
Min; Max	1; 364	7; 364
Treatment dose** (mg)		
Mean (SD)	0.29 (0.19)	2.26 (1.48)
Median	0.25	1.70
Min; Max	0.05; 1.10	0.10; 8.00
Treatment dose** (mg/kg)		
Mean (SD)	0.005 (0.004)	0.033 (0.026)
Median	0.003	0.025
Min; Max	0.001; 0.044	0.001; 0.141
Total Exposure*** (years)	102.9	151.2

SD: Standard deviation
* Exposure days are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan.
** Stable dose at last titration visit. For subjects in 4054 receiving same treatment in main and extension period, only first titration period is included.
*** Including titration period.
Norditropin/somapacitan pool includes subjects exposed to Norditropin or somapacitan treatment in 4043, 4244 and 4054 main trial.

104 Summary of baseline characteristics - Norditropin/somapacitan pool - full analysis set

	Norditropin	Somapacitan	Total
Number of Subjects	166	227	393
Age (years), N	166	227	393
Mean (SD)	47.2 (15.5)	47.4 (14.8)	47.3 (15.1)
Median	47.0	47.0	47.0
Min ; Max	20.0 ; 77.0	19.0 ; 77.0	19.0 ; 77.0
Agegroup, N (%)	166 (100.0)	227 (100.0)	393 (100.0)
18 - 64 years	138 (83.1)	191 (84.1)	329 (83.7)
>= 65 years	28 (16.9)	36 (15.9)	64 (16.3)
Sex, N (%)	166 (100.0)	227 (100.0)	393 (100.0)
Female	82 (49.4)	112 (49.3)	194 (49.4)
Male	84 (50.6)	115 (50.7)	199 (50.6)
Ethnicity, N (%)	166 (100.0)	227 (100.0)	393 (100.0)
Hispanic Or Latino	8 (4.8)	6 (2.6)	14 (3.6)
Not Hispanic Or Latino	149 (89.8)	208 (91.6)	357 (90.8)
NA	9 (5.4)	13 (5.7)	22 (5.6)
Race, N (%)	166 (100.0)	227 (100.0)	393 (100.0)
Asian	58 (34.9)	92 (40.5)	150 (38.2)
White	94 (56.6)	118 (52.0)	212 (53.9)
Black Or African American	3 (1.8)	2 (0.9)	5 (1.3)
Native Hawaiian Or Other Pacific Islander	0	1 (0.4)	1 (0.3)
Other	2 (1.2)	1 (0.4)	3 (0.8)
NA	9 (5.4)	13 (5.7)	22 (5.6)
Country, N (%)	166 (100.0)	227 (100.0)	393 (100.0)
Australia	10 (6.0)	13 (5.7)	23 (5.9)
Denmark	6 (3.6)	16 (7.0)	22 (5.6)
France	7 (4.2)	13 (5.7)	20 (5.1)
Germany	8 (4.8)	11 (4.8)	19 (4.8)
India	11 (6.6)	11 (4.8)	22 (5.6)
Japan	40 (24.1)	75 (33.0)	115 (29.3)
Latvia	1 (0.6)	0	1 (0.3)
Lithuania	3 (1.8)	1 (0.4)	4 (1.0)
Malaysia	3 (1.8)	4 (1.8)	7 (1.8)
Poland	2 (1.2)	8 (3.5)	10 (2.5)
Romania	14 (8.4)	12 (5.3)	26 (6.6)
Russian Federation	6 (3.6)	7 (3.1)	13 (3.3)
South Africa	4 (2.4)	4 (1.8)	8 (2.0)
Sweden	6 (3.6)	4 (1.8)	10 (2.5)
Turkey	1 (0.6)	4 (1.8)	5 (1.3)
Ukraine	1 (0.6)	3 (1.3)	4 (1.0)
United Kingdom	9 (5.4)	10 (4.4)	19 (4.8)
United States	34 (20.5)	31 (13.7)	65 (16.5)
Height (m), N	166	227	393
Mean (SD)	1.65 (0.13)	1.65 (0.11)	1.65 (0.12)
Median	1.65	1.65	1.65
Min ; Max	1.07 ; 1.93	1.30 ; 1.94	1.07 ; 1.94
Body Weight (kg), N	166	227	393
Mean (SD)	76.2 (21.9)	76.4 (20.9)	76.3 (21.3)
Median	74.3	74.0	74.1
Min ; Max	22.5 ; 151	34.5 ; 151	22.5 ; 151

N: Number of subjects, %: Percentage of subjects, SD: Standard deviation
Norditropin/somapacitan pool includes subjects exposed to Norditropin or somapacitan treatment in 4043, 4244 and 4054 main trial.

Summary of baseline characteristics - Norditropin/somapacitan pool - full analysis set

	Norditropin	Somapacitan	Total
BMI (kg/m^2), N	166	227	393
Mean (SD)	27.6 (5.9)	27.8 (6.1)	27.7 (6.0)
Median	26.8	27.0	26.8
Min ; Max	17.0 ; 45.0	17.0 ; 51.9	17.0 ; 51.9
Waist circumference (cm), N	119	120	239
Mean (SD)	94.3 (16.6)	93.9 (15.1)	94.1 (15.8)
Median	94.6	92.9	93.6
Min ; Max	45.3 ; 153	63.5 ; 141	45.3 ; 153
GHD Onset, N (%)	166 (100.0)	227 (100.0)	393 (100.0)
Childhood-Idiopathic	25 (15.1)	31 (13.7)	56 (14.2)
Childhood-Organic	20 (12.0)	40 (17.6)	60 (15.3)
Adulthood	121 (72.9)	156 (68.7)	277 (70.5)
Diabetes Mellitus, N (%)	166 (100.0)	227 (100.0)	393 (100.0)
Diabetic	7 (4.2)	7 (3.1)	14 (3.6)
Non-Diabetic	159 (95.8)	220 (96.9)	379 (96.4)

N: Number of subjects, %: Percentage of subjects, SD: Standard deviation
Norditropin/somapacitan pool includes subjects exposed to Norditropin or somapacitan treatment in 4043, 4244 and 4054 main trial.

105 Adverse events - Cochran-Mantel-Haenszel adjusted vs Naïve - Norditropin/somapacitan pool - safety analysis set

	Norditropin N (%)	E	R	Somapacitan N (%)	E	R	Total N (%)	E	R
Subjects Exposed	166			227			393		
Total patient years	108.0			157.2			265.1		
All adverse events									
Naïve	128 (77.1)	562	520.5	183 (80.6)	692	440.3	311 (79.1)	1254	473.0
CMH adjusted	128 (76.3)	562	508.0	183 (78.4)	692	458.1	311 (78.8)	1254	482.4
Serious adverse events									
Naïve	13 (7.8)	16	14.8	15 (6.6)	20	12.7	28 (7.1)	36	13.6
CMH adjusted	13 (7.4)	16	14.1	15 (6.4)	20	13.5	28 (7.2)	36	14.0
Severity naïve									
Mild	111 (66.9)	391	362.1	161 (70.9)	530	337.2	272 (69.2)	921	347.4
Moderate	51 (30.7)	157	145.4	58 (25.6)	143	91.0	109 (27.7)	300	113.1
Severe	11 (6.6)	14	13.0	12 (5.3)	19	12.1	23 (5.9)	33	12.4
Severity CMH adjusted									
Mild	111 (66.5)	391	359.2	161 (68.4)	530	341.9	272 (68.6)	921	350.0
Moderate	51 (29.4)	157	136.1	58 (26.5)	143	102.9	109 (28.3)	300	119.4
Severe	11 (6.3)	14	12.7	12 (5.6)	19	13.2	23 (6.0)	33	13.0

N: Number of subjects, %: Percentage of exposed subjects having the event, CMH: Cochran-Mantel-Haenszel, E: Number of adverse events reported, R: Event rate per 100 patient years
Proportions and event rates were calculated using the Cochran-Mantel-Haenszel method to account for different exposures in the trials.
If no events are experienced for the subjects in a trial, the subjects contribute with exposure.
The output is based on trials 4244, 4043 and 4054 main period.
MedDRA version 21.0.

106 Serious adverse events - Cochran-Mantel-Haenszel adjusted vs Naïve - Norditropin/somapacitan pool - safety analysis set

	Norditropin			Somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	166			227			393		
Total patient years	108.0			157.2			265.1		
Serious adverse events									
Naïve	13 (7.8)	16	14.8	15 (6.6)	20	12.7	28 (7.1)	36	13.6
CMH adjusted	13 (7.4)	16	14.1	15 (6.4)	20	13.5	28 (7.2)	36	14.0
Severity naïve									
Mild	1 (0.6)	1	0.9	4 (1.8)	4	2.5	5 (1.3)	5	1.9
Moderate	5 (3.0)	5	4.6	6 (2.6)	7	4.5	11 (2.8)	12	4.5
Severe	8 (4.8)	10	9.3	6 (2.6)	9	5.7	14 (3.6)	19	7.2
Severity CMH adjusted									
Mild	1 (0.5)	1	0.8	4 (1.4)	4	2.0	5 (1.2)	5	1.7
Moderate	5 (2.7)	5	4.2	6 (2.8)	7	5.0	11 (2.9)	12	4.8
Severe	8 (4.7)	10	9.1	6 (2.7)	9	6.5	14 (3.7)	19	7.5

N: Number of subjects, %: Percentage of exposed subjects having the event, CMH: Cochran-Mantel-Haenszel, E: Number of adverse events reported, R: Event rate per 100 patient years
Proportions and event rates were calculated using the Cochran-Mantel-Haenszel method to account for different exposures in the trials.
If no events are experienced for the subjects in a trial, the subjects contribute with exposure.
The output is based on trials 4244, 4043 and 4054 main period.
MedDRA version 21.0.

107 Most frequent adverse events (>=5%) by system organ class and preferred term - naive - Norditropin/somapacitan pool - safety analysis set

	Norditropin			Somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	166			227			393		
Total patient years	108.0			157.2			265.1		
General disorders and administration site conditions									
Fatigue	13 (7.8)	13	12.0	9 (4.0)	10	6.4	22 (5.6)	23	8.7
Infections and infestations									
Nasopharyngitis	33 (19.9)	45	41.7	57 (25.1)	88	56.0	90 (22.9)	133	50.2
Upper respiratory tract infection	11 (6.6)	13	12.0	6 (2.6)	7	4.5	17 (4.3)	20	7.5
Musculoskeletal and connective tissue disorders									
Arthralgia	14 (8.4)	14	13.0	16 (7.0)	17	10.8	30 (7.6)	31	11.7
Back pain	6 (3.6)	8	7.4	16 (7.0)	16	10.2	22 (5.6)	24	9.1
Nervous system disorders									
Headache	18 (10.8)	62	57.4	21 (9.3)	60	38.2	39 (9.9)	122	46.0

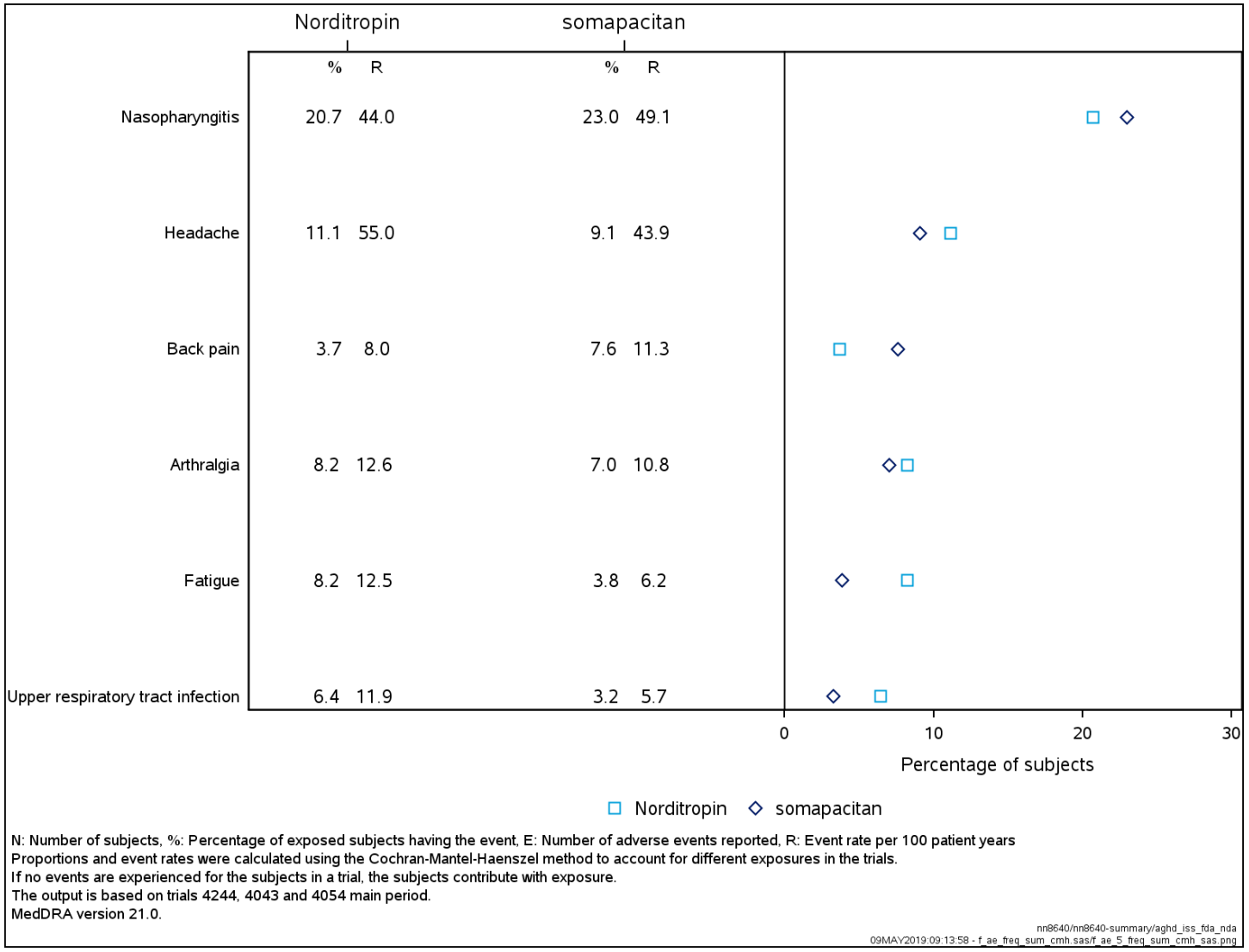
N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
The output is based on trials 4244, 4043 and 4054 main period.
MedDRA version 21.0.

108 Most frequent adverse events (>=5%) by system organ class and preferred term - Cochran-Mantel-Haenszel adjusted - Norditropin/somapacitan po ol - safety analysis set

	Norditropin				Somapacitan				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Subjects Exposed	166				227				393			
Total patient years	108.0				157.2				265.1			
General disorders and administration site conditions												
Fatigue	13	(8.2)	13	12.5	9	(3.8)	10	6.2	22	(5.6)	23	8.8
Infections and infestations												
Nasopharyngitis	33	(20.7)	45	44.0	57	(23.0)	88	49.1	90	(22.1)	133	47.6
Upper respiratory tract infection	11	(6.4)	13	11.9	6	(3.2)	7	5.7	17	(4.5)	20	7.9
Musculoskeletal and connective tissue disorders												
Arthralgia	14	(8.2)	14	12.6	16	(7.0)	17	10.8	30	(7.7)	31	11.8
Back pain	6	(3.7)	8	8.0	16	(7.6)	16	11.3	22	(5.7)	24	9.2
Nervous system disorders												
Headache	18	(11.1)	62	55.0	21	(9.1)	60	43.9	39	(9.9)	122	48.4

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
Proportions and event rates were calculated using the Cochran-Mantel-Haenszel method to account for different exposures in the trials.
If no events are experienced for the subjects in a trial, the subjects contribute with exposure.
The output is based on trials 4244, 4043 and 4054 main period.
MedDRA version 21.0.

109 Most frequent adverse events (>=5%) by system organ class and preferred term -Cochran-Mantel-Haenszel adjusted - Norditropin/somapacitan poo l - safety analysis set



N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
Proportions and event rates were calculated using the Cochran-Mantel-Haenszel method to account for different exposures in the trials.
If no events are experienced for the subjects in a trial, the subjects contribute with exposure.
The output is based on trials 4244, 4043 and 4054 main period.
MedDRA version 21.0.

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110 Adverse events - SMQ - Cochran-Mantel-Haenszel adjusted vs. Naïve - Norditropin/somapacitan pool - safety analysis set

	Norditropin				Somapacitan				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Subjects Exposed	166				227				393			
Total patient years	108.0				157.2				265.1			
All hypothyroidism events												
Naïve	6	(3.6)	6	5.6	2	(0.9)	2	1.3	8	(2.0)	8	3.0
CMH adjusted	6	(3.8)	6	5.8	2	(0.9)	2	1.3	8	(2.1)	8	3.1
All pancreaitis events												
Naïve	0				0				0			
CMH adjusted	0				0				0			
All peripheral oedema events												
Naïve	8	(4.8)	11	10.2	5	(2.2)	7	4.5	13	(3.3)	18	6.8
CMH adjusted	8	(4.4)	11	9.2	5	(2.7)	7	5.7	13	(3.5)	18	7.4
All fatigue/asthenia events												
Naïve	17	(10.2)	17	15.7	18	(7.9)	20	12.7	35	(8.9)	37	14.0
CMH adjusted	17	(10.7)	17	16.4	18	(7.4)	20	12.0	35	(8.8)	37	14.0
All allergic reaction (non-anaphylactic reaction) events												
Naïve	18	(10.8)	20	18.5	11	(4.8)	12	7.6	29	(7.4)	32	12.1
CMH adjusted	18	(11.5)	20	19.2	11	(5.2)	12	8.6	29	(7.3)	32	12.2
All injection site reaction events												
Naïve	9	(5.4)	9	8.3	3	(1.3)	6	3.8	12	(3.1)	15	5.7
CMH adjusted	9	(5.2)	9	7.9	3	(1.4)	6	4.4	12	(3.1)	15	5.9
All lipohypertrophy events												
Naïve	0				4	(1.8)	4	2.5	4	(1.0)	4	1.5
CMH adjusted	0				4	(2.2)	4	3.2	4	(1.1)	4	1.6

N: Number of subjects, %: Percentage of exposed subjects having the event, CMH: Cochran-Mantel-Haenszel, E: Number of adverse events reported, R: Event rate per 100 patient years
Proportions and event rates were calculated using the Cochran-Mantel-Haenszel method to account for different exposures in the trials.
If no events are experienced for the subjects in a trial, the subjects contribute with exposure.
The output is based on trials 4244, 4043 and 4054 main period.
MedDRA version 21.0.

Adverse events - SMQ - Cochran-Mantel-Haenszel adjusted vs. Naïve - Norditropin/somapacitan pool - safety analysis set

	Norditropin			Somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
All lipoatrophy events									
Naïve	1 (0.6)	1	0.9	0			1 (0.3)	1	0.4
CMH adjusted	1 (0.5)	1	0.8	0			1 (0.3)	1	0.4
All blood alkaline phosphatase increased (bone) events									
Naïve	0			1 (0.4)	1	0.6	1 (0.3)	1	0.4
CMH adjusted	0			1 (0.5)	1	0.8	1 (0.3)	1	0.4
All drug specific antibodies events									
Naïve	0			0			0		
CMH adjusted	0			0			0		
All cardiac and vascular investigations incl. arrhythmia									
Naïve	5 (3.0)	8	7.4	1 (0.4)	1	0.6	6 (1.5)	9	3.4
CMH adjusted	5 (2.9)	8	7.2	1 (0.5)	1	0.8	6 (1.6)	9	3.6
All weight increased events									
Naïve	2 (1.2)	2	1.9	7 (3.1)	7	4.5	9 (2.3)	9	3.4
CMH adjusted	2 (1.3)	2	1.9	7 (3.3)	7	4.9	9 (2.3)	9	3.5
All hyperglycemia events									
Naïve	1 (0.6)	4	3.7	1 (0.4)	1	0.6	2 (0.5)	5	1.9
CMH adjusted	1 (0.5)	4	3.3	1 (0.5)	1	0.8	2 (0.5)	5	2.0
All type 2 diabetes events									
Naïve	4 (2.4)	7	6.5	2 (0.9)	2	1.3	6 (1.5)	9	3.4
CMH adjusted	4 (2.4)	7	6.2	2 (0.9)	2	1.3	6 (1.5)	9	3.5
All athralgia events									
Naïve	14 (8.4)	14	13.0	16 (7.0)	17	10.8	30 (7.6)	31	11.7
CMH adjusted	14 (8.2)	14	12.6	16 (7.0)	17	10.8	30 (7.7)	31	11.8

N: Number of subjects, %: Percentage of exposed subjects having the event, CMH: Cochran-Mantel-Haenszel, E: Number of adverse events reported, R: Event rate per 100 patient years
Proportions and event rates were calculated using the Cochran-Mantel-Haenszel method to account for different exposures in the trials.
If no events are experienced for the subjects in a trial, the subjects contribute with exposure.
The output is based on trials 4244, 4043 and 4054 main period.
MedDRA version 21.0.

Adverse events - SMQ - Cochran-Mantel-Haenszel adjusted vs. Naïve - Norditropin/somapacitan pool - safety analysis set

	Norditropin			Somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
All myalgia events									
Naïve	5 (3.0)	5	4.6	2 (0.9)	2	1.3	7 (1.8)	7	2.6
CMH adjusted	5 (3.2)	5	4.8	2 (0.9)	2	1.3	7 (1.8)	7	2.7
All scoliosis events									
Naïve	0			0			0		
CMH adjusted	0			0			0		
All benign, malignant and unspecified neoplasm events									
Naïve	3 (1.8)	3	2.8	2 (0.9)	2	1.3	5 (1.3)	5	1.9
CMH adjusted	3 (1.6)	3	2.5	2 (0.6)	2	0.8	5 (1.2)	5	1.8
All headache events									
Naïve	18 (10.8)	62	57.4	21 (9.3)	60	38.2	39 (9.9)	122	46.0
CMH adjusted	18 (11.1)	62	55.0	21 (9.1)	60	43.9	39 (9.9)	122	48.4
All paraesthesia events									
Naïve	1 (0.6)	1	0.9	4 (1.8)	5	3.2	5 (1.3)	6	2.3
CMH adjusted	1 (0.5)	1	0.8	4 (2.0)	5	3.8	5 (1.3)	6	2.4
All stroke events									
Naïve	0			0			0		
CMH adjusted	0			0			0		
All carpal tunnel syndrome events									
Naïve	0			1 (0.4)	1	0.6	1 (0.3)	1	0.4
CMH adjusted	0			1 (0.4)	1	0.5	1 (0.2)	1	0.4
All benign intracranial hypertension events									
Naïve	0			0			0		
CMH adjusted	0			0			0		

N: Number of subjects, %: Percentage of exposed subjects having the event, CMH: Cochran-Mantel-Haenszel, E: Number of adverse events reported, R: Event rate per 100 patient years
Proportions and event rates were calculated using the Cochran-Mantel-Haenszel method to account for different exposures in the trials.
If no events are experienced for the subjects in a trial, the subjects contribute with exposure.
The output is based on trials 4244, 4043 and 4054 main period.
MedDRA version 21.0.

Adverse events - SMQ - Cochran-Mantel-Haenszel adjusted vs. Naïve - Norditropin/somapacitan pool - safety analysis set

	Norditropin			Somapacitan			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
All rare events									
Naïve	8 (4.8)	13	12.0	5 (2.2)	5	3.2	13 (3.3)	18	6.8
CMH adjusted	8 (4.5)	13	11.3	5 (2.7)	5	4.0	13 (3.5)	18	7.3
All hypersensitivity (anaphylactic reaction) events									
Naïve	0			0			0		
CMH adjusted	0			0			0		
All adrenocortical insufficiency (secondary) events									
Naïve	2 (1.2)	2	1.9	6 (2.6)	6	3.8	8 (2.0)	8	3.0
CMH adjusted	2 (1.1)	2	1.7	6 (2.9)	6	4.3	8 (2.1)	8	3.2
All metabolism disorders - glyceamic control - events									
Naïve	4 (2.4)	7	6.5	2 (0.9)	2	1.3	6 (1.5)	9	3.4
CMH adjusted	4 (2.4)	7	6.2	2 (0.9)	2	1.3	6 (1.5)	9	3.5

N: Number of subjects, %: Percentage of exposed subjects having the event, CMH: Cochran-Mantel-Haenszel, E: Number of adverse events reported, R: Event rate per 100 patient years
Proportions and event rates were calculated using the Cochran-Mantel-Haenszel method to account for different exposures in the trials.
If no events are experienced for the subjects in a trial, the subjects contribute with exposure.
The output is based on trials 4244, 4043 and 4054 main period.
MedDRA version 21.0.

111 Listing of preferred terms used for SMQ 20000160 - Hypothyroidism

Preferred Term Text	Preferred Term ID
Autoimmune hypothyroidism	10076644
Congenital hypothyroidism	10010510
Generalised resistance to thyroid hormone	10018096
Hypothyroidic goitre	10059844
Hypothyroidism	10021114
Myxoedema	10028665
Myxoedema coma	10060819
Post procedural hypothyroidism	10065306
Primary hypothyroidism	10036697
Secondary hypothyroidism	10039840
Tertiary hypothyroidism	10043289
Thyroid atrophy	10043693
Thyroid stimulating hormone deficiency	10078564
Transient hypothyroxinaemia of prematurity	10075901

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112 Listing of preferred terms used for SMQ 20000022 - Pancreatitis

Preferred Term Text	Preferred Term ID
Alcoholic pancreatitis	10056977
Alcoholic pancreopathy	10076384
Autoimmune pancreatitis	10069002
Cullen's sign	10059029
Cytomegalovirus pancreatitis	10049566
Grey Turner's sign	10075426
Haemorrhagic necrotic pancreatitis	10076058
Hereditary pancreatitis	10056976
Ischaemic pancreatitis	10066127
Lupus pancreatitis	10067750
Obstructive pancreatitis	10079822
Oedematous pancreatitis	10052400
Pancreas infection	10051741
Pancreatic abscess	10048984
Pancreatic haemorrhage	10033625
Pancreatic necrosis	10058096
Pancreatic phlegmon	10056975
Pancreatic pseudocyst	10033635
Pancreatic pseudocyst drainage	10033636
Pancreatitis	10033645
Pancreatitis acute	10033647
Pancreatitis bacterial	10065191
Pancreatitis chronic	10033649
Pancreatitis fungal	10065190
Pancreatitis haemorrhagic	10033650
Pancreatitis helminthic	10065189
Pancreatitis mumps	10033653
Pancreatitis necrotising	10033654
Pancreatitis relapsing	10033657
Pancreatitis viral	10065192
Pancreatorenal syndrome	10056277
Radiation pancreatitis	10080726
Traumatic pancreatitis	10074894

MedDRA version 21.0.

113 Listing of preferred terms used for SMQ 20000214 - Allergic reactions (non-anaphylactic reactions)

Preferred Term Text	Preferred Term ID
Acquired C1 inhibitor deficiency	10081035
Acute generalised exanthematous pustulosis	10048799
Administration related reaction	10069773
Administration site dermatitis	10075096
Administration site eczema	10075099
Administration site hypersensitivity	10075102
Administration site rash	10071156
Administration site recall reaction	10075964
Administration site urticaria	10075109
Administration site vasculitis	10075969
Allergic bronchitis	10052613
Allergic colitis	10059447
Allergic cough	10053779
Allergic cystitis	10051394
Allergic eosinophilia	10075185
Allergic gastroenteritis	10075308
Allergic hepatitis	10071198
Allergic keratitis	10057380
Allergic oedema	10060934
Allergic otitis externa	10075072
Allergic otitis media	10061557
Allergic pharyngitis	10050639
Allergic reaction to excipient	10078853
Allergic respiratory disease	10063532
Allergic respiratory symptom	10063527
Allergic sinusitis	10049153
Allergic stomatitis	10079554
Allergic transfusion reaction	10066173
Allergy alert test positive	10075479
Allergy test positive	10056352
Allergy to immunoglobulin therapy	10074079
Allergy to surgical sutures	10077279
Allergy to vaccine	10055048
Alveolitis allergic	10001890
Anaphylactic reaction	10002198
Anaphylactic shock	10002199
Anaphylactic transfusion reaction	10067113
Anaphylactoid reaction	10002216
Anaphylactoid shock	10063119
Anaphylaxis treatment	10002222
Angioedema	10002424
Anti-neutrophil cytoplasmic antibody positive vasculitis	10050894
Antiallergic therapy	10064059
Antiendomysial antibody positive	10065514
Application site dermatitis	10003036
Application site eczema	10050099
Application site hypersensitivity	10063683
Application site rash	10003054
Application site recall reaction	10076024
Application site urticaria	10050104
Application site vasculitis	10076027
Arthritis allergic	10061430
Aspirin-exacerbated respiratory disease	10075084
Atopy	10003645
Blepharitis allergic	10005149
Blood immunoglobulin E abnormal	10005589
Blood immunoglobulin E increased	10005591
Bromoderma	10006404
Bronchospasm	10006482
Catheter site dermatitis	10073992
Catheter site eczema	10073995
Catheter site hypersensitivity	10073998
Catheter site rash	10052271

MedDRA version 21.0.

Listing of preferred terms used for SMQ 20000214 - Allergic reactions (non-anaphylactic reactions)

Preferred Term Text	Preferred Term ID
Catheter site urticaria	10052272
Catheter site vasculitis	10074014
Chronic eosinophilic rhinosinusitis	10071399
Chronic hyperplastic eosinophilic sinusitis	10071380
Circulatory collapse	10009192
Circumoral oedema	10052250
Conjunctival oedema	10010726
Conjunctivitis allergic	10010744
Contact stomatitis	10067510
Contrast media allergy	10066973
Contrast media reaction	10010836
Corneal oedema	10011033
Cutaneous vasculitis	10011686
Dennie-Morgan fold	10062918
Dermatitis	10012431
Dermatitis acneiform	10012432
Dermatitis allergic	10012434
Dermatitis atopic	10012438
Dermatitis bullous	10012441
Dermatitis contact	10012442
Dermatitis exfoliative	10012455
Dermatitis exfoliative generalised	10012456
Dermatitis herpetiformis	10012468
Dermatitis infected	10012470
Dermatitis psoriasiform	10058675
Device allergy	10072867
Dialysis membrane reaction	10076665
Distributive shock	10070559
Documented hypersensitivity to administered product	10076470
Drug eruption	10013687
Drug hypersensitivity	10013700
Drug provocation test	10074350
Drug reaction with eosinophilia and systemic symptoms	10073508
Eczema	10014184
Eczema infantile	10014198
Eczema nummular	10014201
Eczema vaccinatum	10066042
Eczema vesicular	10058681
Eczema weeping	10055182
Encephalitis allergic	10056387
Encephalopathy allergic	10014627
Eosinophilic granulomatosis with polyangiitis	10078117
Epidermal necrosis	10059284
Epidermolysis	10053177
Epidermolysis bullosa	10014989
Epiglottic oedema	10015029
Erythema multiforme	10015218
Erythema nodosum	10015226
Exfoliative rash	10064579
Eye allergy	10015907
Eye oedema	10052139
Eye swelling	10015967
Eyelid oedema	10015993
Face oedema	10016029
Fixed eruption	10016741
Giant papillary conjunctivitis	10018258
Gingival oedema	10049305
Gingival swelling	10018291
Gleich's syndrome	10066837
Haemorrhagic urticaria	10059499
Hand dermatitis	10058898
Henoch-Schonlein purpura	10019617
Henoch-Schonlein purpura nephritis	10069440

MedDRA version 21.0.

Listing of preferred terms used for SMQ 20000214 - Allergic reactions (non-anaphylactic reactions)

Preferred Term Text	Preferred Term ID
Heparin-induced thrombocytopenia	10062506
Hereditary angioedema	10019860
Hereditary angioedema with C1 esterase inhibitor deficiency	10080955
Hypersensitivity	10020751
Hypersensitivity myocarditis	10081004
Hypersensitivity vasculitis	10020764
Idiopathic urticaria	10021247
Immediate post-injection reaction	10067142
Immune thrombocytopenic purpura	10074667
Immune tolerance induction	10070581
Immune-mediated adverse reaction	10077665
Implant site dermatitis	10063855
Implant site hypersensitivity	10063858
Implant site rash	10063786
Implant site urticaria	10063787
Incision site dermatitis	10073168
Incision site rash	10073411
Infusion related reaction	10051792
Infusion site dermatitis	10065458
Infusion site eczema	10074850
Infusion site hypersensitivity	10065471
Infusion site rash	10059830
Infusion site recall reaction	10076085
Infusion site urticaria	10065490
Infusion site vasculitis	10074851
Injection related reaction	10071152
Injection site dermatitis	10022056
Injection site eczema	10066221
Injection site hypersensitivity	10022071
Injection site rash	10022094
Injection site recall reaction	10066797
Injection site urticaria	10022107
Injection site vasculitis	10067995
Instillation site hypersensitivity	10073612
Instillation site rash	10073622
Instillation site urticaria	10073627
Interstitial granulomatous dermatitis	10067972
Intestinal angioedema	10076229
Iodine allergy	10052098
Kaposi's varicelliform eruption	10051891
Kounis syndrome	10069167
Laryngeal oedema	10023845
Laryngitis allergic	10064866
Laryngospasm	10023891
Laryngotracheal oedema	10023893
Limbal swelling	10070492
Lip oedema	10024558
Lip swelling	10024570
Mast cell degranulation present	10076606
Medical device site dermatitis	10075572
Medical device site eczema	10075575
Medical device site hypersensitivity	10075579
Medical device site rash	10075585
Medical device site recall reaction	10076140
Medical device site urticaria	10075588
Mouth swelling	10075203
Mucocutaneous rash	10056671
Multiple allergies	10028164
Nephritis allergic	10029120
Nikolsky's sign	10029415
Nodular rash	10075807
Oculomucocutaneous syndrome	10030081
Oculorespiratory syndrome	10067317

MedDRA version 21.0.

Listing of preferred terms used for SMQ 20000214 - Allergic reactions (non-anaphylactic reactions)

Preferred Term Text	Preferred Term ID
Oedema mouth	10030110
Oral allergy syndrome	10068355
Oropharyngeal blistering	10067950
Oropharyngeal oedema	10078783
Oropharyngeal spasm	10031111
Oropharyngeal swelling	10031118
Palatal oedema	10056998
Palatal swelling	10074403
Palisaded neutrophilic granulomatous dermatitis	10068809
Palpable purpura	10056872
Pathergy reaction	10074332
Perioral dermatitis	10034541
Periorbital oedema	10034545
Pharyngeal oedema	10034829
Procedural shock	10080894
Pruritus allergic	10063438
Radioallergosorbent test positive	10037789
Rash	10037844
Rash erythematous	10037855
Rash follicular	10037857
Rash generalised	10037858
Rash macular	10037867
Rash maculo-papular	10037868
Rash maculovesicular	10050004
Rash morbilliform	10037870
Rash neonatal	10037871
Rash papulosquamous	10037879
Rash pruritic	10037884
Rash pustular	10037888
Rash rubelliform	10057984
Rash scarlatiniform	10037890
Rash vesicular	10037898
Reaction to azo-dyes	10037973
Reaction to colouring	10037974
Reaction to excipient	10079925
Reaction to preservatives	10064788
Red man syndrome	10038192
Rhinitis allergic	10039085
Scleral oedema	10057431
Scleritis allergic	10051126
Scrotal oedema	10039755
Serum sickness	10040400
Serum sickness-like reaction	10040402
Shock	10040560
Shock symptom	10040581
Skin necrosis	10040893
Skin reaction	10040914
Skin test positive	10040934
Solar urticaria	10041307
Solvent sensitivity	10041316
Stevens-Johnson syndrome	10042033
Stoma site hypersensitivity	10074509
Stoma site rash	10059071
Swelling face	10042682
Swollen tongue	10042727
Symmetrical drug-related intertriginous and flexural exanthema	10078325
Therapeutic product cross-reactivity	10079645
Tongue oedema	10043967
Toxic epidermal necrolysis	10044223
Toxic skin eruption	10057970
Tracheal oedema	10044296
Type I hypersensitivity	10045240
Type II hypersensitivity	10054000

MedDRA version 21.0.

Listing of preferred terms used for SMQ 20000214 - Allergic reactions (non-anaphylactic reactions)

Preferred Term Text	Preferred Term ID
Type III immune complex mediated reaction	10053614
Type IV hypersensitivity reaction	10053613
Urticaria	10046735
Urticaria cholinergic	10046740
Urticaria chronic	10052568
Urticaria contact	10046742
Urticaria papular	10046750
Urticaria physical	10046751
Urticaria pigmentosa	10046752
Urticaria vesiculosa	10046755
Urticarial vasculitis	10048820
Vaccination site dermatitis	10069477
Vaccination site eczema	10076161
Vaccination site exfoliation	10069489
Vaccination site hypersensitivity	10068880
Vaccination site rash	10069482
Vaccination site recall reaction	10076188
Vaccination site urticaria	10069622
Vaccination site vasculitis	10076191
Vaccination site vesicles	10069623
Vaginal exfoliation	10064483
Vaginal ulceration	10046943
Vasculitic rash	10047111
Vernal keratoconjunctivitis	10081000
Vessel puncture site rash	10077117
Vessel puncture site vesicles	10077813
Vulval ulceration	10047768
Vulvovaginal rash	10071588
Vulvovaginal ulceration	10050181
Vulvovaginitis allergic	10080783

MedDRA version 21.0.

114 Listing of preferred terms used for SMQ 20000060 - Stroke

Preferred Term Text	Preferred Term ID
Amaurosis fugax	10001903
Balint's syndrome	10057375
Basal ganglia haematoma	10077031
Basal ganglia haemorrhage	10067057
Basal ganglia infarction	10069020
Basal ganglia stroke	10071043
Basilar artery aneurysm	10077607
Basilar artery occlusion	10048963
Basilar artery perforation	10075736
Basilar artery stenosis	10004163
Basilar artery thrombosis	10063093
Brachiocephalic arteriosclerosis	10075449
Brachiocephalic artery occlusion	10069694
Brachiocephalic artery stenosis	10075450
Brain hypoxia	10006127
Brain stem embolism	10074422
Brain stem haematoma	10073230
Brain stem haemorrhage	10006145
Brain stem infarction	10006147
Brain stem ischaemia	10006148
Brain stem microhaemorrhage	10071205
Brain stem stroke	10068644
Brain stem thrombosis	10062573
Brain stent insertion	10080887
CSF bilirubin positive	10071326
Capsular warning syndrome	10067744
Carotid aneurysm rupture	10051328
Carotid angioplasty	10071260
Carotid arterial embolus	10007684
Carotid arteriosclerosis	10067116
Carotid artery aneurysm	10007686
Carotid artery bypass	10053003
Carotid artery disease	10061744
Carotid artery dissection	10050403
Carotid artery insufficiency	10064949
Carotid artery occlusion	10048964
Carotid artery perforation	10075728
Carotid artery restenosis	10072558
Carotid artery stenosis	10007687
Carotid artery stent insertion	10066102
Carotid artery stent removal	10069952
Carotid artery thrombosis	10007688
Carotid endarterectomy	10007692
Carotid revascularisation	10072559
Central nervous system haemorrhage	10072043
Cerebellar artery occlusion	10053633
Cerebellar artery thrombosis	10008023
Cerebellar embolism	10067167
Cerebellar haematoma	10061038
Cerebellar haemorrhage	10008030
Cerebellar infarction	10008034
Cerebellar ischaemia	10068621
Cerebellar microhaemorrhage	10071206
Cerebellar stroke	10079062
Cerebral aneurysm perforation	10075394
Cerebral aneurysm ruptured syphilitic	10008076
Cerebral arteriosclerosis	10065559
Cerebral arteriovenous malformation haemorrhagic	10008086
Cerebral arteritis	10008087
Cerebral artery embolism	10008088
Cerebral artery occlusion	10008089
Cerebral artery perforation	10075734
Cerebral artery restenosis	10075423

MedDRA version 21.0.

Listing of preferred terms used for SMQ 20000060 - Stroke

Preferred Term Text	Preferred Term ID
Cerebral artery stenosis	10063648
Cerebral artery thrombosis	10008092
Cerebral capillary telangiectasia	10075633
Cerebral circulatory failure	10008097
Cerebral congestion	10076929
Cerebral endovascular aneurysm repair	10077079
Cerebral gas embolism	10070813
Cerebral haematoma	10053942
Cerebral haemorrhage	10008111
Cerebral haemorrhage foetal	10050157
Cerebral haemorrhage neonatal	10008112
Cerebral hypoperfusion	10065384
Cerebral infarction	10008118
Cerebral infarction foetal	10008119
Cerebral ischaemia	10008120
Cerebral microembolism	10078311
Cerebral microhaemorrhage	10067277
Cerebral reperfusion injury	10075401
Cerebral revascularisation	10071508
Cerebral septic infarct	10070671
Cerebral small vessel ischaemic disease	10070878
Cerebral thrombosis	10008132
Cerebral vascular occlusion	10076895
Cerebral vasoconstriction	10059109
Cerebral venous thrombosis	10008138
Cerebral ventricular rupture	10075249
Cerebrovascular accident	10008190
Cerebrovascular accident prophylaxis	10049165
Cerebrovascular disorder	10008196
Cerebrovascular insufficiency	10058842
Cerebrovascular stenosis	10061751
Charcot-Bouchard microaneurysms	10054749
Congenital hemiparesis	10071359
Delayed ischaemic neurological deficit	10078388
Dural arteriovenous fistula	10074462
Embolic cerebral infarction	10060839
Embolic stroke	10014498
Epidural haemorrhage	10073681
Extra-axial haemorrhage	10078254
Extradural haematoma	10015769
Extraischaemic cerebral haematoma	10080347
Haemorrhage intracranial	10018985
Haemorrhagic cerebral infarction	10019005
Haemorrhagic stroke	10019016
Haemorrhagic transformation stroke	10055677
Hemianaesthesia	10077170
Hemiasomatognosia	10077171
Hemihyperaesthesia	10080713
Hemiparaesthesia	10078746
Hemiparesis	10019465
Hemiplegia	10019468
Hypoxic-ischaemic encephalopathy	10070511
Inner ear infarction	10070754
Intra-cerebral aneurysm operation	10022736
Intracerebral haematoma evacuation	10062025
Intracranial aneurysm	10022758
Intracranial haematoma	10059491
Intracranial tumour haemorrhage	10022775
Intracranial venous sinus thrombosis	10061251
Intraventricular haemorrhage	10022840
Intraventricular haemorrhage neonatal	10022841
Ischaemic cerebral infarction	10060840
Ischaemic stroke	10061256

MedDRA version 21.0.

Listing of preferred terms used for SMQ 20000060 - Stroke

Preferred Term Text	Preferred Term ID
Lacunar infarction	10051078
Lacunar stroke	10076994
Lateral medullary syndrome	10024033
Meningorrhagia	10052593
Migrainous infarction	10056237
Millard-Gubler syndrome	10067462
Moyamoya disease	10028047
Perinatal stroke	10073945
Periventricular haemorrhage neonatal	10076706
Pituitary haemorrhage	10049760
Post cardiac arrest syndrome	10078202
Post procedural stroke	10066591
Post stroke depression	10070606
Posthaemorrhagic hydrocephalus	10079859
Precerebral arteriosclerosis	10077033
Precerebral artery occlusion	10036511
Putamen haemorrhage	10058940
Reversible cerebral vasoconstriction syndrome	10073240
Reversible ischaemic neurological deficit	10050496
Ruptured cerebral aneurysm	10039330
Spinal artery embolism	10049440
Spinal artery thrombosis	10071316
Spinal cord haematoma	10076051
Spinal cord haemorrhage	10048992
Spinal epidural haematoma	10050162
Spinal epidural haemorrhage	10049236
Spinal subarachnoid haemorrhage	10073564
Spinal subdural haematoma	10050164
Spinal subdural haemorrhage	10073563
Stroke in evolution	10059613
Subarachnoid haematoma	10076701
Subarachnoid haemorrhage	10042316
Subarachnoid haemorrhage neonatal	10042317
Subclavian steal syndrome	10042335
Subdural haematoma	10042361
Subdural haematoma evacuation	10042363
Subdural haemorrhage	10042364
Subdural haemorrhage neonatal	10042365
Superior sagittal sinus thrombosis	10042567
Thalamic infarction	10064961
Thalamus haemorrhage	10058939
Thrombotic cerebral infarction	10067347
Thrombotic stroke	10043647
Transient ischaemic attack	10044390
Transverse sinus thrombosis	10044457
Vascular encephalopathy	10063661
Vascular stent occlusion	10077143
Vascular stent stenosis	10077144
Vasculitis cerebral	10047119
Vein of Galen aneurysmal malformation	10077889
Vertebral artery aneurysm	10077498
Vertebral artery dissection	10071716
Vertebral artery occlusion	10048965
Vertebral artery perforation	10075735
Vertebral artery stenosis	10047330
Vertebral artery thrombosis	10057777
Vertebrobasilar insufficiency	10047334

MedDRA version 21.0.

115 Listing of preferred terms used for SMQ 20000021 - Hypersensitivity (Anaphylactic reactions)

Preferred Term Text	Preferred Term ID
Anaphylactic reaction	10002198
Anaphylactic shock	10002199
Anaphylactic transfusion reaction	10067113
Anaphylactoid reaction	10002216
Anaphylactoid shock	10063119
Circulatory collapse	10009192
Dialysis membrane reaction	10076665
Kounis syndrome	10069167
Procedural shock	10080894
Shock	10040560
Shock symptom	10040581
Type I hypersensitivity	10045240

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116 Listing of preferred terms used for NNMQ - Peripheral oedema

Preferred Term Text	Preferred Term ID
Oedema peripheral	10030124
Peripheral swelling	10048959

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117 Listing of preferred terms used for NNMQ - Fatique/Asthenia

Preferred Term Text	Preferred Term ID
Adult failure to thrive	10077257
Asthenia	10003549
Autonomic nervous system imbalance	10003840
Cachexia	10006895
Chronic fatigue syndrome	10008874
Decreased activity	10011953
Fatigue	10016256
Lethargy	10024264
Listless	10024642
Malaise	10025482
Post treatment Lyme disease syndrome	10079060
Sluggishness	10041052

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118 Listing of preferred terms used for NNMQ - Weight increased

Preferred Term Text	Preferred Term ID
Weight increased	10047899

MedDRA version 21.0.

119 Listing of preferred terms used for NNMQ - Injection site reaction

Preferred Term Text	Preferred Term ID
Embolia cutis medicamentosa	10058729
Injected limb mobility decreased	10057664
Injection site abscess	10022044
Injection site abscess sterile	10022045
Injection site anaesthesia	10022046
Injection site bruising	10022052
Injection site calcification	10054812
Injection site cellulitis	10050057
Injection site coldness	10050082
Injection site cyst	10022055
Injection site deformation	10079275
Injection site dermatitis	10022056
Injection site discharge	10065600
Injection site discolouration	10051572
Injection site discomfort	10054266
Injection site dryness	10067252
Injection site dysaesthesia	10069124
Injection site eczema	10066221
Injection site erosion	10022059
Injection site erythema	10022061
Injection site exfoliation	10068689
Injection site extravasation	10022062
Injection site fibrosis	10022064
Injection site granuloma	10022065
Injection site haematoma	10022066
Injection site haemorrhage	10022067
Injection site hyperaesthesia	10073418
Injection site hypersensitivity	10022071
Injection site hypertrichosis	10075313
Injection site hypoaesthesia	10074586
Injection site indentation	10079277
Injection site induration	10022075
Injection site infection	10022076
Injection site inflammation	10022078
Injection site injury	10066083
Injection site irritation	10022079
Injection site ischaemia	10048648
Injection site joint discomfort	10073459
Injection site joint effusion	10064494
Injection site joint erythema	10076327
Injection site joint infection	10074703
Injection site joint inflammation	10064111
Injection site joint movement impairment	10053979
Injection site joint pain	10049261
Injection site joint swelling	10049260
Injection site joint warmth	10049262
Injection site laceration	10067253
Injection site lymphadenopathy	10057665
Injection site macule	10067255
Injection site mass	10022081
Injection site movement impairment	10056250
Injection site necrosis	10022082
Injection site nerve damage	10022083
Injection site nodule	10057880
Injection site oedema	10022085
Injection site pain	10022086
Injection site pallor	10066041
Injection site papule	10066044
Injection site paraesthesia	10022088
Injection site phlebitis	10022090
Injection site photosensitivity reaction	10053396
Injection site plaque	10073174
Injection site pruritus	10022093

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Listing of preferred terms used for NNMQ - Injection site reaction

Preferred Term Text	Preferred Term ID
Injection site pustule	10054994
Injection site rash	10022094
Injection site reaction	10022095
Injection site recall reaction	10066797
Injection site scab	10066210
Injection site scar	10059009
Injection site streaking	10066778
Injection site swelling	10053425
Injection site telangiectasia	10079124
Injection site thrombosis	10022104
Injection site ulcer	10022105
Injection site urticaria	10022107
Injection site vasculitis	10067995
Injection site vesicles	10022111
Injection site warmth	10022112
Malabsorption from injection site	10025478

MedDRA version 21.0.

120 Listing of preferred terms used for NNMQ - Lipohypertrophy

Preferred Term Text	Preferred Term ID
Injection site hypertrophy	10022072
Lipodystrophy acquired	10049287
Lipohypertrophy	10062315

MedDRA version 21.0.

121 Listing of preferred terms used for NNMQ - Lipoatrophy

Preferred Term Text	Preferred Term ID
Fat tissue decreased	10073170
Injection site atrophy	10022048
Lipoatrophy	10024604

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122 Listing of preferred terms used for NNMQ - Blood alkaline phosphatase increased (bone)

Preferred Term Text	Preferred Term ID
Blood alkaline phosphatase increased	10059570

MedDRA version 21.0.

123 Listing of preferred terms used for NNMQ - Drug specific antibodies present

Preferred Term Text	Preferred Term ID
Agglutination test	10080821
Allergy test	10053462
Allergy test negative	10056362
Allergy test positive	10056352
Angiotensin II receptor type 1 antibody positive	10079737
Anti-interferon antibody	10072886
Anti-interferon antibody negative	10072887
Anti-interferon antibody positive	10072888
Antibody test	10060979
Antibody test abnormal	10061425
Antibody test negative	10061426
Antibody test normal	10061429
Antibody test positive	10061427
Antiendomysial antibody positive	10065514
Antiendomysial antibody test	10076977
Basophil degranulation test	10069524
Charcot-Leyden crystals	10008413
Donor specific antibody present	10075992
Drug provocation test	10074350
Histamine release test	10080590
Human anti-human antibody test	10066932
Human anti-mouse antibody increased	10065605
Human anti-mouse antibody positive	10065248
Human anti-mouse antibody test	10066929
Human antichimeric antibody negative	10069373
Human antichimeric antibody positive	10069375
Human antichimeric antibody test	10066928
Immune agglutinins	10062011
Immune complex assay	10063326
Immune complex level increased	10064650
Immunology test	10062297
Immunology test abnormal	10061214
Immunology test normal	10062502
Inhibiting antibodies	10058032
Inhibiting antibodies negative	10073772
Inhibiting antibodies positive	10073771
Leukotriene decreased	10064664
Leukotriene increased	10064663
Leukotriene test	10072335
Lymphocytotoxic antibody positive	10048774
Mast cell degranulation present	10076606
Mast cell degranulation test	10069536
Neutralising antibodies	10058063
Neutralising antibodies negative	10064981
Neutralising antibodies positive	10064980
Non-neutralising antibodies	10076383
Non-neutralising antibodies negative	10076382
Non-neutralising antibodies positive	10064982
Panel-reactive antibody	10058280
Panel-reactive antibody increased	10058278
Streptokinase antibody increased	10053797
Tryptase	10063240
Tryptase decreased	10063343
Tryptase increased	10063342

MedDRA version 21.0.

124 Listing of preferred terms used for NNMQ - Cardiac and vascular investigations incl. arrhythmia

Preferred Term Text	Preferred Term ID
Abdominal bruit	10063943
Accelerated idioventricular rhythm	10049003
Accessory cardiac pathway	10067618
Adams-Stokes syndrome	10001115
Agonal rhythm	10054015
Allen's test	10053463
Angiocardiogram	10080743
Angiogram	10061637
Angiogram abnormal	10060956
Angiogram normal	10061638
Angiogram peripheral	10057452
Angiogram peripheral abnormal	10057517
Angiogram peripheral normal	10057516
Angioscopy	10068866
Ankle brachial index	10062762
Ankle brachial index abnormal	10077378
Ankle brachial index decreased	10062760
Ankle brachial index increased	10076877
Ankle brachial index normal	10062761
Anomalous atrioventricular excitation	10002611
Aortic bruit	10051832
Aortogram	10057775
Aortogram abnormal	10057794
Aortogram normal	10057795
Arrhythmia	10003119
Arrhythmia neonatal	10003124
Arrhythmia supraventricular	10003130
Arterial bruit	10057895
Arterial catheterisation abnormal	10003149
Arterial catheterisation normal	10003150
Arterial segmental pressure test	10073986
Arteriogram	10061658
Arteriogram abnormal	10061659
Arteriogram carotid	10003194
Arteriogram carotid abnormal	10003195
Arteriogram carotid normal	10003196
Arteriogram coronary	10003200
Arteriogram coronary abnormal	10003201
Arteriogram coronary normal	10003202
Arteriogram normal	10061682
Atrial conduction time prolongation	10064191
Atrial fibrillation	10003658
Atrial flutter	10003662
Atrial parasystole	10071666
Atrial pressure	10050641
Atrial pressure increased	10049785
Atrial tachycardia	10003668
Atrioventricular block	10003671
Atrioventricular block complete	10003673
Atrioventricular block first degree	10003674
Atrioventricular block second degree	10003677
Atrioventricular conduction time shortened	10068180
Atrioventricular dissociation	10069571
Atrioventricular node dispersion	10077893
Baseline foetal heart rate variability disorder	10074638
Bezold-Jarisch reflex	10076999
Bifascicular block	10057393
Biopsy artery	10051409
Biopsy artery abnormal	10058364
Biopsy artery normal	10058393
Biopsy blood vessel	10052663
Biopsy blood vessel abnormal	10058410
Biopsy blood vessel normal	10058409

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Cardiac and vascular investigations incl. arrhythmia

Preferred Term Text	Preferred Term ID
Biopsy heart	10004779
Biopsy heart abnormal	10004780
Biopsy heart normal	10004781
Biopsy pericardium	10004842
Biopsy pericardium abnormal	10004843
Biopsy pericardium normal	10004844
Blood pressure abnormal	10005728
Blood pressure ambulatory	10005729
Blood pressure ambulatory abnormal	10005730
Blood pressure ambulatory decreased	10005731
Blood pressure ambulatory increased	10005732
Blood pressure ambulatory normal	10005733
Blood pressure decreased	10005734
Blood pressure diastolic	10005735
Blood pressure diastolic abnormal	10005736
Blood pressure diastolic decreased	10005737
Blood pressure diastolic increased	10005739
Blood pressure diastolic normal	10005741
Blood pressure difference of extremities	10071052
Blood pressure immeasurable	10005748
Blood pressure increased	10005750
Blood pressure measurement	10076581
Blood pressure normal	10005754
Blood pressure orthostatic	10053352
Blood pressure orthostatic abnormal	10053354
Blood pressure orthostatic decreased	10053356
Blood pressure orthostatic increased	10053355
Blood pressure orthostatic normal	10053353
Blood pressure systolic	10005756
Blood pressure systolic abnormal	10005757
Blood pressure systolic decreased	10005758
Blood pressure systolic increased	10005760
Blood pressure systolic inspiratory decreased	10005761
Blood pressure systolic inspiratory normal	10005762
Blood pressure systolic normal	10005764
Brachial pulse	10053929
Brachial pulse abnormal	10053931
Brachial pulse decreased	10053899
Brachial pulse increased	10053900
Brachial pulse normal	10053930
Bradyarrhythmia	10049765
Bradycardia	10006093
Bradycardia foetal	10006094
Bradycardia neonatal	10056471
Brugada syndrome	10059027
Bundle branch block	10006578
Bundle branch block bilateral	10006579
Bundle branch block left	10006580
Bundle branch block right	10006582
Capillary nail refill test	10065130
Capillary nail refill test abnormal	10069381
Caprini risk score	10079595
Caprini risk score high	10079594
Caprini risk score low	10079596
Cardiac arrest	10007515
Cardiac arrest neonatal	10007516
Cardiac death	10049993
Cardiac electrophysiologic study	10061739
Cardiac electrophysiologic study abnormal	10061808
Cardiac electrophysiologic study normal	10061807
Cardiac fibrillation	10061592
Cardiac flutter	10052840
Cardiac function test	10058470

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Cardiac and vascular investigations incl. arrhythmia

Preferred Term Text	Preferred Term ID
Cardiac function test abnormal	10058479
Cardiac function test normal	10058478
Cardiac imaging procedure	10053451
Cardiac imaging procedure abnormal	10053453
Cardiac imaging procedure normal	10053452
Cardiac index	10007575
Cardiac index abnormal	10007576
Cardiac index decreased	10007577
Cardiac index increased	10007578
Cardiac index normal	10007579
Cardiac monitoring	10053438
Cardiac monitoring abnormal	10053440
Cardiac monitoring normal	10053439
Cardiac murmur	10007586
Cardiac murmur functional	10007587
Cardiac output	10007594
Cardiac output decreased	10007595
Cardiac output increased	10007596
Cardiac pacemaker evaluation	10053441
Cardiac pharmacologic stress test	10054017
Cardiac stress test	10061027
Cardiac stress test abnormal	10055014
Cardiac stress test normal	10055063
Cardiac telemetry	10053448
Cardiac telemetry abnormal	10053450
Cardiac telemetry normal	10053449
Cardiac ventriculogram	10053445
Cardiac ventriculogram abnormal	10053447
Cardiac ventriculogram left	10053497
Cardiac ventriculogram left abnormal	10053499
Cardiac ventriculogram left normal	10053498
Cardiac ventriculogram normal	10053446
Cardiac ventriculogram right	10053442
Cardiac ventriculogram right abnormal	10053444
Cardiac ventriculogram right normal	10053443
Cardio-ankle vascular index	10078807
Cardio-respiratory arrest	10007617
Cardio-respiratory arrest neonatal	10007618
Cardiothoracic ratio	10068336
Cardiothoracic ratio increased	10007646
Cardiovascular evaluation	10053046
Cardiovascular function test	10060858
Cardiovascular function test abnormal	10007651
Cardiovascular function test normal	10007652
Carotid bruit	10048777
Carotid intima-media thickness increased	10064582
Carotid pulse	10053926
Carotid pulse abnormal	10053928
Carotid pulse decreased	10053897
Carotid pulse increased	10053898
Carotid pulse normal	10053927
Catheterisation cardiac	10007815
Catheterisation cardiac abnormal	10007816
Catheterisation cardiac normal	10007817
Central bradycardia	10078310
Central venous pressure	10007977
Central venous pressure abnormal	10007978
Central venous pressure decreased	10007979
Central venous pressure increased	10007980
Central venous pressure normal	10007981
Chronotropic incompetence	10068627
Computerised tomogram coronary artery	10060804
Computerised tomogram coronary artery abnormal	10060806

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Cardiac and vascular investigations incl. arrhythmia

Preferred Term Text	Preferred Term ID
Computerised tomogram coronary artery normal	10060805
Conduction disorder	10010276
Decreased ventricular afterload	10050906
Decreased ventricular preload	10050905
Defect conduction intraventricular	10012118
Directional Doppler flow tests	10013047
Directional Doppler flow tests abnormal	10013048
Directional Doppler flow tests normal	10013049
ECG P wave inverted	10057526
ECG electrically inactive area	10072252
ECG signs of myocardial infarction	10075299
ECG signs of myocardial ischaemia	10058317
ECG signs of ventricular hypertrophy	10050998
Echocardiogram	10014113
Echocardiogram abnormal	10061593
Echocardiogram normal	10014115
Ejection fraction	10050527
Ejection fraction abnormal	10014331
Ejection fraction decreased	10050528
Ejection fraction normal	10064144
Electrocardiogram	10014362
Electrocardiogram J wave	10075349
Electrocardiogram J wave abnormal	10075347
Electrocardiogram J wave increased	10075348
Electrocardiogram P pulmonale	10064209
Electrocardiogram P wave abnormal	10050384
Electrocardiogram P wave biphasic	10056962
Electrocardiogram P wave normal	10050383
Electrocardiogram PQ interval	10059215
Electrocardiogram PQ interval prolonged	10053656
Electrocardiogram PQ interval shortened	10075328
Electrocardiogram PR interval	10050656
Electrocardiogram PR prolongation	10053657
Electrocardiogram PR shortened	10014374
Electrocardiogram Q wave abnormal	10051177
Electrocardiogram Q waves	10014375
Electrocardiogram Q waves normal	10014376
Electrocardiogram QRS complex	10014377
Electrocardiogram QRS complex abnormal	10014378
Electrocardiogram QRS complex normal	10014379
Electrocardiogram QRS complex prolonged	10014380
Electrocardiogram QRS complex shortened	10051158
Electrocardiogram QT interval	10014385
Electrocardiogram QT interval abnormal	10063748
Electrocardiogram QT interval normal	10014386
Electrocardiogram QT prolonged	10014387
Electrocardiogram QT shortened	10014388
Electrocardiogram R on T phenomenon	10048883
Electrocardiogram RR interval prolonged	10067652
Electrocardiogram ST segment	10014389
Electrocardiogram ST segment abnormal	10014390
Electrocardiogram ST segment depression	10014391
Electrocardiogram ST segment elevation	10014392
Electrocardiogram ST segment normal	10014393
Electrocardiogram ST-T change	10061117
Electrocardiogram ST-T segment abnormal	10052333
Electrocardiogram ST-T segment depression	10049224
Electrocardiogram ST-T segment elevation	10049225
Electrocardiogram T wave abnormal	10050380
Electrocardiogram T wave alternans	10079358
Electrocardiogram T wave amplitude decreased	10014394
Electrocardiogram T wave amplitude increased	10051159
Electrocardiogram T wave biphasic	10050382

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Cardiac and vascular investigations incl. arrhythmia

Preferred Term Text	Preferred Term ID
Electrocardiogram T wave inversion	10014395
Electrocardiogram T wave normal	10050381
Electrocardiogram T wave peaked	10014396
Electrocardiogram U wave inversion	10062314
Electrocardiogram U wave present	10057913
Electrocardiogram U-wave abnormality	10055032
Electrocardiogram U-wave prominent	10080090
Electrocardiogram abnormal	10014363
Electrocardiogram ambulatory	10014368
Electrocardiogram ambulatory abnormal	10014369
Electrocardiogram ambulatory normal	10014370
Electrocardiogram change	10061116
Electrocardiogram delta waves abnormal	10014372
Electrocardiogram high voltage	10076278
Electrocardiogram low voltage	10062311
Electrocardiogram normal	10014373
Electrocardiogram pacemaker spike	10057999
Electrocardiogram repolarisation abnormality	10052464
Exercise electrocardiogram	10015644
Exercise electrocardiogram abnormal	10015645
Exercise electrocardiogram normal	10015646
Exercise test	10015652
Exercise test abnormal	10015653
Exercise test normal	10015654
Extrasystoles	10015856
Femoral bruit	10049431
Femoral pulse	10053932
Femoral pulse abnormal	10053934
Femoral pulse decreased	10053901
Femoral pulse increased	10053902
Femoral pulse normal	10053933
Foetal arrhythmia	10016847
Foetal heart rate acceleration abnormality	10074642
Foetal heart rate deceleration abnormality	10074636
Foetal heart rate disorder	10061158
Foetal tachyarrhythmia	10077575
Fractional flow reserve	10077343
Gated single photon emission computerised tomogram	10076888
Haemodynamic test	10061189
Haemodynamic test abnormal	10057457
Haemodynamic test normal	10057522
Heart alternation	10058155
Heart block congenital	10019263
Heart rate	10019299
Heart rate abnormal	10019300
Heart rate decreased	10019301
Heart rate increased	10019303
Heart rate irregular	10019304
Heart rate normal	10019306
Heart sounds	10069168
Heart sounds abnormal	10019311
Heart sounds normal	10019312
Homans' sign	10051013
Homans' sign negative	10071193
Homans' sign positive	10051031
Iliac bruit	10051833
Increased ventricular afterload	10050901
Increased ventricular preload	10050900
Inherited cardiac conduction disorder	10070294
Intracardiac pressure increased	10079904
Junctional ectopic tachycardia	10074640
Laser speckle contrast imaging	10075009
Left ventricular end-diastolic pressure	10060065

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Cardiac and vascular investigations incl. arrhythmia

Preferred Term Text	Preferred Term ID
Left ventricular end-diastolic pressure decreased	10060089
Left ventricular end-diastolic pressure increased	10060088
Lenegre's disease	10071710
Long QT syndrome	10024803
Long QT syndrome congenital	10057926
Lown-Ganong-Levine syndrome	10024984
Lymphangiogram	10025215
Lymphangiogram abnormal	10025216
Lymphangiogram normal	10025217
Lymphatic mapping	10072871
Maximum heart rate	10050312
Maximum heart rate decreased	10072477
Maximum heart rate increased	10072476
Mean arterial pressure	10026982
Mean arterial pressure decreased	10026983
Mean arterial pressure increased	10026985
Multiple gated acquisition scan	10028211
Multiple gated acquisition scan abnormal	10028212
Multiple gated acquisition scan normal	10028213
Myocardial strain	10066954
Neonatal tachycardia	10049775
Nodal arrhythmia	10029458
Nodal rhythm	10029470
Nonreassuring foetal heart rate pattern	10074641
Nuclear magnetic resonance imaging heart	10076374
Orthostatic heart rate response increased	10069431
Orthostatic heart rate test	10079786
Pacemaker generated arrhythmia	10053486
Pacemaker syndrome	10051994
Parasystole	10033929
Paroxysmal arrhythmia	10050106
Paroxysmal atrioventricular block	10077503
Pedal pulse abnormal	10062995
Pedal pulse decreased	10062993
Pericardial drainage test	10049185
Pericardial drainage test abnormal	10056459
Pericardial drainage test normal	10056463
Peripheral arteriogram	10075250
Peripheral pulse decreased	10048718
Popliteal pulse	10053938
Popliteal pulse abnormal	10053940
Popliteal pulse decreased	10053905
Popliteal pulse increased	10053906
Popliteal pulse normal	10053939
Postural orthostatic tachycardia syndrome	10063080
Pulmonary arterial pressure	10060196
Pulmonary arterial pressure abnormal	10060233
Pulmonary arterial pressure decreased	10060231
Pulmonary arterial pressure increased	10037324
Pulmonary arterial pressure normal	10060232
Pulmonary arterial wedge pressure	10037325
Pulmonary arterial wedge pressure abnormal	10037326
Pulmonary arterial wedge pressure decreased	10037327
Pulmonary arterial wedge pressure increased	10037329
Pulmonary arterial wedge pressure normal	10037331
Pulse abnormal	10037466
Pulse absent	10037469
Pulse pressure abnormal	10037478
Pulse pressure decreased	10037480
Pulse pressure increased	10037482
Pulse pressure normal	10037483
Pulse volume decreased	10069583
Pulse waveform	10061488

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Cardiac and vascular investigations incl. arrhythmia

Preferred Term Text	Preferred Term ID
Pulse waveform abnormal	10061475
Pulse waveform normal	10061487
Pulseless electrical activity	10058151
QRS axis	10057622
QRS axis abnormal	10057624
QRS axis normal	10057623
Radial pulse	10053935
Radial pulse abnormal	10053937
Radial pulse decreased	10053903
Radial pulse increased	10053904
Radial pulse normal	10053936
Rebound tachycardia	10067207
Renal bruit	10049432
Reperfusion arrhythmia	10058156
Respiratory sinus arrhythmia magnitude	10079114
Respiratory sinus arrhythmia magnitude abnormal	10079117
Respiratory sinus arrhythmia magnitude decreased	10079116
Respiratory sinus arrhythmia magnitude increased	10079115
Retrograde p-waves	10071187
Rhythm idioventricular	10039111
Right atrial pressure increased	10067283
Right ventricular ejection fraction decreased	10075337
Right ventricular systolic pressure	10060199
Right ventricular systolic pressure decreased	10060237
Right ventricular systolic pressure increased	10060236
SI QIII TIII pattern	10068479
Scan myocardial perfusion	10054082
Scan myocardial perfusion abnormal	10061501
Scan myocardial perfusion normal	10061514
Schellong test	10067771
Sinoatrial block	10040736
Sinus arrest	10040738
Sinus arrhythmia	10040739
Sinus bradycardia	10040741
Sinus node dysfunction	10075889
Sinus rhythm	10048815
Sinus tachycardia	10040752
Sinusoidal foetal heart rate pattern	10074643
Stress echocardiogram	10050241
Stress echocardiogram abnormal	10070746
Stress echocardiogram normal	10070745
Stroke volume	10042245
Stroke volume decreased	10042246
Stroke volume increased	10042248
Stroke volume normal	10042250
Sudden cardiac death	10049418
Sudden death	10042434
Supraventricular extrasystoles	10042602
Supraventricular tachyarrhythmia	10065342
Supraventricular tachycardia	10042604
Tachyarrhythmia	10049447
Tachycardia	10043071
Tachycardia foetal	10043074
Tachycardia paroxysmal	10043079
Tilt table test	10052700
Tilt table test normal	10072466
Tilt table test positive	10072467
Timothy syndrome	10079205
Toe brachial index abnormal	10080802
Toe brachial index decreased	10080805
Toe brachial index increased	10080801
Toe brachial index normal	10080806
Torsade de pointes	10044066

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Cardiac and vascular investigations incl. arrhythmia

Preferred Term Text	Preferred Term ID
Transvalvular pressure gradient	10075232
Transvalvular pressure gradient abnormal	10079127
Transvalvular pressure gradient decreased	10079129
Transvalvular pressure gradient increased	10079128
Transvalvular pressure gradient normal	10079126
Trifascicular block	10044644
Ultrasonic angiogram	10045384
Ultrasonic angiogram abnormal	10061604
Ultrasonic angiogram normal	10061605
Ultrasound Doppler	10045412
Ultrasound Doppler abnormal	10045413
Ultrasound Doppler normal	10045414
Vascular imaging	10052677
Vascular resistance pulmonary	10075164
Vascular resistance pulmonary decreased	10047103
Vascular resistance pulmonary increased	10067285
Vascular resistance pulmonary normal	10047104
Vascular resistance systemic	10047105
Vascular resistance systemic decreased	10047106
Vascular resistance systemic increased	10047107
Vascular resistance systemic normal	10047108
Vascular test	10062172
Vascular test abnormal	10057458
Vascular test normal	10057523
Vascular waterfall	10078820
Venogram	10047208
Venogram abnormal	10047209
Venogram normal	10047210
Venous bruit	10065565
Venous pressure	10060091
Venous pressure abnormal	10047234
Venous pressure decreased	10047235
Venous pressure increased	10047236
Venous pressure jugular	10047237
Venous pressure jugular abnormal	10047238
Venous pressure jugular decreased	10047239
Venous pressure jugular increased	10047240
Venous pressure jugular normal	10047241
Venous pressure normal	10062176
Ventricular arrhythmia	10047281
Ventricular asystole	10047284
Ventricular extrasystoles	10047289
Ventricular fibrillation	10047290
Ventricular flutter	10047294
Ventricular internal diameter	10057921
Ventricular internal diameter abnormal	10057922
Ventricular internal diameter normal	10057923
Ventricular parasystole	10058184
Ventricular pre-excitation	10049761
Ventricular tachyarrhythmia	10065341
Ventricular tachycardia	10047302
Wall motion score index	10079014
Wall motion score index abnormal	10079016
Wall motion score index normal	10079015
Wandering pacemaker	10047818
Withdrawal arrhythmia	10047997
Wolff-Parkinson-White syndrome	10048015
Wolff-Parkinson-White syndrome congenital	10049291

MedDRA version 21.0.

125 Listing of preferred terms used for NNMQ - Hyperglycaemia

Preferred Term Text	Preferred Term ID
Blood 1,5-anhydroglucitol test	10078005
Blood galactose	10060022
Blood galactose abnormal	10060037
Blood galactose decreased	10060039
Blood galactose increased	10060038
Blood galactose normal	10060036
Blood glucose	10005553
Blood glucose abnormal	10005554
Blood glucose decreased	10005555
Blood glucose false positive	10005556
Blood glucose fluctuation	10049803
Blood glucose normal	10005558
Carbohydrate tolerance decreased	10007218
Carbohydrate tolerance increased	10064424
Continuous glucose monitoring	10079764
Dawn phenomenon	10052097
Fructosamine	10017393
Fructosamine decreased	10017394
Fructosamine normal	10017396
Fructose	10063255
Fructose decreased	10063256
Fructose increased	10063257
Galactose urine	10017606
Galactose urine abnormal	10017607
Galactose urine decreased	10017608
Galactose urine increased	10017609
Glucose tolerance decreased	10018428
Glucose tolerance increased	10018431
Glucose tolerance test	10018432
Glucose tolerance test abnormal	10018433
Glucose tolerance test normal	10018435
Glycolysis increased	10018471
Glycosylated haemoglobin	10018480
Glycosylated haemoglobin decreased	10018482
Glycosylated haemoglobin normal	10018485
HAIR-AN syndrome	10067378
Hypoinsulinaemia	10070070
Hypoinsulinaemia postoperative	10021014
Impaired insulin secretion	10052341
Indeterminate glucose tolerance	10078582
Insulin resistance test	10069403
Lactose tolerance test	10052986
Lactose tolerance test abnormal	10056561
Lactose tolerance test normal	10056568
Stool reducing substances increased	10064232
Stool reducing substances test	10079899
Urine glucose false positive	10046644

MedDRA version 21.0.

126 Listing of preferred terms used for NNMQ - Type 2 diabetes

Preferred Term Text	Preferred Term ID
Acquired lipoatrophic diabetes	10073667
Blood 1,5-anhydroglucitol decreased	10065367
Blood glucose increased	10005557
Blood insulin increased	10005614
Diabetes complicating pregnancy	10012596
Diabetes mellitus	10012601
Diabetes mellitus inadequate control	10012607
Diabetes with hyperosmolarity	10012631
Diabetic arteritis	10077357
Diabetic coma	10012650
Diabetic coronary microangiopathy	10080788
Diabetic hepatopathy	10071265
Diabetic hyperglycaemic coma	10012668
Diabetic hyperosmolar coma	10012669
Diabetic ketoacidosis	10012671
Diabetic ketoacidotic hyperglycaemic coma	10012672
Diabetic ketosis	10012673
Diabetic metabolic decompensation	10074309
Euglycaemic diabetic ketoacidosis	10080061
Fructosamine increased	10017395
Fulminant type 1 diabetes mellitus	10072628
Gestational diabetes	10018209
Glucose tolerance impaired	10018429
Glucose tolerance impaired in pregnancy	10018430
Glucose urine present	10018478
Glycosuria	10018473
Glycosuria during pregnancy	10018475
Glycosylated haemoglobin increased	10018484
Hyperglycaemia	10020635
Hyperglycaemic hyperosmolar nonketotic syndrome	10063554
Hyperglycaemic seizure	10071394
Hyperglycaemic unconsciousness	10071286
Impaired fasting glucose	10056997
Insulin resistance	10022489
Insulin resistance syndrome	10022490
Insulin resistant diabetes	10022491
Insulin-requiring type 2 diabetes mellitus	10053247
Ketoacidosis	10023379
Ketonuria	10023388
Ketosis	10023391
Ketosis-prone diabetes mellitus	10023392
Latent autoimmune diabetes in adults	10066389
Metabolic syndrome	10052066
Monogenic diabetes	10075980
Neonatal diabetes mellitus	10028933
Pancreatogenous diabetes	10033660
Type 1 diabetes mellitus	10067584
Type 2 diabetes mellitus	10067585
Type 3 diabetes mellitus	10072659
Urine ketone body present	10057597

MedDRA version 21.0.

127 Listing of preferred terms used for NNMQ - Athralgia

Preferred Term Text	Preferred Term ID
Arthralgia	10003239

MedDRA version 21.0.

128 Listing of preferred terms used for NNMQ - Myalgia

Preferred Term Text	Preferred Term ID
Myalgia	10028411

MedDRA version 21.0.

129 Listing of preferred terms used for NNMQ - Scoliosis

Preferred Term Text	Preferred Term ID
Kyphoscoliosis	10023506
Scoliosis	10039722

MedDRA version 21.0.

130 Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
5q minus syndrome	10068532
ACTH-producing pituitary tumour	10000613
APUDoma	10003069
Abdominal neoplasm	10060925
Abdominal wall cyst	10051634
Abdominal wall neoplasm	10061610
Abdominal wall neoplasm benign	10071022
Abdominal wall neoplasm malignant	10071023
Acanthoma	10059394
Acanthosis nigricans	10000350
Acinar cell carcinoma of pancreas	10073363
Acinic cell carcinoma of salivary gland	10073369
Acoustic neuroma	10000523
Acquired C1 inhibitor deficiency	10081035
Acquired bronchial cyst	10051545
Acquired thalassaemia	10072108
Acral lentiginous melanoma	10000583
Acral lentiginous melanoma stage I	10000585
Acral lentiginous melanoma stage II	10000586
Acral lentiginous melanoma stage III	10000587
Acral lentiginous melanoma stage IV	10000588
Acrochordon	10000591
Acrokeratosis paraneoplastica	10065247
Acute bilineal leukaemia	10080323
Acute biphenotypic leukaemia	10067399
Acute leukaemia	10000830
Acute leukaemia in remission	10060930
Acute lymphocytic leukaemia	10000846
Acute lymphocytic leukaemia (in remission)	10000847
Acute lymphocytic leukaemia recurrent	10063620
Acute lymphocytic leukaemia refractory	10076866
Acute megakaryocytic leukaemia	10000860
Acute megakaryocytic leukaemia (in remission)	10057194
Acute monocytic leukaemia	10000871
Acute monocytic leukaemia (in remission)	10000872
Acute myeloid leukaemia	10000880
Acute myeloid leukaemia (in remission)	10000881
Acute myeloid leukaemia recurrent	10059034
Acute myelomonocytic leukaemia	10000890
Acute promyelocytic leukaemia	10001019
Acute undifferentiated leukaemia	10073479
Adenocarcinoma	10001141
Adenocarcinoma gastric	10001150
Adenocarcinoma of appendix	10073359
Adenocarcinoma of colon	10001167
Adenocarcinoma of salivary gland	10068068
Adenocarcinoma of the cervix	10001197
Adenocarcinoma pancreas	10052747
Adenoid cystic carcinoma	10053231
Adenoid cystic carcinoma of external auditory canal	10078057
Adenoid cystic carcinoma of salivary gland	10073370
Adenolipoma	10057341
Adenolymphoma	10070460
Adenoma benign	10001233
Adenomatous polyposis coli	10056981
Adenosquamous carcinoma of the cervix	10001244
Adenosquamous carcinoma of vagina	10073978
Adenosquamous cell carcinoma	10068873
Adenosquamous cell lung cancer	10001245
Adenosquamous cell lung cancer recurrent	10001247
Adenosquamous cell lung cancer stage 0	10001248
Adenosquamous cell lung cancer stage I	10001249
Adenosquamous cell lung cancer stage II	10001250

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Adenosquamous cell lung cancer stage III	10001251
Adenosquamous cell lung cancer stage IV	10001254
Administration site cyst	10075927
Adnexa uteri cyst	10050203
Adrenal adenoma	10001323
Adrenal cyst	10049647
Adrenal gland cancer	10073152
Adrenal gland cancer metastatic	10055095
Adrenal neoplasm	10061588
Adrenocortical carcinoma	10001388
Adult T-cell lymphoma/leukaemia	10001413
Adult T-cell lymphoma/leukaemia recurrent	10001416
Adult T-cell lymphoma/leukaemia refractory	10001417
Adult T-cell lymphoma/leukaemia stage I	10001418
Adult T-cell lymphoma/leukaemia stage II	10001419
Adult T-cell lymphoma/leukaemia stage III	10001420
Adult T-cell lymphoma/leukaemia stage IV	10001421
Aesthesioneuroblastoma	10001433
Aleukaemic leukaemia	10001660
Alveolar rhabdomyosarcoma	10065867
Alveolar soft part sarcoma	10001882
Alveolar soft part sarcoma metastatic	10001884
Alveolar soft part sarcoma recurrent	10001887
Ameloblastoma	10066796
Ampullary polyp	10076972
Amyloidoma	10059047
Anal cancer	10061424
Anal cancer metastatic	10055096
Anal cancer recurrent	10002133
Anal cancer stage 0	10002134
Anal cancer stage I	10002135
Anal cancer stage II	10002136
Anal cancer stage III	10002137
Anal cancer stage IV	10002138
Anal neoplasm	10061629
Anal polyp	10002168
Anal squamous cell carcinoma	10073358
Anaplastic astrocytoma	10002224
Anaplastic large cell lymphoma T- and null-cell types	10002227
Anaplastic large cell lymphoma T- and null-cell types recurrent	10002229
Anaplastic large cell lymphoma T- and null-cell types refractory	10002230
Anaplastic large cell lymphoma T- and null-cell types stage I	10002231
Anaplastic large cell lymphoma T- and null-cell types stage II	10002232
Anaplastic large cell lymphoma T- and null-cell types stage III	10002233
Anaplastic large cell lymphoma T- and null-cell types stage IV	10002234
Anaplastic large-cell lymphoma	10073478
Anaplastic meningioma	10073127
Anaplastic oligodendroglioma	10073128
Anaplastic thyroid cancer	10002240
Aneurysmal bone cyst	10002362
Angiocentric glioma	10073129
Angiocentric lymphoma	10002411
Angiocentric lymphoma recurrent	10002414
Angiocentric lymphoma refractory	10002415
Angiocentric lymphoma stage I	10002416
Angiocentric lymphoma stage II	10002417
Angiocentric lymphoma stage III	10002418
Angiocentric lymphoma stage IV	10002419
Angiofibroma	10002429
Angioimmunoblastic T-cell lymphoma	10002449
Angioimmunoblastic T-cell lymphoma recurrent	10002452
Angioimmunoblastic T-cell lymphoma refractory	10002453
Angioimmunoblastic T-cell lymphoma stage I	10002454

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Angioimmunoblastic T-cell lymphoma stage II	10002455
Angioimmunoblastic T-cell lymphoma stage III	10002456
Angioimmunoblastic T-cell lymphoma stage IV	10002457
Angiolipoma	10048945
Angiomyofibroblastoma	10074730
Angiomyolipoma	10051810
Angiomyxoma	10076892
Angiosarcoma	10002476
Angiosarcoma metastatic	10002477
Angiosarcoma non-metastatic	10057700
Angiosarcoma recurrent	10002480
Anogenital warts	10059313
Apocrine breast carcinoma	10066206
Appendix adenoma	10076206
Appendix cancer	10073360
Application site cyst	10076002
Arachnoid cyst	10049005
Astroblastoma	10079366
Astrocytoma	10003571
Astrocytoma malignant	10060971
Astrocytoma, low grade	10065869
Atypical fibroxanthoma	10064755
Atypical teratoid/rhabdoid tumour of CNS	10065907
Aural cystadenoma	10052241
Aural polyp	10003794
B precursor type acute leukaemia	10003890
B-cell lymphoma	10003899
B-cell lymphoma recurrent	10003902
B-cell lymphoma refractory	10003903
B-cell lymphoma stage I	10003904
B-cell lymphoma stage II	10003905
B-cell lymphoma stage III	10003906
B-cell lymphoma stage IV	10003907
B-cell prolymphocytic leukaemia	10073480
B-cell small lymphocytic lymphoma	10003908
B-cell small lymphocytic lymphoma recurrent	10003911
B-cell small lymphocytic lymphoma refractory	10003912
B-cell small lymphocytic lymphoma stage I	10003913
B-cell small lymphocytic lymphoma stage II	10003914
B-cell small lymphocytic lymphoma stage III	10003915
B-cell small lymphocytic lymphoma stage IV	10003916
B-cell type acute leukaemia	10003917
B-cell unclassifiable lymphoma high grade	10003922
B-cell unclassifiable lymphoma low grade	10003923
Bannayan-Riley-Ruvalcaba syndrome	10080314
Bartholin's cyst	10004140
Basal cell carcinoma	10004146
Basal cell naevus syndrome	10062804
Basosquamous carcinoma	10004178
Basosquamous carcinoma of skin	10004179
Becker's naevus	10004192
Bence Jones proteinuria	10004231
Benign abdominal neoplasm	10078771
Benign anorectal neoplasm	10060992
Benign biliary neoplasm	10056514
Benign bone neoplasm	10060993
Benign breast neoplasm	10004243
Benign cardiac neoplasm	10004245
Benign cartilage neoplasm	10072915
Benign duodenal neoplasm	10004251
Benign ear neoplasm	10069051
Benign endocrine neoplasm	10060994
Benign fallopian tube neoplasm	10053865

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Benign female reproductive tract neoplasm	10060995
Benign gastric neoplasm	10004267
Benign gastrointestinal neoplasm	10060996
Benign genitourinary tract neoplasm	10074418
Benign hepatic neoplasm	10004269
Benign hepatobiliary neoplasm	10077922
Benign hydatidiform mole	10004272
Benign joint neoplasm	10078143
Benign laryngeal neoplasm	10004278
Benign lung neoplasm	10004280
Benign lymph node neoplasm	10060997
Benign male reproductive tract neoplasm	10060998
Benign mediastinal neoplasm	10004288
Benign mesenteric neoplasm	10072024
Benign mesothelioma	10061691
Benign middle ear neoplasm	10004292
Benign muscle neoplasm	10061692
Benign neoplasm	10060999
Benign neoplasm of adrenal gland	10004300
Benign neoplasm of ampulla of Vater	10077045
Benign neoplasm of bladder	10004302
Benign neoplasm of cervix uteri	10004312
Benign neoplasm of choroid	10004313
Benign neoplasm of conjunctiva	10004315
Benign neoplasm of cornea	10004316
Benign neoplasm of epididymis	10004323
Benign neoplasm of eye	10004325
Benign neoplasm of eyelid	10063707
Benign neoplasm of islets of Langerhans	10004334
Benign neoplasm of lacrimal duct	10004337
Benign neoplasm of lacrimal gland	10004338
Benign neoplasm of optic nerve	10057424
Benign neoplasm of orbit	10004355
Benign neoplasm of pineal gland	10004380
Benign neoplasm of prostate	10004385
Benign neoplasm of retina	10004390
Benign neoplasm of scrotum	10004395
Benign neoplasm of seminal vesicle	10068125
Benign neoplasm of skin	10004398
Benign neoplasm of spinal cord	10004406
Benign neoplasm of testis	10004410
Benign neoplasm of thymus	10004411
Benign neoplasm of thyroid gland	10004412
Benign neoplasm of ureter	10004418
Benign neoplasm of urethra	10004419
Benign nipple neoplasm	10072040
Benign oesophageal neoplasm	10004428
Benign ovarian tumour	10004433
Benign pancreatic neoplasm	10061000
Benign penile neoplasm	10004437
Benign pericardium neoplasm	10054947
Benign peritoneal neoplasm	10004438
Benign pleural mesothelioma	10004442
Benign pleural neoplasm	10004443
Benign renal neoplasm	10061001
Benign respiratory tract neoplasm	10061002
Benign salivary gland neoplasm	10004453
Benign small intestinal neoplasm	10061003
Benign soft tissue neoplasm	10061004
Benign spleen tumour	10059425
Benign tracheal neoplasm	10004466
Benign urinary tract neoplasm	10061006
Benign uterine neoplasm	10061007

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Benign vaginal neoplasm	10004472
Benign vascular neoplasm	10056253
Benign vulval neoplasm	10004475
Bile duct adenocarcinoma	10004585
Bile duct adenosquamous carcinoma	10004589
Bile duct cancer	10004593
Bile duct cancer recurrent	10004596
Bile duct cancer stage 0	10059384
Bile duct cancer stage I	10059373
Bile duct cancer stage II	10059374
Bile duct cancer stage III	10059375
Bile duct cancer stage IV	10059376
Bile duct squamous cell carcinoma	10004633
Biliary adenoma	10048798
Biliary cancer metastatic	10055111
Biliary cyst	10052384
Biliary hamartoma	10074610
Biliary neoplasm	10004668
Biliary polyp	10068356
Biphasic mesothelioma	10073062
Birt-Hogg-Dube syndrome	10067736
Bladder adenocarcinoma recurrent	10004986
Bladder adenocarcinoma stage 0	10004987
Bladder adenocarcinoma stage I	10004988
Bladder adenocarcinoma stage II	10004989
Bladder adenocarcinoma stage III	10004990
Bladder adenocarcinoma stage IV	10004991
Bladder adenocarcinoma stage unspecified	10004992
Bladder cancer	10005003
Bladder cancer recurrent	10005005
Bladder cancer stage 0, with cancer in situ	10005006
Bladder cancer stage 0, without cancer in situ	10005007
Bladder cancer stage I, with cancer in situ	10005008
Bladder cancer stage I, without cancer in situ	10005009
Bladder cancer stage II	10005010
Bladder cancer stage III	10005011
Bladder cancer stage IV	10005012
Bladder cyst	10058524
Bladder neoplasm	10005056
Bladder papilloma	10005064
Bladder squamous cell carcinoma recurrent	10005075
Bladder squamous cell carcinoma stage 0	10005076
Bladder squamous cell carcinoma stage I	10005077
Bladder squamous cell carcinoma stage II	10005078
Bladder squamous cell carcinoma stage III	10005079
Bladder squamous cell carcinoma stage IV	10005080
Bladder squamous cell carcinoma stage unspecified	10005081
Bladder transitional cell carcinoma	10005084
Bladder transitional cell carcinoma metastatic	10071664
Bladder transitional cell carcinoma recurrent	10066750
Bladder transitional cell carcinoma stage 0	10066749
Bladder transitional cell carcinoma stage I	10066751
Bladder transitional cell carcinoma stage II	10066753
Bladder transitional cell carcinoma stage III	10066754
Bladder transitional cell carcinoma stage IV	10066752
Blast cell crisis	10053747
Blast cell proliferation	10005089
Blast crisis in myelogenous leukaemia	10050282
Blastic plasmacytoid dendritic cell neoplasia	10075460
Blepharal papilloma	10057885
Bone cancer	10005949
Bone cancer metastatic	10055101
Bone cyst	10005952

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Bone giant cell tumour	10005969
Bone giant cell tumour benign	10005970
Bone giant cell tumour malignant	10073106
Bone marrow leukaemic cell infiltration	10049557
Bone marrow reticulin fibrosis	10069678
Bone marrow tumour cell infiltration	10049556
Bone neoplasm	10005995
Bone sarcoma	10006007
Borderline mucinous tumour of ovary	10073266
Borderline ovarian tumour	10006032
Borderline serous tumour of ovary	10073267
Bowen's disease	10006059
Bowenoid papulosis	10006060
Brain cancer metastatic	10055093
Brain neoplasm	10061019
Brain neoplasm benign	10006129
Brain neoplasm malignant	10006131
Brain sarcoma	10073857
Brain stem glioma	10006143
Brain stem glioma benign	10006144
Brain teratoma	10068394
Branchial cyst	10006164
Breakthrough pain	10064556
Breast adenoma	10063087
Breast angiosarcoma	10072813
Breast angiosarcoma metastatic	10072814
Breast cancer	10006187
Breast cancer female	10057654
Breast cancer in situ	10006189
Breast cancer male	10061020
Breast cancer metastatic	10055113
Breast cancer recurrent	10006198
Breast cancer stage I	10006199
Breast cancer stage II	10006200
Breast cancer stage III	10006201
Breast cancer stage IV	10006202
Breast cyst	10006220
Breast cyst rupture	10072812
Breast fibroma	10063088
Breast neoplasm	10006279
Breast sarcoma	10068582
Breast sarcoma metastatic	10068583
Breast sarcoma recurrent	10068584
Brenner tumour	10073258
Bronchial carcinoma	10006417
Bronchial neoplasm	10052245
Bronchial neoplasm benign	10052247
Bronchial polyp	10057346
Bronchioloalveolar carcinoma	10058354
Buccal polyp	10051411
Burkitt's leukaemia	10067184
Burkitt's lymphoma	10006595
Burkitt's lymphoma recurrent	10006598
Burkitt's lymphoma refractory	10006599
Burkitt's lymphoma stage I	10006600
Burkitt's lymphoma stage II	10006601
Burkitt's lymphoma stage III	10006602
Burkitt's lymphoma stage IV	10006603
Buschke-Lowenstein's tumour	10059427
CNS germinoma	10065852
Cachexia	10006895
Calcifying fibrous pseudotumour	10064280
Cancer in remission	10065305

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Cancer pain	10058019
Carcinogenic effect in offspring	10007268
Carcinoid crisis	10072251
Carcinoid heart disease	10069010
Carcinoid syndrome	10007270
Carcinoid tumour	10007275
Carcinoid tumour of the appendix	10007277
Carcinoid tumour of the caecum	10007278
Carcinoid tumour of the duodenum	10050110
Carcinoid tumour of the gastrointestinal tract	10007279
Carcinoid tumour of the pancreas	10055007
Carcinoid tumour of the prostate	10007280
Carcinoid tumour of the small bowel	10052819
Carcinoid tumour of the stomach	10007281
Carcinoid tumour pulmonary	10007282
Carcinoma ex-pleomorphic adenoma	10077435
Carcinoma in situ	10061450
Carcinoma in situ of eye	10007368
Carcinoma in situ of penis	10007384
Carcinoma in situ of skin	10007390
Carcinoma in situ of trachea	10007401
Carcinomatous polyarthritis	10069494
Cardiac fibroma	10055009
Cardiac haemangioma benign	10055011
Cardiac lymphangioma	10055010
Cardiac myxoma	10061005
Cardiac neoplasm malignant	10061025
Cardiac neoplasm unspecified	10051549
Cardiac neurofibroma	10055012
Cardiac teratoma	10057456
Cardiac valve fibroelastoma	10068699
Carney complex	10076601
Carotid body tumour	10007690
Cartilage neoplasm	10061746
Castleman's disease	10050251
Cementoblastoma	10062564
Central nervous system dermoid tumour	10007942
Central nervous system leukaemia	10066231
Central nervous system lymphoma	10007953
Central nervous system melanoma	10077160
Central nervous system neoplasm	10007958
Central nervous system neuroblastoma	10073130
Cerebellar haemangioma	10059273
Cerebellar tumour	10061750
Cerebellopontine angle tumour	10069726
Cerebral cyst	10061445
Cerebral haemangioma	10048788
Cervical cyst	10008254
Cervical polyp	10008297
Cervix adenomatous polyp	10008338
Cervix cancer metastatic	10055094
Cervix carcinoma	10008342
Cervix carcinoma recurrent	10008344
Cervix carcinoma stage 0	10061809
Cervix carcinoma stage I	10008345
Cervix carcinoma stage II	10008346
Cervix carcinoma stage III	10008347
Cervix carcinoma stage IV	10008348
Cervix neoplasm	10008354
Cervix warts	10063815
Chemodectoma	10051227
Chest wall cyst	10051649
Chest wall tumour	10072960

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Chiasma syndrome	10067348
Chloroma	10008583
Chloroma (in remission)	10008584
Cholangioadenoma	10008592
Cholangiocarcinoma	10008593
Cholangiosarcoma	10077861
Choledochal cyst	10008625
Cholesteatoma	10008642
Cholesterin granuloma of middle ear	10008649
Cholesterol granuloma	10008660
Chondroblastoma	10008686
Chondroma	10008725
Chondromatosis	10051503
Chondrosarcoma	10008734
Chondrosarcoma metastatic	10008736
Chondrosarcoma recurrent	10008738
Chordoma	10008747
Choriocarcinoma	10008757
Choroid fissure cyst	10079494
Choroid melanoma	10008773
Choroid neoplasm	10057405
Choroid plexus carcinoma	10067478
Choroid plexus papilloma	10008777
Choroidal haemangioma	10070957
Chromophobe renal cell carcinoma	10080544
Chronic eosinophilic leukaemia	10065854
Chronic leukaemia	10008943
Chronic leukaemia in remission	10061042
Chronic lymphocytic leukaemia	10008958
Chronic lymphocytic leukaemia (in remission)	10008959
Chronic lymphocytic leukaemia recurrent	10008961
Chronic lymphocytic leukaemia refractory	10008962
Chronic lymphocytic leukaemia stage 0	10008963
Chronic lymphocytic leukaemia stage 1	10008964
Chronic lymphocytic leukaemia stage 2	10008965
Chronic lymphocytic leukaemia stage 3	10008966
Chronic lymphocytic leukaemia stage 4	10008967
Chronic lymphocytic leukaemia transformation	10058717
Chronic myeloid leukaemia	10009013
Chronic myeloid leukaemia (in remission)	10009014
Chronic myeloid leukaemia recurrent	10075081
Chronic myeloid leukaemia transformation	10068232
Chronic myelomonocytic leukaemia	10009018
Chronic myelomonocytic leukaemia (in remission)	10009019
Chronic rhinosinusitis with nasal polyps	10080060
Clear cell carcinoma of cervix	10074909
Clear cell endometrial carcinoma	10009252
Clear cell renal cell carcinoma	10073251
Clear cell sarcoma of soft tissue	10073140
Clear cell sarcoma of the kidney	10009253
Clonal evolution	10065163
Colloid brain cyst	10074613
Colon adenoma	10048832
Colon cancer	10009944
Colon cancer metastatic	10055114
Colon cancer recurrent	10009952
Colon cancer stage 0	10063523
Colon cancer stage I	10009953
Colon cancer stage II	10009954
Colon cancer stage III	10009955
Colon cancer stage IV	10009956
Colon neoplasm	10061045
Colorectal adenocarcinoma	10052360

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Colorectal cancer	10061451
Colorectal cancer metastatic	10052358
Colorectal cancer recurrent	10010030
Colorectal cancer stage I	10010032
Colorectal cancer stage II	10010033
Colorectal cancer stage III	10010034
Colorectal cancer stage IV	10010035
Colorectal carcinoma stage 0	10010038
Composite lymphoma	10073957
Congenital acrochordon	10050730
Congenital benign neoplasm	10073493
Congenital cerebral cyst	10054954
Congenital cerebral haemangioma	10048924
Congenital choroid plexus cyst	10048785
Congenital cyst	10062328
Congenital cystic disease of liver	10010427
Congenital cystic kidney disease	10010428
Congenital eye naevus	10051050
Congenital fibrosarcoma	10065859
Congenital malignant neoplasm	10073492
Congenital melanocytic naevus	10072036
Congenital naevus	10067248
Congenital neoplasm	10078557
Congenital renal cyst	10010607
Congenital retinoblastoma	10073470
Congenital teratoma	10052012
Congenital vaginal cyst	10063457
Conjunctival cyst	10010703
Conjunctival melanoma	10066384
Conjunctival neoplasm	10057406
Conjunctival primary acquired melanosis	10066925
Connective tissue neoplasm	10061088
Corneal cyst	10061787
Corneoconjunctival intraepithelial neoplasia	10071076
Cowden's disease	10051906
Cranial nerve neoplasm benign	10061095
Craniopharyngioma	10011318
Craniopharyngioma benign	10011319
Cronkhite-Canada syndrome	10062907
Cutaneous lymphoma	10079945
Cyst	10011732
Cyst rupture	10061803
Cystadenocarcinoma ovary	10054912
Cystadenocarcinoma pancreas	10065908
Cystadenofibroma of fallopian tube	10080257
Cystic angiomatosis	10079371
Cystic eyeball, congenital	10011761
Cystic lymphangioma	10058949
Dedifferentiated liposarcoma	10073135
Dental cyst	10075995
Denys-Drash syndrome	10070179
Dermal cyst	10012426
Dermatofibrosarcoma protuberans	10057070
Dermatofibrosarcoma protuberans metastatic	10073574
Dermoid cyst	10012522
Desmoid tumour	10059352
Desmoplastic melanoma	10072449
Desmoplastic mesothelioma	10073063
Desmoplastic small round cell tumour	10064581
Diaphragm neoplasm	10051932
Diffuse large B-cell lymphoma	10012818
Diffuse large B-cell lymphoma recurrent	10012821
Diffuse large B-cell lymphoma refractory	10012822

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Diffuse large B-cell lymphoma stage I	10012823
Diffuse large B-cell lymphoma stage II	10012824
Diffuse large B-cell lymphoma stage III	10012825
Diffuse large B-cell lymphoma stage IV	10012826
Diffuse uveal melanocytic proliferation	10078228
Disseminated large cell lymphoma	10054951
Double hit lymphoma	10080202
Ductal adenocarcinoma of pancreas	10073364
Duodenal neoplasm	10061825
Duodenal polyp	10013833
Dysplastic naevus	10062805
Dysplastic naevus syndrome	10013960
Ear neoplasm	10055016
Ear neoplasm malignant	10055017
Eccrine carcinoma	10069680
Ectopic ACTH syndrome	10014146
Ectopic aldosterone secretion	10014148
Ectopic antidiuretic hormone secretion	10014149
Ectopic calcitonin production	10014152
Ectopic chorionic gonadotrophin secretion	10014153
Ectopic growth hormone secretion	10014158
Ectopic hormone secretion	10061115
Ectopic parathyroid hormone production	10014165
Ectopic prolactin secretion	10014170
Ectopic renin secretion	10014171
Elastofibroma	10079215
Elephantiasis nostras verrucosa	10071025
Embryonal rhabdomyosarcoma	10065868
Encephalitis autoimmune	10072378
Enchondromatosis	10014642
Endobronchial lipoma	10014654
Endocrine neoplasm	10061121
Endocrine neoplasm malignant	10061122
Endometrial adenocarcinoma	10014720
Endometrial adenoma	10014728
Endometrial cancer	10014733
Endometrial cancer metastatic	10014734
Endometrial cancer recurrent	10014736
Endometrial cancer stage 0	10014737
Endometrial cancer stage I	10014738
Endometrial cancer stage II	10014739
Endometrial cancer stage III	10014740
Endometrial cancer stage IV	10014741
Endometrial neoplasm	10014759
Endometrial sarcoma	10057649
Endometrial sarcoma metastatic	10067065
Endometrial sarcoma recurrent	10067064
Endometrial stromal sarcoma	10048397
Endotheliomatosis	10076868
Enteropathy-associated T-cell lymphoma	10073481
Eosinophilic leukaemia	10014958
Ependymoma	10014967
Ependymoma benign	10014969
Ependymoma malignant	10014968
Epidermal naevus syndrome	10077952
Epididymal cancer	10073115
Epididymal cyst	10014994
Epididymal neoplasm	10069101
Epiglottic carcinoma	10057438
Epiglottic cyst	10057437
Epithelioid mesothelioma	10073064
Epithelioid sarcoma	10015099
Epithelioid sarcoma metastatic	10015101

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Epithelioid sarcoma recurrent	10015104
Epithelioma adenoides cysticum	10015106
Epstein Barr virus positive mucocutaneous ulcer	10079386
Epstein-Barr virus associated lymphoma	10071441
Epstein-Barr virus associated lymphoproliferative disorder	10068349
Erdheim-Chester disease	10060801
Erythraemic myelosis (in remission)	10015246
Erythroleukaemia	10015281
Erythroplasia	10063121
Erythroplasia of lip	10052826
Erythroplasia of penis	10052824
Erythroplasia of vulva	10052825
Essential thrombocythaemia	10015493
Ewing's sarcoma	10015560
Ewing's sarcoma metastatic	10015562
Ewing's sarcoma recurrent	10015564
Extra-osseous Ewing's sarcoma	10015759
Extra-osseous Ewing's sarcoma metastatic	10015761
Extra-osseous Ewing's sarcoma recurrent	10015764
Extradural neoplasm	10058955
Extragonadal primary embryonal carcinoma	10015789
Extragonadal primary germ cell tumour	10073055
Extragonadal primary germ cell tumour mixed	10073056
Extragonadal primary germ cell tumour mixed stage I	10015800
Extragonadal primary germ cell tumour mixed stage II	10015801
Extragonadal primary germ cell tumour mixed stage III	10015802
Extragonadal primary malignant teratoma	10061848
Extragonadal primary non-seminoma	10061849
Extragonadal primary non-seminoma stage I	10015805
Extragonadal primary non-seminoma stage II	10015806
Extragonadal primary non-seminoma stage III	10015809
Extragonadal primary non-seminoma stage IV	10015810
Extragonadal primary seminoma (pure)	10073057
Extragonadal primary seminoma (pure) stage I	10015811
Extragonadal primary seminoma (pure) stage II	10015812
Extragonadal primary seminoma (pure) stage III	10015815
Extragonadal primary seminoma (pure) stage IV	10015816
Extramammary Paget's disease	10068223
Extranodal marginal zone B-cell lymphoma (MALT type)	10061850
Extranodal marginal zone B-cell lymphoma (MALT type) recurrent	10015823
Extranodal marginal zone B-cell lymphoma (MALT type) refractory	10015824
Extranodal marginal zone B-cell lymphoma (MALT type) stage I	10015825
Extranodal marginal zone B-cell lymphoma (MALT type) stage II	10015826
Extranodal marginal zone B-cell lymphoma (MALT type) stage III	10015827
Extranodal marginal zone B-cell lymphoma (MALT type) stage IV	10015828
Extraocular retinoblastoma	10015831
Extraskeletal chondrosarcoma metastatic	10015840
Extraskeletal chondrosarcoma recurrent	10015843
Extraskeletal myxoid chondrosarcoma	10073134
Extraskeletal osteosarcoma	10015847
Extraskeletal osteosarcoma metastatic	10015849
Extraskeletal osteosarcoma recurrent	10015852
Eye haemangioma	10071053
Eye naevus	10051045
Eyelid haemangioma	10071054
Eyelid naevus	10080691
Eyelid tumour	10050497
Fallopian tube cancer	10016180
Fallopian tube cancer metastatic	10016182
Fallopian tube cancer stage I	10016184
Fallopian tube cancer stage II	10016185
Fallopian tube cancer stage III	10016186
Fallopian tube cancer stage IV	10016187

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Fallopian tube cyst	10050697
Fallopian tube leiomyoma	10079928
Fallopian tube neoplasm	10061855
Familial acromegaly	10080509
Familial haemophagocytic lymphohistiocytosis	10070904
Familial medullary thyroid cancer	10073153
Female reproductive neoplasm	10061153
Female reproductive tract carcinoma in situ	10061154
Fibroadenoma of breast	10016613
Fibrocystic breast disease	10016621
Fibroma	10016629
Fibromatosis	10049444
Fibrosarcoma	10016632
Fibrosarcoma metastatic	10016635
Fibrous cortical defect	10052753
Fibrous histiocytoma	10053717
Focal nodular hyperplasia	10052285
Foetal cystic hygroma	10052011
Follicle centre lymphoma diffuse small cell lymphoma	10061957
Follicle centre lymphoma diffuse small cell lymphoma recurrent	10016897
Follicle centre lymphoma diffuse small cell lymphoma refractory	10016898
Follicle centre lymphoma diffuse small cell lymphoma stage I	10016899
Follicle centre lymphoma diffuse small cell lymphoma stage II	10016900
Follicle centre lymphoma diffuse small cell lymphoma stage III	10016901
Follicle centre lymphoma diffuse small cell lymphoma stage IV	10016902
Follicle centre lymphoma, follicular grade I, II, III	10061170
Follicle centre lymphoma, follicular grade I, II, III recurrent	10016905
Follicle centre lymphoma, follicular grade I, II, III refractory	10016906
Follicle centre lymphoma, follicular grade I, II, III stage I	10016907
Follicle centre lymphoma, follicular grade I, II, III stage II	10016908
Follicle centre lymphoma, follicular grade I, II, III stage III	10016909
Follicle centre lymphoma, follicular grade I, II, III stage IV	10016910
Follicular dendritic cell sarcoma	10075332
Follicular thyroid cancer	10016935
Frasier syndrome	10080313
Fungating wound	10068834
Gallbladder adenocarcinoma	10058286
Gallbladder adenoma	10076240
Gallbladder adenosquamous carcinoma	10073067
Gallbladder cancer	10017614
Gallbladder cancer metastatic	10066879
Gallbladder cancer recurrent	10017619
Gallbladder cancer stage 0	10059316
Gallbladder cancer stage I	10059317
Gallbladder cancer stage II	10058281
Gallbladder cancer stage III	10058282
Gallbladder cancer stage IV	10058283
Gallbladder neoplasm	10073072
Gallbladder papilloma	10073347
Gallbladder polyp	10049704
Gallbladder squamous cell carcinoma	10073068
Gammopathy	10061964
Ganglioglioma	10017701
Ganglioneuroblastoma	10017708
Ganglioneuroma	10017709
Garcin syndrome	10076032
Gastric adenoma	10060850
Gastric cancer	10017758
Gastric cancer recurrent	10017761
Gastric cancer stage 0	10017762
Gastric cancer stage I	10017763
Gastric cancer stage II	10017764
Gastric cancer stage III	10017765

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Gastric cancer stage IV	10061967
Gastric cyst	10056978
Gastric haemangioma	10075848
Gastric leiomyoma	10081041
Gastric neoplasm	10061968
Gastric polyps	10017817
Gastric sarcoma	10055008
Gastrinoma	10017852
Gastrinoma malignant	10051709
Gastroenteropancreatic neuroendocrine tumour disease	10077559
Gastrointestinal adenocarcinoma	10081003
Gastrointestinal cancer metastatic	10053548
Gastrointestinal carcinoma	10017940
Gastrointestinal carcinoma in situ	10061168
Gastrointestinal lymphoma	10017973
Gastrointestinal melanoma	10077167
Gastrointestinal neoplasm	10061174
Gastrointestinal polyp	10079055
Gastrointestinal polyp haemorrhage	10074437
Gastrointestinal stromal cancer	10071653
Gastrointestinal stromal tumour	10051066
Gastrointestinal submucosal tumour	10072581
Gastrointestinal tract adenoma	10051635
Gastrooesophageal cancer	10062878
Genital cancer male	10073116
Genital cancer male in situ	10073124
Genital cyst	10053178
Genital neoplasm malignant female	10018160
Genitourinary melanoma	10077166
Genitourinary tract neoplasm	10061183
Germ cell cancer	10061184
Germ cell cancer metastatic	10068971
Germ cell neoplasm	10075292
Gestational trophoblastic tumour	10061988
Giant cell tumour of tendon sheath	10018255
Gingival cancer	10067807
Gingival cyst	10055018
Gingival polyp	10018288
Glioblastoma	10018336
Glioblastoma multiforme	10018337
Glioma	10018338
Gliomatosis cerebri	10066254
Glioneuronal tumour	10068601
Gliosarcoma	10018340
Glomus jugulare tumour	10056563
Glomus tumour	10018381
Glomus tympanicum tumour	10069919
Glottis carcinoma	10018395
Glucagonoma	10018404
Good syndrome	10079838
Gorham's disease	10071283
Granular cell tumour	10060980
Granulosa cell tumour of the testis	10078131
Growth hormone-producing pituitary tumour	10018758
HER-2 positive breast cancer	10065430
HER-2 positive gastric cancer	10066896
Haemangioblastoma	10018813
Haemangioma	10018814
Haemangioma congenital	10018818
Haemangioma of bone	10072572
Haemangioma of breast	10018820
Haemangioma of liver	10018821
Haemangioma of retina	10018822

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Haemangioma of skin	10018823
Haemangioma of spleen	10068123
Haemangioma-thrombocytopenia syndrome	10058423
Haemangiopericytoma	10018825
Haemangiopericytoma of meninges	10018826
Haematological malignancy	10066476
Haematopoietic neoplasm	10061187
Haemophilic pseudotumour	10073770
Haemorrhagic breast cyst	10077443
Haemorrhagic cyst	10059189
Haemorrhagic hepatic cyst	10067796
Haemorrhagic ovarian cyst	10060781
Haemorrhagic thyroid cyst	10072256
Haemorrhagic tumour necrosis	10054096
Hair follicle tumour benign	10019043
Hairy cell leukaemia	10019053
Hairy cell leukaemia recurrent	10077403
Hamartoma	10061193
Hamartoma vascular	10019106
Head and neck cancer	10067821
Head and neck cancer metastatic	10071540
Head and neck cancer stage I	10071539
Head and neck cancer stage II	10071538
Head and neck cancer stage III	10071537
Head and neck cancer stage IV	10071536
Heavy chain disease	10019350
Hepatic adenoma	10019629
Hepatic angiosarcoma	10067388
Hepatic cancer	10073069
Hepatic cancer metastatic	10055110
Hepatic cancer recurrent	10073070
Hepatic cancer stage I	10059318
Hepatic cancer stage II	10059319
Hepatic cancer stage III	10059324
Hepatic cancer stage IV	10059325
Hepatic cyst	10019646
Hepatic cyst infection	10051705
Hepatic cyst ruptured	10053973
Hepatic haemangioma rupture	10054885
Hepatic hamartoma	10079685
Hepatic neoplasm	10019695
Hepatobiliary cancer	10073073
Hepatobiliary cancer in situ	10073074
Hepatobiliary cyst	10079889
Hepatobiliary neoplasm	10061203
Hepatoblastoma	10062001
Hepatoblastoma recurrent	10019823
Hepatocellular carcinoma	10073071
Hepatosplenic T-cell lymphoma	10066957
Hereditary leiomyomatosis renal cell carcinoma	10067944
Hereditary multiple osteochondromas	10079019
Hereditary non-polyposis colorectal cancer syndrome	10051922
Hereditary papillary renal carcinoma	10067943
Hidradenocarcinoma	10073088
High grade B-cell lymphoma Burkitt-like lymphoma	10020067
High grade B-cell lymphoma Burkitt-like lymphoma recurrent	10020070
High grade B-cell lymphoma Burkitt-like lymphoma refractory	10020071
High grade B-cell lymphoma Burkitt-like lymphoma stage I	10020072
High grade B-cell lymphoma Burkitt-like lymphoma stage II	10020073
High grade B-cell lymphoma Burkitt-like lymphoma stage III	10020074
High grade B-cell lymphoma Burkitt-like lymphoma stage IV	10020075
High-grade B-cell lymphoma	10080215
Histiocytic medullary reticulosis	10068785

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Histiocytic necrotising lymphadenitis	10069070
Histiocytic sarcoma	10076876
Histiocytosis	10020117
Hodgkin's disease	10020206
Hodgkin's disease lymphocyte depletion stage I site unspecified	10020208
Hodgkin's disease lymphocyte depletion stage I subdiaphragm	10020209
Hodgkin's disease lymphocyte depletion stage I supradiaphragm	10020210
Hodgkin's disease lymphocyte depletion stage II site unspecified	10020211
Hodgkin's disease lymphocyte depletion stage II subdiaphragm	10020212
Hodgkin's disease lymphocyte depletion stage II supradiaphragm	10020213
Hodgkin's disease lymphocyte depletion type recurrent	10020215
Hodgkin's disease lymphocyte depletion type refractory	10020216
Hodgkin's disease lymphocyte depletion type stage III	10020217
Hodgkin's disease lymphocyte depletion type stage IV	10020218
Hodgkin's disease lymphocyte depletion type stage unspecified	10020219
Hodgkin's disease lymphocyte predominance stage I site unspec	10020220
Hodgkin's disease lymphocyte predominance stage I subdiaphragm	10020221
Hodgkin's disease lymphocyte predominance stage I supradiaphragm	10020222
Hodgkin's disease lymphocyte predominance stage II site unspec	10020223
Hodgkin's disease lymphocyte predominance stage II subdiaphragm	10020224
Hodgkin's disease lymphocyte predominance stage II supradiaphragm	10020225
Hodgkin's disease lymphocyte predominance type recurrent	10020227
Hodgkin's disease lymphocyte predominance type refractory	10020228
Hodgkin's disease lymphocyte predominance type stage III	10020229
Hodgkin's disease lymphocyte predominance type stage IV	10020230
Hodgkin's disease lymphocyte predominance type stage unspecified	10020231
Hodgkin's disease mixed cellularity recurrent	10020233
Hodgkin's disease mixed cellularity refractory	10020234
Hodgkin's disease mixed cellularity stage I site unspecified	10020235
Hodgkin's disease mixed cellularity stage I subdiaphragmatic	10020236
Hodgkin's disease mixed cellularity stage I supradiaphragmatic	10020237
Hodgkin's disease mixed cellularity stage II subdiaphragmatic	10020238
Hodgkin's disease mixed cellularity stage II supradiaphragmatic	10020239
Hodgkin's disease mixed cellularity stage III	10020240
Hodgkin's disease mixed cellularity stage IV	10020241
Hodgkin's disease mixed cellularity stage unspecified	10020242
Hodgkin's disease nodular sclerosis	10020244
Hodgkin's disease nodular sclerosis recurrent	10020245
Hodgkin's disease nodular sclerosis refractory	10020246
Hodgkin's disease nodular sclerosis stage I	10073535
Hodgkin's disease nodular sclerosis stage II	10073534
Hodgkin's disease nodular sclerosis stage III	10020252
Hodgkin's disease nodular sclerosis stage IV	10020253
Hodgkin's disease recurrent	10020266
Hodgkin's disease refractory	10020267
Hodgkin's disease stage I	10020268
Hodgkin's disease stage II	10020269
Hodgkin's disease stage III	10020270
Hodgkin's disease stage IV	10061597
Hodgkin's disease unclassifiable	10020271
Hormone refractory breast cancer	10076935
Hormone-dependent prostate cancer	10071119
Hormone-refractory prostate cancer	10062904
Hormone-secreting ovarian tumour	10020391
Horner's syndrome	10020392
Huerthle cell carcinoma	10066136
Hygroma colli	10050249
Hypercalcaemia of malignancy	10020584
Hypercalcitoninaemia	10072001
Hypergammaglobulinaemia benign monoclonal	10020631
Hyperreactio luteinalis	10074866
Hypertrophic osteoarthropathy	10020877
Hypopharyngeal cancer	10021042

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Hypopharyngeal cancer recurrent	10021044
Hypopharyngeal cancer stage 0	10021045
Hypopharyngeal cancer stage I	10021046
Hypopharyngeal cancer stage II	10021047
Hypopharyngeal cancer stage III	10021048
Hypopharyngeal cancer stage IV	10021049
Hypopharyngeal neoplasm	10056305
Hypopharyngeal neoplasm benign	10021051
Hypothalamic hamartoma	10078217
Immune reconstitution inflammatory syndrome associated Kaposi's sarcoma	10072796
Immunoblastic lymphoma	10053574
Implant site cyst	10063854
Infantile haemangioma	10075378
Infantile septic granulomatosis	10048708
Infected cyst	10058015
Infected dermal cyst	10071367
Infected lymphocele	10059359
Infected naevus	10050500
Infected neoplasm	10058014
Inferior vena cava syndrome	10070911
Inflammatory carcinoma of breast recurrent	10021977
Inflammatory carcinoma of breast stage III	10021978
Inflammatory carcinoma of breast stage IV	10021979
Inflammatory carcinoma of the breast	10021980
Inflammatory malignant fibrous histiocytoma	10073142
Inflammatory myofibroblastic tumour	10067917
Inflammatory pseudotumour	10068331
Infusion site cyst	10065457
Injection site cyst	10022055
Insulinoma	10022498
Intestinal T-cell lymphoma recurrent	10022706
Intestinal T-cell lymphoma refractory	10022707
Intestinal T-cell lymphoma stage I	10022708
Intestinal T-cell lymphoma stage II	10022709
Intestinal T-cell lymphoma stage III	10022710
Intestinal T-cell lymphoma stage IV	10022711
Intestinal adenocarcinoma	10051925
Intestinal angioma	10078319
Intestinal cyst	10062023
Intestinal metastasis	10080311
Intestinal polyp	10048616
Intra-abdominal haemangioma	10022728
Intracranial germ cell tumour	10073751
Intracranial haemangioma	10022759
Intracranial meningioma malignant	10022770
Intracranial tumour haemorrhage	10022775
Intracystic breast papilloma	10078162
Intraductal papillary breast neoplasm	10073540
Intraductal papillary mucinous neoplasm	10070999
Intraductal papillary-mucinous carcinoma of pancreas	10073365
Intraductal papilloma of breast	10022781
Intraductal proliferative breast lesion	10073094
Intraneural cyst	10051086
Intraocular melanoma	10061252
Intraosseous angioma	10048846
Intratumoural aneurysm	10072808
Intravascular lipoma	10073293
Intravascular papillary endothelial hyperplasia	10060711
Intravenous leiomyomatosis	10071677
Invasive breast carcinoma	10075713
Invasive ductal breast carcinoma	10073095
Invasive lobular breast carcinoma	10073096

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Invasive papillary breast carcinoma	10073098
Iris cyst	10022949
Iris melanoma	10073086
Iris neoplasm	10057412
Jaw cyst	10023146
Joint neoplasm	10078144
Juvenile angiofibroma	10073678
Juvenile chronic myelomonocytic leukaemia	10023249
Juvenile melanoma benign	10023256
Kaposi's sarcoma	10023284
Kaposi's sarcoma AIDS related	10023286
Kaposi's sarcoma classical type	10023288
Keratinising squamous cell carcinoma of nasopharynx	10073324
Keratoacanthoma	10023347
Kidney angiomyolipoma	10077284
Knuckle pads	10070650
Lacrimal cyst	10061260
Lacrimal duct neoplasm	10057408
Langerhans cell sarcoma	10078782
Langerhans' cell histiocytosis	10069698
Large cell lung cancer	10023774
Large cell lung cancer metastatic	10069730
Large cell lung cancer recurrent	10023775
Large cell lung cancer stage 0	10023776
Large cell lung cancer stage I	10023777
Large cell lung cancer stage II	10023778
Large cell lung cancer stage III	10023779
Large cell lung cancer stage IV	10023780
Large granular lymphocytosis	10023791
Large intestine benign neoplasm	10073394
Large intestine fibroma	10051655
Large intestine polyp	10051589
Laryngeal cancer	10023825
Laryngeal cancer metastatic	10070902
Laryngeal cancer recurrent	10023828
Laryngeal cancer stage 0	10023829
Laryngeal cancer stage I	10023830
Laryngeal cancer stage II	10023831
Laryngeal cancer stage III	10023832
Laryngeal cancer stage IV	10023833
Laryngeal cyst	10051848
Laryngeal neoplasm	10023841
Laryngeal papilloma	10023849
Laryngeal polyp	10023851
Laryngeal squamous cell carcinoma	10023856
Leiomyoma	10024184
Leiomyosarcoma	10024189
Leiomyosarcoma metastatic	10024191
Leiomyosarcoma recurrent	10024194
Lentigo maligna	10024218
Lentigo maligna recurrent	10024220
Lentigo maligna stage I	10024221
Lentigo maligna stage II	10024222
Lentigo maligna stage III	10024223
Lentigo maligna stage IV	10024224
Leptomeningeal myelomatosis	10078282
Leser-Trelat sign	10065415
Leukaemia	10024288
Leukaemia basophilic	10024293
Leukaemia cutis	10053180
Leukaemia granulocytic	10024299
Leukaemia in remission	10061220
Leukaemia monocytic	10024305

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Leukaemia recurrent	10062489
Leukaemic cardiac infiltration	10077563
Leukaemic infiltration	10069360
Leukaemic infiltration extramedullary	10067117
Leukaemic infiltration gingiva	10067431
Leukaemic infiltration hepatic	10058671
Leukaemic infiltration ovary	10075853
Leukaemic infiltration pulmonary	10052368
Leukaemic infiltration renal	10069359
Leukaemic lymphoma	10024325
Leukaemic retinopathy	10059239
Leukoerythroblastosis	10024383
Leukostasis syndrome	10074608
Leydig cell tumour of the testis	10024407
Light chain disease	10024459
Limbic encephalitis	10078012
Linitis plastica	10024520
Lip and/or oral cavity cancer	10061523
Lip and/or oral cavity cancer recurrent	10024535
Lip and/or oral cavity cancer stage 0	10024536
Lip and/or oral cavity cancer stage I	10024537
Lip and/or oral cavity cancer stage II	10024538
Lip and/or oral cavity cancer stage III	10024539
Lip and/or oral cavity cancer stage IV	10024540
Lip neoplasm	10062038
Lip neoplasm benign	10024556
Lip neoplasm malignant stage unspecified	10024557
Lip squamous cell carcinoma	10064055
Lipoblastoma	10074547
Lipodermoid tumour	10073484
Lipofibroma	10067852
Lipoma	10024612
Lipoma of breast	10024616
Liposarcoma	10024627
Liposarcoma metastatic	10024629
Liposarcoma recurrent	10024632
Liver carcinoma ruptured	10050842
Lobular breast carcinoma in situ	10073099
Lung adenocarcinoma	10025031
Lung adenocarcinoma recurrent	10025033
Lung adenocarcinoma stage 0	10025034
Lung adenocarcinoma stage I	10025035
Lung adenocarcinoma stage II	10025036
Lung adenocarcinoma stage III	10025037
Lung adenocarcinoma stage IV	10025038
Lung cancer metastatic	10050017
Lung carcinoma cell type unspecified recurrent	10025065
Lung carcinoma cell type unspecified stage 0	10025066
Lung carcinoma cell type unspecified stage I	10025067
Lung carcinoma cell type unspecified stage II	10025068
Lung carcinoma cell type unspecified stage III	10025069
Lung carcinoma cell type unspecified stage IV	10025070
Lung cyst	10068749
Lung infiltration malignant	10062041
Lung neoplasm	10062042
Lung neoplasm malignant	10058467
Lung squamous cell carcinoma metastatic	10071533
Lung squamous cell carcinoma recurrent	10025120
Lung squamous cell carcinoma stage 0	10025121
Lung squamous cell carcinoma stage I	10025122
Lung squamous cell carcinoma stage II	10025123
Lung squamous cell carcinoma stage III	10025124
Lung squamous cell carcinoma stage IV	10025125

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Lymphangioma	10025219
Lymphangiosarcoma	10025223
Lymphangiosis carcinomatosa	10053132
Lymphatic system neoplasm	10062044
Lymphocele	10048642
Lymphocytic leukaemia	10025270
Lymphocytic lymphoma	10052178
Lymphohistiocytosis	10049646
Lymphoid leukaemia (in remission)	10025300
Lymphoma	10025310
Lymphoma AIDS related	10025312
Lymphoma transformation	10064344
Lymphoplasmacytoid lymphoma/immunocytoma	10025342
Lymphoplasmacytoid lymphoma/immunocytoma recurrent	10025345
Lymphoplasmacytoid lymphoma/immunocytoma refractory	10025346
Lymphoplasmacytoid lymphoma/immunocytoma stage I	10025347
Lymphoplasmacytoid lymphoma/immunocytoma stage II	10025348
Lymphoplasmacytoid lymphoma/immunocytoma stage III	10025349
Lymphoplasmacytoid lymphoma/immunocytoma stage IV	10025350
Lymphoproliferative disorder	10061232
Lymphoproliferative disorder in remission	10061233
Male reproductive tract neoplasm	10061236
Malignant anorectal neoplasm	10061237
Malignant ascites	10025538
Malignant blue naevus	10072448
Malignant bowel obstruction	10075918
Malignant connective tissue neoplasm	10074340
Malignant cranial nerve neoplasm	10061238
Malignant dysphagia	10067576
Malignant exophthalmos	10075386
Malignant fibrous histiocytoma	10025552
Malignant fibrous histiocytoma metastatic	10025554
Malignant fibrous histiocytoma of bone	10025557
Malignant fibrous histiocytoma recurrent	10025561
Malignant genitourinary tract neoplasm	10074419
Malignant giant cell fibrous histiocytoma	10073141
Malignant glioma	10065443
Malignant haemangiopericytoma	10025566
Malignant haemangiopericytoma metastatic	10025567
Malignant haemangiopericytoma recurrent	10025570
Malignant histiocytosis	10025581
Malignant hydatidiform mole	10025598
Malignant joint neoplasm	10078145
Malignant lymphoid neoplasm	10061240
Malignant lymphoma unclassifiable high grade	10025635
Malignant lymphoma unclassifiable low grade	10025636
Malignant mast cell neoplasm	10025638
Malignant mediastinal neoplasm	10061241
Malignant melanoma	10025650
Malignant melanoma in situ	10025652
Malignant melanoma of eyelid	10063706
Malignant melanoma of sites other than skin	10025654
Malignant melanoma stage I	10025668
Malignant melanoma stage II	10025669
Malignant melanoma stage III	10025670
Malignant melanoma stage IV	10025671
Malignant meningioma metastatic	10077758
Malignant mesenchymoma	10061526
Malignant mesenchymoma metastatic	10025674
Malignant mesenchymoma recurrent	10025677
Malignant mesenteric neoplasm	10067369
Malignant middle ear neoplasm	10061267
Malignant muscle neoplasm	10062050

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Malignant neoplasm of ampulla of Vater	10025697
Malignant neoplasm of auricular cartilage	10057272
Malignant neoplasm of choroid	10025839
Malignant neoplasm of conjunctiva	10025861
Malignant neoplasm of cornea	10025871
Malignant neoplasm of eye	10025910
Malignant neoplasm of eyelid	10063693
Malignant neoplasm of islets of Langerhans	10025997
Malignant neoplasm of lacrimal duct	10026030
Malignant neoplasm of lacrimal gland	10026031
Malignant neoplasm of orbit	10026183
Malignant neoplasm of paraurethral glands	10026326
Malignant neoplasm of placenta	10026350
Malignant neoplasm of pleura	10026351
Malignant neoplasm of pleura metastatic	10072432
Malignant neoplasm of renal pelvis	10026426
Malignant neoplasm of retina	10026432
Malignant neoplasm of seminal vesicle	10068124
Malignant neoplasm of spermatic cord	10026470
Malignant neoplasm of spinal cord	10026472
Malignant neoplasm of thorax	10026532
Malignant neoplasm of thymus	10026533
Malignant neoplasm of unknown primary site	10073059
Malignant neoplasm of uterine adnexa	10026616
Malignant neoplasm papilla of Vater	10077303
Malignant neoplasm progression	10051398
Malignant nervous system neoplasm	10061268
Malignant nipple neoplasm	10062051
Malignant nipple neoplasm female	10053129
Malignant nipple neoplasm male	10053128
Malignant oligodendroglioma	10026659
Malignant ovarian cyst	10026662
Malignant palate neoplasm	10026663
Malignant pericardial neoplasm	10054946
Malignant peritoneal neoplasm	10061269
Malignant pituitary tumour	10026672
Malignant pleural effusion	10026673
Malignant polyp	10078695
Malignant psoas syndrome	10077755
Malignant respiratory tract neoplasm	10061270
Malignant splenic neoplasm	10026702
Malignant sweat gland neoplasm	10073087
Malignant transformation	10064912
Malignant urinary tract neoplasm	10061272
Malignant urinary tract obstruction	10080015
Mantle cell lymphoma	10061275
Mantle cell lymphoma recurrent	10026800
Mantle cell lymphoma refractory	10026801
Mantle cell lymphoma stage I	10026802
Mantle cell lymphoma stage II	10026803
Mantle cell lymphoma stage III	10026804
Mantle cell lymphoma stage IV	10026805
Marginal zone lymphoma	10076596
Marginal zone lymphoma recurrent	10077533
Marginal zone lymphoma refractory	10077534
Marginal zone lymphoma stage I	10077529
Marginal zone lymphoma stage II	10077530
Marginal zone lymphoma stage III	10077531
Marginal zone lymphoma stage IV	10077532
Marjolin's ulcer	10076248
Marrow hyperplasia	10026851
Mastocytic leukaemia	10056450
Mastocytoma	10026890

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Mastoid cyst	10077793
Maternal cancer in pregnancy	10079877
Mature B-cell type acute leukaemia	10026945
Maxillofacial sinus neoplasm	10026956
Mediastinal cyst	10050168
Mediastinum neoplasm	10027086
Medical device site cyst	10076100
Medullary carcinoma of breast	10027095
Medullary thyroid cancer	10027105
Medulloblastoma	10027107
Medulloblastoma recurrent	10066594
Meigs' syndrome	10027139
Melanocytic naevus	10027145
Melanoma recurrent	10066600
Meningeal neoplasm	10061282
Meningioma	10027191
Meningioma benign	10027192
Meningioma malignant	10027193
Meniscus cyst	10072157
Mesenteric cyst	10079196
Mesenteric neoplasm	10072025
Mesoblastic nephroma	10070665
Mesonephric duct cyst	10027405
Mesothelioma	10027406
Mesothelioma malignant	10027407
Mesothelioma malignant recurrent	10027411
Metaplastic breast carcinoma	10073100
Metastases to Eustachian tube	10051666
Metastases to abdominal cavity	10027450
Metastases to abdominal wall	10051664
Metastases to adrenals	10027451
Metastases to biliary tract	10062195
Metastases to bladder	10049722
Metastases to bone	10027452
Metastases to bone marrow	10051662
Metastases to breast	10027454
Metastases to central nervous system	10059282
Metastases to chest wall	10051663
Metastases to diaphragm	10051665
Metastases to eye	10049724
Metastases to fallopian tube	10049727
Metastases to gallbladder	10051667
Metastases to gastrointestinal tract	10062196
Metastases to heart	10049717
Metastases to kidney	10027455
Metastases to larynx	10051668
Metastases to liver	10027457
Metastases to lung	10027458
Metastases to lymph nodes	10027459
Metastases to meninges	10051696
Metastases to mouth	10051669
Metastases to muscle	10049730
Metastases to nasal sinuses	10051670
Metastases to neck	10027460
Metastases to nervous system	10061287
Metastases to oesophagus	10051671
Metastases to ovary	10027462
Metastases to pancreas	10049721
Metastases to pelvis	10070913
Metastases to penis	10051672
Metastases to perineum	10051673
Metastases to peripheral nervous system	10051674
Metastases to peripheral vascular system	10058307

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Metastases to peritoneum	10051676
Metastases to pharynx	10051677
Metastases to pituitary gland	10049728
Metastases to placenta	10049725
Metastases to pleura	10027463
Metastases to prostate	10051678
Metastases to rectum	10051679
Metastases to reproductive organ	10061288
Metastases to retroperitoneum	10051680
Metastases to salivary gland	10051681
Metastases to skin	10027465
Metastases to soft tissue	10062197
Metastases to spinal cord	10078267
Metastases to spine	10027468
Metastases to spleen	10051682
Metastases to stomach	10049718
Metastases to testicle	10051683
Metastases to the mediastinum	10027469
Metastases to the respiratory system	10061600
Metastases to thorax	10051684
Metastases to thyroid	10049723
Metastases to tonsils	10077476
Metastases to trachea	10051685
Metastases to urinary tract	10056251
Metastases to uterus	10049726
Metastases to vagina	10075555
Metastasis	10062194
Metastatic bronchial carcinoma	10058306
Metastatic carcinoid tumour	10068115
Metastatic carcinoma of the bladder	10057352
Metastatic choriocarcinoma	10071532
Metastatic gastric cancer	10063916
Metastatic glioma	10063157
Metastatic glucagonoma	10075245
Metastatic lymphoma	10071541
Metastatic malignant melanoma	10027480
Metastatic neoplasm	10061289
Metastatic nervous system neoplasm	10077703
Metastatic ocular melanoma	10068117
Metastatic pulmonary embolism	10069909
Metastatic renal cell carcinoma	10050513
Metastatic salivary gland cancer	10066882
Metastatic squamous cell carcinoma	10063569
Metastatic uterine cancer	10068116
Microsatellite instability cancer	10079618
Minimal residual disease	10079987
Mismatch repair cancer syndrome	10077888
Mixed adenoneuroendocrine carcinoma	10076748
Mixed hepatocellular cholangiocarcinoma	10027761
Mixed-type liposarcoma	10073136
Monoclonal gammopathy	10060880
Monocytic leukaemia in remission	10061295
Mouth cyst	10028020
Mucinous adenocarcinoma of appendix	10073361
Mucinous breast carcinoma	10073101
Mucinous cystadenocarcinoma ovary	10054914
Mucinous endometrial carcinoma	10028076
Mucoepidermoid carcinoma	10057269
Mucoepidermoid carcinoma of salivary gland	10073371
Mucosal cyst of postmastoidectomy cavity	10028108
Mueller's mixed tumour	10066057
Muir-Torre syndrome	10063042
Multicentric reticulohistiocytosis	10070595

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Multinucleate cell angiohistiocytoma	10077003
Multiple cutaneous and uterine leiomyomatosis	10077859
Multiple endocrine neoplasia	10051747
Multiple endocrine neoplasia Type 1	10073150
Multiple endocrine neoplasia Type 2	10073149
Multiple endocrine neoplasia Type 2A	10073148
Multiple endocrine neoplasia Type 2B	10073151
Muscle neoplasm	10070956
Musculoskeletal cancer	10077675
Myasthenic syndrome	10028424
Mycosis fungoides	10028483
Mycosis fungoides recurrent	10028501
Mycosis fungoides refractory	10028502
Mycosis fungoides stage I	10028503
Mycosis fungoides stage II	10028504
Mycosis fungoides stage III	10028505
Mycosis fungoides stage IV	10028506
Myeloblastoma	10051141
Myelodysplastic syndrome	10028533
Myelodysplastic syndrome transformation	10067387
Myelodysplastic syndrome unclassifiable	10028535
Myelofibrosis	10028537
Myeloid leukaemia	10028549
Myeloid leukaemia in remission	10061301
Myeloid metaplasia	10028561
Myelolipoma	10077376
Myeloma cast nephropathy	10073599
Myeloproliferative neoplasm	10077465
Myolipoma	10054837
Myxofibrosarcoma	10066948
Myxoid liposarcoma	10073137
NUT midline carcinoma	10078295
Naevoid melanoma	10079054
Naevus haemorrhage	10062955
Naevus lipomatosus cutaneous superficialis	10077916
Nasal cavity cancer	10028729
Nasal cyst	10051712
Nasal neoplasm	10060768
Nasal neoplasm benign	10051711
Nasal polyps	10028756
Nasal sinus cancer	10028767
Nasopharyngeal cancer	10061306
Nasopharyngeal cancer metastatic	10079104
Nasopharyngeal cancer recurrent	10028787
Nasopharyngeal cancer stage 0	10028788
Nasopharyngeal cancer stage I	10028789
Nasopharyngeal cancer stage II	10028790
Nasopharyngeal cancer stage III	10028791
Nasopharyngeal cancer stage IV	10028792
Nasopharyngeal neoplasm benign	10028802
Nasopharyngeal polyp	10076420
Natural killer-cell leukaemia	10028811
Natural killer-cell lymphoblastic lymphoma	10058975
Necrolytic migratory erythema	10060821
Neonatal leukaemia	10028958
Neonatal neuroblastoma	10049793
Neoplasm	10028980
Neoplasm malignant	10028997
Neoplasm of appendix	10056288
Neoplasm of cornea unspecified malignancy	10052903
Neoplasm of orbit	10061863
Neoplasm of thymus	10056296
Neoplasm progression	10061309

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Neoplasm prostate	10029096
Neoplasm recurrence	10061864
Neoplasm skin	10029098
Neoplasm swelling	10059049
Nephroblastoma	10029145
Nervous system cyst	10078167
Nervous system neoplasm	10061311
Nervous system neoplasm benign	10061283
Neurilemmoma benign	10029235
Neuroblastoma	10029260
Neuroblastoma recurrent	10066595
Neuroectodermal neoplasm	10056672
Neuroendocrine breast tumour	10073103
Neuroendocrine carcinoma	10057270
Neuroendocrine carcinoma metastatic	10071542
Neuroendocrine carcinoma of the bladder	10078341
Neuroendocrine carcinoma of the skin	10029266
Neuroendocrine tumour	10052399
Neuroendocrine tumour of the lung	10078174
Neuroendocrine tumour of the lung metastatic	10078175
Neurofibroma	10029267
Neurofibromatosis	10029268
Neurofibrosarcoma	10061527
Neurofibrosarcoma metastatic	10029274
Neurofibrosarcoma recurrent	10029277
Neurogenic tumour	10080963
Neuroma	10029308
Neuromyotonia	10072359
Neurotensinoma	10029341
Nipple neoplasm	10056286
Nodal marginal zone B-cell lymphoma	10029460
Nodal marginal zone B-cell lymphoma recurrent	10029463
Nodal marginal zone B-cell lymphoma refractory	10029464
Nodal marginal zone B-cell lymphoma stage I	10029465
Nodal marginal zone B-cell lymphoma stage II	10029466
Nodal marginal zone B-cell lymphoma stage III	10029467
Nodal marginal zone B-cell lymphoma stage IV	10029468
Nodular fasciitis	10065988
Nodular lymphocyte predominant Hodgkin lymphoma	10080201
Nodular melanoma	10029488
Non-Hodgkin's lymphoma	10029547
Non-Hodgkin's lymphoma metastatic	10071535
Non-Hodgkin's lymphoma recurrent	10029600
Non-Hodgkin's lymphoma refractory	10029601
Non-Hodgkin's lymphoma stage I	10029602
Non-Hodgkin's lymphoma stage II	10029603
Non-Hodgkin's lymphoma stage III	10029604
Non-Hodgkin's lymphoma stage IV	10029605
Non-Hodgkin's lymphoma transformed recurrent	10061871
Non-Hodgkin's lymphoma unspecified histology aggressive	10063908
Non-Hodgkin's lymphoma unspecified histology aggressive recurrent	10029609
Non-Hodgkin's lymphoma unspecified histology aggressive refractory	10029610
Non-Hodgkin's lymphoma unspecified histology aggressive stage I	10029611
Non-Hodgkin's lymphoma unspecified histology aggressive stage II	10029612
Non-Hodgkin's lymphoma unspecified histology aggressive stage III	10029613
Non-Hodgkin's lymphoma unspecified histology aggressive stage IV	10029614
Non-Hodgkin's lymphoma unspecified histology indolent	10065856
Non-Hodgkin's lymphoma unspecified histology indolent stage I	10029622
Non-Hodgkin's lymphoma unspecified histology indolent stage II	10029623
Non-Hodgkin's lymphoma unspecified histology indolent stage III	10029624
Non-Hodgkin's lymphoma unspecified histology indolent stage IV	10029625
Non-renal cell carcinoma of kidney	10061872
Non-secretory adenoma of pituitary	10029556

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Non-small cell lung cancer	10061873
Non-small cell lung cancer metastatic	10059515
Non-small cell lung cancer recurrent	10029515
Non-small cell lung cancer stage 0	10029516
Non-small cell lung cancer stage I	10029517
Non-small cell lung cancer stage II	10029518
Non-small cell lung cancer stage III	10029519
Non-small cell lung cancer stage IIIA	10029520
Non-small cell lung cancer stage IIIB	10029521
Non-small cell lung cancer stage IV	10029522
Nongerminomatous germ cell tumour of the CNS	10065871
Nonkeratinising carcinoma of nasopharynx	10073325
Numb chin syndrome	10066930
Ocular cancer metastatic	10055099
Ocular haemangiopericytoma	10057416
Ocular lymphoma	10075324
Ocular neoplasm	10052448
Odontogenic cyst	10063413
Oesophageal adenocarcinoma	10030137
Oesophageal adenocarcinoma recurrent	10030140
Oesophageal adenocarcinoma stage 0	10030141
Oesophageal adenocarcinoma stage I	10030142
Oesophageal adenocarcinoma stage II	10030143
Oesophageal adenocarcinoma stage III	10030144
Oesophageal adenocarcinoma stage IV	10030145
Oesophageal cancer metastatic	10055102
Oesophageal carcinoma	10030155
Oesophageal carcinoma recurrent	10030159
Oesophageal carcinoma stage 0	10030162
Oesophageal cyst	10079063
Oesophageal neoplasm	10061882
Oesophageal papilloma	10071192
Oesophageal polyp	10051935
Oesophageal squamous cell carcinoma	10061534
Oesophageal squamous cell carcinoma metastatic	10058527
Oesophageal squamous cell carcinoma recurrent	10030187
Oesophageal squamous cell carcinoma stage 0	10030188
Oesophageal squamous cell carcinoma stage I	10030189
Oesophageal squamous cell carcinoma stage II	10030190
Oesophageal squamous cell carcinoma stage III	10030191
Oesophageal squamous cell carcinoma stage IV	10030192
Oestrogen receptor positive breast cancer	10070577
Oligoastrocytoma	10073131
Oligodendroglioma	10030286
Oligodendroglioma benign	10030287
Omenn syndrome	10069097
Oncocytoma	10048757
Oncogenic osteomalacia	10077950
Oncologic complication	10067777
Optic glioma	10073338
Optic nerve neoplasm	10053645
Oral cavity cancer metastatic	10055098
Oral fibroma	10051656
Oral haemangioma	10077632
Oral neoplasm	10061325
Oral neoplasm benign	10031000
Oral papilloma	10068322
Oropharyngeal cancer	10031096
Oropharyngeal cancer recurrent	10031098
Oropharyngeal cancer stage 0	10031099
Oropharyngeal cancer stage I	10031100
Oropharyngeal cancer stage II	10031101
Oropharyngeal cancer stage III	10031102

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Oropharyngeal cancer stage IV	10064099
Oropharyngeal lymphoepithelioma	10031104
Oropharyngeal neoplasm	10057444
Oropharyngeal neoplasm benign	10031110
Oropharyngeal squamous cell carcinoma	10031112
Osteochondroma	10059587
Osteofibroma	10073852
Osteoma	10031249
Osteoma cutis	10048902
Osteosarcoma	10031291
Osteosarcoma metastatic	10031294
Osteosarcoma recurrent	10031296
Ota's naevus	10051713
Otic cancer metastatic	10055100
Ovarian Sertoli-Leydig cell tumour	10073270
Ovarian adenoma	10048991
Ovarian cancer	10033128
Ovarian cancer metastatic	10057529
Ovarian cancer recurrent	10066697
Ovarian cancer stage I	10070905
Ovarian cancer stage II	10070906
Ovarian cancer stage III	10070907
Ovarian cancer stage IV	10070908
Ovarian clear cell carcinoma	10073268
Ovarian cyst	10033132
Ovarian cyst ruptured	10033136
Ovarian cyst torsion	10049670
Ovarian dysgerminoma stage I	10033144
Ovarian dysgerminoma stage II	10033148
Ovarian dysgerminoma stage III	10033152
Ovarian dysgerminoma stage IV	10033156
Ovarian dysgerminoma stage unspecified	10052759
Ovarian embryonal carcinoma	10056266
Ovarian endometrioid carcinoma	10073269
Ovarian epithelial cancer	10061328
Ovarian epithelial cancer metastatic	10033158
Ovarian epithelial cancer recurrent	10033160
Ovarian epithelial cancer stage I	10033161
Ovarian epithelial cancer stage II	10033162
Ovarian epithelial cancer stage III	10033163
Ovarian epithelial cancer stage IV	10033164
Ovarian fibroma	10064257
Ovarian germ cell cancer	10061893
Ovarian germ cell cancer stage I	10061894
Ovarian germ cell cancer stage II	10061895
Ovarian germ cell cancer stage III	10061896
Ovarian germ cell cancer stage IV	10061897
Ovarian germ cell choriocarcinoma	10073262
Ovarian germ cell choriocarcinoma stage I	10033183
Ovarian germ cell choriocarcinoma stage II	10033187
Ovarian germ cell choriocarcinoma stage III	10033191
Ovarian germ cell choriocarcinoma stage IV	10033195
Ovarian germ cell embryonal carcinoma stage I	10033196
Ovarian germ cell embryonal carcinoma stage II	10033200
Ovarian germ cell embryonal carcinoma stage III	10033204
Ovarian germ cell embryonal carcinoma stage IV	10033208
Ovarian germ cell endodermal sinus tumour	10073263
Ovarian germ cell endodermal sinus tumour stage I	10033218
Ovarian germ cell endodermal sinus tumour stage II	10033219
Ovarian germ cell endodermal sinus tumour stage III	10033220
Ovarian germ cell endodermal sinus tumour stage IV	10033221
Ovarian germ cell polyembryoma	10073264
Ovarian germ cell polyembryoma stage I	10033223

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Ovarian germ cell polyembryoma stage II	10033227
Ovarian germ cell polyembryoma stage III	10033231
Ovarian germ cell polyembryoma stage IV	10033235
Ovarian germ cell teratoma	10073265
Ovarian germ cell teratoma benign	10033236
Ovarian germ cell teratoma stage I	10033237
Ovarian germ cell teratoma stage II	10033241
Ovarian germ cell teratoma stage III	10033245
Ovarian germ cell teratoma stage IV	10033249
Ovarian germ cell tumour	10075812
Ovarian germ cell tumour mixed	10073259
Ovarian granulosa cell tumour	10073260
Ovarian granulosa-theca cell tumour	10057376
Ovarian low malignant potential tumour	10033268
Ovarian neoplasm	10061535
Ovarian stromal cancer	10065858
Ovarian theca cell tumour	10073261
PHACES syndrome	10068032
POEMS syndrome	10053869
Paget's disease of nipple	10033364
Paget's disease of penis	10033365
Paget's disease of the vulva	10033369
Palmar fasciitis	10067366
Pancoast's syndrome	10065249
Pancoast's tumour	10033572
Pancreatic carcinoma	10033609
Pancreatic carcinoma metastatic	10033610
Pancreatic carcinoma recurrent	10033613
Pancreatic carcinoma stage 0	10059320
Pancreatic carcinoma stage I	10059321
Pancreatic carcinoma stage II	10059322
Pancreatic carcinoma stage III	10059323
Pancreatic carcinoma stage IV	10059326
Pancreatic cyst	10033615
Pancreatic cyst rupture	10071369
Pancreatic neoplasm	10061902
Pancreatic neuroendocrine tumour	10067517
Pancreatic neuroendocrine tumour metastatic	10068909
Pancreatic sarcoma	10055006
Pancreatoblastoma	10073367
Papillary cystadenoma lymphomatosum	10074291
Papillary renal cell carcinoma	10078493
Papillary serous endometrial carcinoma	10033700
Papillary thyroid cancer	10033701
Papillary tumour of renal pelvis	10033702
Papilloma	10033713
Papilloma conjunctival	10067127
Paracancerous pneumonia	10080986
Paraganglion neoplasm	10061332
Paraganglion neoplasm benign	10033790
Paraganglion neoplasm malignant	10033791
Paranasal cyst	10062321
Paranasal sinus and nasal cavity malignant neoplasm	10061909
Paranasal sinus and nasal cavity malignant neoplasm recurrent	10033855
Paranasal sinus and nasal cavity malignant neoplasm stage 0	10033856
Paranasal sinus and nasal cavity malignant neoplasm stage I	10033857
Paranasal sinus and nasal cavity malignant neoplasm stage II	10033858
Paranasal sinus and nasal cavity malignant neoplasm stage III	10033859
Paranasal sinus and nasal cavity malignant neoplasm stage IV	10033860
Paranasal sinus benign neoplasm	10057447
Paranasal sinus neoplasm	10057448
Paraneoplastic arthritis	10077507
Paraneoplastic dermatomyositis	10066267

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Paraneoplastic dermatosis	10078237
Paraneoplastic encephalomyelitis	10069587
Paraneoplastic glomerulonephritis	10076749
Paraneoplastic myelopathy	10080965
Paraneoplastic nephrotic syndrome	10075626
Paraneoplastic neurological syndrome	10072106
Paraneoplastic pemphigus	10057056
Paraneoplastic pleural effusion	10075715
Paraneoplastic rash	10074687
Paraneoplastic retinopathy	10065311
Paraneoplastic syndrome	10059420
Paraneoplastic thrombosis	10079251
Paraproteinaemia	10061333
Parathyroid cyst	10067772
Parathyroid tumour	10033963
Parathyroid tumour benign	10033964
Parathyroid tumour malignant	10033965
Pathological fracture	10034156
Pearly penile papules	10075021
Pelvic cyst	10072715
Pelvic neoplasm	10061336
Penile cancer	10034299
Penile neoplasm	10061913
Penile squamous cell carcinoma	10059631
Penile wart	10034325
Penis carcinoma metastatic	10034329
Penis carcinoma recurrent	10034331
Penis carcinoma stage I	10034332
Penis carcinoma stage II	10034333
Penis carcinoma stage III	10034334
Penis carcinoma stage IV	10034335
Pericardial cyst	10051730
Pericardial effusion malignant	10048630
Pericardial mesothelioma malignant	10073066
Pericardial mesothelioma malignant recurrent	10034480
Pericardial neoplasm	10054945
Pericarditis malignant	10034491
Perineal cyst	10066058
Perineurial cyst	10051766
Peripheral T-cell lymphoma unspecified	10034623
Peripheral T-cell lymphoma unspecified recurrent	10034625
Peripheral T-cell lymphoma unspecified refractory	10034626
Peripheral T-cell lymphoma unspecified stage I	10034627
Peripheral T-cell lymphoma unspecified stage II	10034628
Peripheral T-cell lymphoma unspecified stage III	10034629
Peripheral T-cell lymphoma unspecified stage IV	10034630
Peripheral nerve sheath tumour malignant	10034590
Peripheral nervous system neoplasm	10062069
Peripheral neuroepithelioma of bone	10061342
Peripheral neuroepithelioma of bone metastatic	10034603
Peripheral neuroepithelioma of bone recurrent	10034605
Peripheral neuroepithelioma of soft tissue	10057646
Peripheral primitive neuroectodermal bone tumour	10073107
Peripheral primitive neuroectodermal tumour of soft tissue	10073144
Peritoneal carcinoma metastatic	10068974
Peritoneal cyst	10051942
Peritoneal gliomatosis	10070561
Peritoneal mesothelioma malignant	10056558
Peritoneal mesothelioma malignant recurrent	10034671
Peritoneal neoplasm	10061344
Peritoneal sarcoma	10051949
Peritumoural oedema	10072360
Peutz-Jeghers syndrome	10034764

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Phaeochromocytoma	10034800
Phaeochromocytoma crisis	10068778
Phaeochromocytoma malignant	10051710
Phakomatosis	10048734
Pharyngeal cancer	10034811
Pharyngeal cancer metastatic	10055104
Pharyngeal cancer recurrent	10034813
Pharyngeal cancer stage 0	10034814
Pharyngeal cancer stage I	10034815
Pharyngeal cancer stage II	10034816
Pharyngeal cancer stage III	10034817
Pharyngeal cancer stage IV	10034818
Pharyngeal cyst	10034821
Pharyngeal neoplasm	10062075
Pharyngeal neoplasm benign	10034828
Pharyngeal polyp	10051943
Phosphaturic mesenchymal tumour	10079470
Phyllodes tumour	10071776
Pilomatrix carcinoma	10075614
Pineal germinoma	10035052
Pineal gland cyst	10068650
Pineal neoplasm	10061348
Pineal parenchymal neoplasm malignant	10061537
Pinealoblastoma	10050487
Pinealoma	10035057
Pineocytoma	10035059
Pituitary cancer metastatic	10055106
Pituitary cyst	10051687
Pituitary neoplasm malignant recurrent	10057838
Pituitary tumour	10035104
Pituitary tumour benign	10061538
Pituitary tumour recurrent	10057316
Placental chorioangioma	10056718
Placental neoplasm	10061349
Placental polyp	10035142
Plasma cell leukaemia	10035222
Plasma cell leukaemia in remission	10060406
Plasma cell myeloma	10035226
Plasma cell myeloma in remission	10073132
Plasma cell myeloma recurrent	10073133
Plasmablastic lymphoma	10065039
Plasmacytoma	10035484
Pleomorphic adenoma	10073372
Pleomorphic liposarcoma	10073138
Pleomorphic malignant fibrous histiocytoma	10073143
Pleural cyst	10071257
Pleural mesothelioma	10035603
Pleural mesothelioma malignant	10059518
Pleural mesothelioma malignant recurrent	10035607
Pleural neoplasm	10061352
Pleural sarcoma	10051950
Pleuropulmonary blastoma	10080682
Polycythaemia vera	10036057
Polyneuropathy in malignant disease	10036115
Polyp	10061529
Poorly differentiated thyroid carcinoma	10076603
Porocarcinoma	10063609
Post transplant lymphoproliferative disorder	10051358
Postcricoid cancer	10036334
Precursor B-lymphoblastic lymphoma	10036523
Precursor B-lymphoblastic lymphoma recurrent	10060910
Precursor B-lymphoblastic lymphoma refractory	10060911
Precursor B-lymphoblastic lymphoma stage I	10036532

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Precursor B-lymphoblastic lymphoma stage II	10036533
Precursor B-lymphoblastic lymphoma stage III	10036534
Precursor B-lymphoblastic lymphoma stage IV	10036535
Precursor T-lymphoblastic lymphoma/leukaemia	10036543
Precursor T-lymphoblastic lymphoma/leukaemia recurrent	10036546
Precursor T-lymphoblastic lymphoma/leukaemia refractory	10036547
Precursor T-lymphoblastic lymphoma/leukaemia stage I	10036548
Precursor T-lymphoblastic lymphoma/leukaemia stage II	10036549
Precursor T-lymphoblastic lymphoma/leukaemia stage III	10036550
Precursor T-lymphoblastic lymphoma/leukaemia stage IV	10036551
Primary breast lymphoma	10081036
Primary cardiac lymphoma	10075993
Primary effusion lymphoma	10065857
Primary gastrointestinal follicular lymphoma	10078972
Primary mediastinal large B-cell lymphoma	10036710
Primary mediastinal large B-cell lymphoma recurrent	10036713
Primary mediastinal large B-cell lymphoma refractory	10036714
Primary mediastinal large B-cell lymphoma stage I	10036715
Primary mediastinal large B-cell lymphoma stage II	10036716
Primary mediastinal large B-cell lymphoma stage III	10036717
Primary mediastinal large B-cell lymphoma stage IV	10036718
Primary myelofibrosis	10077161
Primary pulmonary melanoma	10080717
Primitive neuroectodermal tumour	10057846
Primitive neuroectodermal tumour metastatic	10068910
Prolactin-producing pituitary tumour	10036831
Prolymphocytic leukaemia	10036888
Prostate cancer	10060862
Prostate cancer metastatic	10036909
Prostate cancer recurrent	10036911
Prostate cancer stage 0	10036912
Prostate cancer stage I	10036917
Prostate cancer stage II	10036918
Prostate cancer stage III	10036919
Prostate cancer stage IV	10036920
Prostatic adenoma	10036940
Prostatic cyst	10067640
Prostatic polyp	10075248
Pseudoachalasia	10075246
Pseudocirrhosis	10076501
Pseudomyxoma peritonei	10037138
Pseudosarcoma	10051807
Pulmonary tumour thrombotic microangiopathy	10079988
Pyoderma gangrenosum	10037635
Pyogenic granuloma	10037649
Queyrat erythroplasia	10037732
Rectal adenocarcinoma	10038019
Rectal adenoma	10048829
Rectal cancer	10038038
Rectal cancer metastatic	10055097
Rectal cancer recurrent	10038046
Rectal cancer stage 0	10038047
Rectal cancer stage I	10038048
Rectal cancer stage II	10038049
Rectal cancer stage III	10038050
Rectal cancer stage IV	10038051
Rectal neoplasm	10062099
Rectal polyp	10038074
Rectosigmoid cancer	10038086
Rectosigmoid cancer metastatic	10069728
Rectosigmoid cancer recurrent	10038094
Rectosigmoid cancer stage 0	10038095
Rectosigmoid cancer stage I	10038096

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Rectosigmoid cancer stage II	10038097
Rectosigmoid cancer stage III	10038098
Rectosigmoid cancer stage IV	10038099
Recurrent cancer	10038111
Refractory anaemia with an excess of blasts	10038270
Refractory anaemia with ringed sideroblasts	10038272
Refractory cancer	10070308
Refractory cytopenia with multilineage dysplasia	10067959
Refractory cytopenia with unilineage dysplasia	10072684
Renal adenoma	10051948
Renal cancer	10038389
Renal cancer metastatic	10050018
Renal cancer recurrent	10038390
Renal cancer stage I	10038391
Renal cancer stage II	10038392
Renal cancer stage III	10038393
Renal cancer stage IV	10038394
Renal cell carcinoma	10067946
Renal cell carcinoma recurrent	10038410
Renal cell carcinoma stage I	10038411
Renal cell carcinoma stage II	10038412
Renal cell carcinoma stage III	10038413
Renal cell carcinoma stage IV	10038414
Renal cyst	10038423
Renal cyst haemorrhage	10059846
Renal cyst infection	10058596
Renal cyst ruptured	10049814
Renal haemangioma	10069908
Renal neoplasm	10061482
Renal oncocytoma	10050176
Respiratory papilloma	10038707
Respiratory tract carcinoma in situ	10038724
Respiratory tract neoplasm	10061486
Retention cyst	10060721
Retinal melanocytoma	10057428
Retinal melanoma	10038878
Retinal neoplasm	10057407
Retinoblastoma	10038916
Retro-orbital neoplasm	10038956
Retroperitoneal cancer	10038977
Retroperitoneal neoplasm	10056664
Retroperitoneal neoplasm metastatic	10062485
Retroperitoneum cyst	10051689
Rhabdoid tumour	10073334
Rhabdoid tumour of the kidney	10039019
Rhabdomyoma	10039021
Rhabdomyosarcoma	10039022
Rhabdomyosarcoma recurrent	10039027
Richter's syndrome	10058728
Rosai-Dorfman syndrome	10063397
Round cell liposarcoma	10073139
Salivary gland adenoma	10051636
Salivary gland cancer	10061934
Salivary gland cancer recurrent	10039398
Salivary gland cancer stage 0	10039399
Salivary gland cancer stage I	10039400
Salivary gland cancer stage II	10039401
Salivary gland cancer stage III	10039402
Salivary gland cancer stage IV	10039403
Salivary gland cyst	10052248
Salivary gland neoplasm	10061497
Sarcoma	10039491
Sarcoma metastatic	10068595

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Sarcoma of skin	10039495
Sarcoma uterus	10039497
Sarcomatoid carcinoma	10080324
Sarcomatoid mesothelioma	10073065
Sarcomatosis	10039500
Schwannoma	10039667
Scrotal cancer	10039744
Scrotal cyst	10065670
Sebaceous adenoma	10062919
Sebaceous carcinoma	10068784
Seborrhoeic keratosis	10039796
Second primary malignancy	10039801
Secondary cerebellar degeneration	10074943
Secretory adenoma of pituitary	10039893
Seminal vesicular cyst	10052480
Seminoma	10039956
Serous cystadenocarcinoma ovary	10054913
Sertoli cell testicular tumour	10073117
Signet-ring cell carcinoma	10057266
Silicon granuloma	10040677
Sinonasal papilloma	10071665
Sinus cancer metastatic	10055105
Sinus polyp	10040749
Sinus polyp degeneration	10040750
Skin angiosarcoma	10072891
Skin cancer	10040808
Skin cancer metastatic	10055115
Skin neoplasm bleeding	10060712
Skin papilloma	10040907
Skin squamous cell carcinoma metastatic	10077314
Small cell carcinoma	10041056
Small cell carcinoma of the cervix	10041057
Small cell lung cancer	10041067
Small cell lung cancer extensive stage	10041068
Small cell lung cancer limited stage	10041069
Small cell lung cancer metastatic	10059514
Small cell lung cancer recurrent	10041070
Small intestine adenocarcinoma	10073373
Small intestine carcinoma	10054184
Small intestine carcinoma metastatic	10041121
Small intestine carcinoma recurrent	10041124
Small intestine carcinoma stage 0	10059368
Small intestine carcinoma stage I	10059369
Small intestine carcinoma stage II	10059370
Small intestine carcinoma stage III	10059371
Small intestine carcinoma stage IV	10059372
Small intestine leiomyosarcoma	10041127
Small intestine polyp	10073395
Smooth muscle cell neoplasm	10062253
Soft tissue neoplasm	10068771
Soft tissue sarcoma	10075333
Solid pseudopapillary tumour of the pancreas	10069345
Solitary epithelioid histiocytoma	10069378
Somatostatinoma	10041329
Spermatocele	10041490
Spermatocytic seminoma	10073118
Spinal cord lipoma	10064898
Spinal cord neoplasm	10062261
Spinal meningeal cyst	10067375
Spinal meningioma benign	10041579
Spinal meningioma malignant	10041580
Spindle cell sarcoma	10049067
Splenic cyst	10051169

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Splenic hamartoma	10076586
Splenic marginal zone lymphoma	10062113
Splenic marginal zone lymphoma recurrent	10041652
Splenic marginal zone lymphoma refractory	10041653
Splenic marginal zone lymphoma stage I	10041654
Splenic marginal zone lymphoma stage II	10041655
Splenic marginal zone lymphoma stage III	10041656
Splenic marginal zone lymphoma stage IV	10041657
Splenic neoplasm malignancy unspecified	10053190
Squamous cell breast carcinoma	10079307
Squamous cell carcinoma	10041823
Squamous cell carcinoma of head and neck	10060121
Squamous cell carcinoma of lung	10041826
Squamous cell carcinoma of pharynx	10066471
Squamous cell carcinoma of skin	10041834
Squamous cell carcinoma of the cervix	10041848
Squamous cell carcinoma of the hypopharynx	10041849
Squamous cell carcinoma of the oral cavity	10041857
Squamous cell carcinoma of the tongue	10041865
Squamous cell carcinoma of the vagina	10041866
Squamous cell carcinoma of the vulva	10041875
Squamous endometrial carcinoma	10041883
Stauffer's syndrome	10069107
Steatocystoma multiplex	10048905
Stewart-Treves syndrome	10059498
Stoma site polyp	10077702
Superficial spreading melanoma stage I	10042549
Superficial spreading melanoma stage II	10042550
Superficial spreading melanoma stage III	10042551
Superficial spreading melanoma stage IV	10042552
Superficial spreading melanoma stage unspecified	10042553
Superior vena cava syndrome	10042569
Sweat gland tumour	10042658
Synovial cyst	10042858
Synovial sarcoma	10042863
Synovial sarcoma metastatic	10042864
Synovial sarcoma recurrent	10042867
T-cell chronic lymphocytic leukaemia	10042970
T-cell lymphoma	10042971
T-cell lymphoma recurrent	10042979
T-cell lymphoma refractory	10042980
T-cell lymphoma stage I	10042981
T-cell lymphoma stage II	10042982
T-cell lymphoma stage III	10042983
T-cell lymphoma stage IV	10042984
T-cell prolymphocytic leukaemia	10042985
T-cell type acute leukaemia	10042987
T-cell unclassifiable lymphoma high grade	10042989
T-cell unclassifiable lymphoma low grade	10042990
TEMPI syndrome	10075076
Tendon neoplasm	10061377
Teratoma	10043276
Teratoma benign	10048460
Testicle adenoma	10051637
Testicular cancer metastatic	10055103
Testicular choriocarcinoma	10062122
Testicular choriocarcinoma recurrent	10069812
Testicular choriocarcinoma stage I	10043303
Testicular choriocarcinoma stage II	10043304
Testicular choriocarcinoma stage III	10043305
Testicular cyst	10048872
Testicular embryonal carcinoma	10062123
Testicular embryonal carcinoma stage I	10043309

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Testicular embryonal carcinoma stage II	10043310
Testicular embryonal carcinoma stage III	10043311
Testicular germ cell cancer	10061378
Testicular germ cell cancer metastatic	10068694
Testicular germ cell tumour	10075811
Testicular germ cell tumour mixed	10073119
Testicular germ cell tumour mixed stage I	10043331
Testicular germ cell tumour mixed stage II	10043332
Testicular germ cell tumour mixed stage III	10043333
Testicular leiomyosarcoma	10057340
Testicular malignant teratoma	10073120
Testicular malignant teratoma stage I	10043339
Testicular malignant teratoma stage II	10043340
Testicular malignant teratoma stage III	10043341
Testicular neoplasm	10061379
Testicular papilloma	10055033
Testicular seminoma (pure)	10062124
Testicular seminoma (pure) stage I	10043350
Testicular seminoma (pure) stage II	10043351
Testicular seminoma (pure) stage III	10043352
Testicular teratoma benign	10043355
Testicular yolk sac tumour	10073121
Testicular yolk sac tumour stage I	10043357
Testicular yolk sac tumour stage II	10043358
Testicular yolk sac tumour stage III	10043359
Testis cancer	10057644
Testis cancer recurrent	10069813
Throat cancer	10043515
Thymic cancer metastatic	10055108
Thymic cyst	10079570
Thymoma	10043670
Thymoma malignant	10061031
Thymoma malignant recurrent	10043674
Thyroglossal cyst	10051320
Thyroid B-cell lymphoma	10072613
Thyroid adenoma	10043688
Thyroid cancer	10066474
Thyroid cancer metastatic	10055107
Thyroid cancer recurrent	10072162
Thyroid cancer stage 0	10070567
Thyroid cancer stage I	10071027
Thyroid cancer stage II	10071028
Thyroid cancer stage III	10071029
Thyroid cancer stage IV	10071030
Thyroid cyst	10043706
Thyroid neoplasm	10043744
Thyroid stimulating hormone-producing pituitary tumour	10043772
Tongue cancer metastatic	10055109
Tongue cancer recurrent	10071251
Tongue carcinoma stage 0	10058429
Tongue carcinoma stage I	10058430
Tongue carcinoma stage II	10058431
Tongue carcinoma stage III	10058432
Tongue carcinoma stage IV	10058433
Tongue cyst	10051879
Tongue neoplasm	10062129
Tongue neoplasm benign	10043965
Tongue neoplasm malignant stage unspecified	10043966
Tongue polyp	10074778
Tonsil cancer	10044002
Tonsil cancer metastatic	10072792
Tonsillar cyst	10057451
Tonsillar neoplasm	10062131

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Tonsillar neoplasm benign	10044004
Tornwaldt cyst	10078492
Tracheal cancer	10044285
Tracheal neoplasm	10062133
Tracheal papilloma	10067203
Transformation to acute myeloid leukaemia	10079107
Transitional cell cancer of renal pelvis and ureter metastatic	10044406
Transitional cell cancer of the renal pelvis and ureter	10044407
Transitional cell cancer of the renal pelvis and ureter localised	10044408
Transitional cell cancer of the renal pelvis and ureter recurrent	10044410
Transitional cell cancer of the renal pelvis and ureter regional	10044411
Transitional cell carcinoma	10044412
Transitional cell carcinoma metastatic	10071080
Transitional cell carcinoma recurrent	10077051
Transitional cell carcinoma urethra	10044426
Trichoblastic carcinoma	10080660
Triple hit lymphoma	10080200
Triple negative breast cancer	10075566
Trisomy 12	10063092
Trousseau's syndrome	10060905
Tuberous sclerosis complex	10080584
Tubular breast carcinoma	10073104
Tumour associated fever	10052243
Tumour budding	10076969
Tumour cavitation	10080086
Tumour cell mobilisation	10070894
Tumour compression	10068268
Tumour embolism	10045168
Tumour exudation	10075825
Tumour fistulisation	10072830
Tumour flare	10045169
Tumour haemorrhage	10049750
Tumour hyperprogression	10081037
Tumour inflammation	10078786
Tumour invasion	10064390
Tumour lysis syndrome	10045170
Tumour necrosis	10054094
Tumour obstruction	10077313
Tumour of ampulla of Vater	10073851
Tumour pain	10045171
Tumour perforation	10064938
Tumour pruritus	10077704
Tumour pseudoprogression	10077472
Tumour rupture	10070627
Tumour thrombosis	10068067
Tumour ulceration	10050283
Ulcerated haemangioma	10075629
Umbilical cord cyst	10079122
Undifferentiated carcinoma of colon	10073362
Undifferentiated nasopharyngeal carcinoma	10073328
Undifferentiated sarcoma	10045515
Ureteral cyst	10065914
Ureteral neoplasm	10062221
Ureteral polyp	10051506
Ureteric cancer	10046392
Ureteric cancer local	10046393
Ureteric cancer metastatic	10046394
Ureteric cancer recurrent	10046396
Ureteric cancer regional	10046397
Ureteric papilloma	10076386
Urethral adenoma	10051638
Urethral cancer	10046431
Urethral cancer metastatic	10046433

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
Urethral cancer recurrent	10046435
Urethral cyst	10049502
Urethral melanoma metastatic	10072793
Urethral neoplasm	10062223
Urethral papilloma	10046462
Urethral polyp	10051507
Urinary bladder adenoma	10051639
Urinary bladder polyp	10049794
Urinary bladder sarcoma	10051690
Urinary tract carcinoma in situ	10061396
Urinary tract neoplasm	10061398
Urinary tract polyp	10079493
Uterine cancer	10046766
Uterine carcinoma in situ	10046770
Uterine cyst	10048931
Uterine leiomyoma	10046798
Uterine leiomyosarcoma	10046799
Uterine myoma expulsion	10074467
Uterine neoplasm	10046803
Uterine polyp	10046811
Vaccination site cyst	10076158
Vaginal adenocarcinoma	10065349
Vaginal cancer	10046885
Vaginal cancer metastatic	10046887
Vaginal cancer recurrent	10046889
Vaginal cancer stage 0	10046890
Vaginal cancer stage I	10046891
Vaginal cancer stage II	10046892
Vaginal cancer stage III	10046893
Vaginal cancer stage IVA	10046894
Vaginal cancer stage IVB	10046895
Vaginal cyst	10046900
Vaginal neoplasm	10062165
Vaginal polyp	10046939
Vascular neoplasm	10055031
Venous angioma of brain	10053485
Vipoma	10047430
Viral acanthoma	10077282
Vitreous cyst	10072892
Vocal cord cyst	10051515
Vocal cord neoplasm	10057038
Vocal cord polyp	10047675
Vulva cyst	10050475
Vulval cancer	10047741
Vulval cancer metastatic	10047742
Vulval cancer recurrent	10047744
Vulval cancer stage 0	10047745
Vulval cancer stage I	10047746
Vulval cancer stage II	10047747
Vulval cancer stage III	10047748
Vulval cancer stage IV	10047749
Vulval neoplasm	10062135
Vulval polyp	10047765
Vulvar adenocarcinoma	10063536
Vulvovaginal warts	10047793
Waldenstrom's macroglobulinaemia	10047801
Waldenstrom's macroglobulinaemia recurrent	10047804
Waldenstrom's macroglobulinaemia refractory	10047805
Waldenstrom's macroglobulinaemia stage I	10047806
Waldenstrom's macroglobulinaemia stage II	10047807
Waldenstrom's macroglobulinaemia stage III	10047808
Waldenstrom's macroglobulinaemia stage IV	10047809
Warty dyskeratoma	10068856

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - All benign, malignant and unspecified neoplasms

Preferred Term Text	Preferred Term ID
White sponge naevus	10072666
X-linked lymphoproliferative syndrome	10068348
Xanthogranuloma	10051251
Yolk sac tumour site unspecified	10048251

MedDRA version 21.0.

131 Listing of preferred terms used for NNMQ - Headache

Preferred Term Text	Preferred Term ID
Cervicogenic headache	10064888
Chronic paroxysmal hemicrania	10009094
Cluster headache	10059133
Cold-stimulus headache	10071151
Craniocervical syndrome	10077374
Drug withdrawal headache	10013753
Eagle's syndrome	10066835
Exertional headache	10068614
External compression headache	10076669
Headache	10019211
Medication overuse headache	10072720
New daily persistent headache	10076678
Occipital neuralgia	10068106
Ophthalmoplegic migraine	10050122
Post lumbar puncture syndrome	10060854
Post-traumatic headache	10036313
Postictal headache	10052470
Premenstrual headache	10049122
Primary cough headache	10076707
Primary headache associated with sexual activity	10079056
Procedural headache	10066965
SUNCT syndrome	10061981
Sinus headache	10040744
Stroke-like migraine attacks after radiation therapy	10073775
Temporomandibular joint syndrome	10043220
Tension headache	10043269
Thunderclap headache	10075481
Typical aura without headache	10071669
Vascular headache	10047077

MedDRA version 21.0.

132 Listing of preferred terms used for NNMQ - Paraesthesia

Preferred Term Text	Preferred Term ID
Paraesthesia	10033775

MedDRA version 21.0.

133 Listing of preferred terms used for NNMQ - Carpal tunnel syndrome

Preferred Term Text	Preferred Term ID
Carpal tunnel syndrome	10007697

MedDRA version 21.0.

134 Listing of preferred terms used for NNMQ - Benign intracranial hypertension

Preferred Term Text	Preferred Term ID
Brain compression	10006112
Brain oedema	10048962
Cerebral ventricle collapse	10073706
Cerebrospinal fluid circulation disorder	10075604
Cerebrospinal fluid retention	10065532
Cerebrospinal thrombotic tamponade	10052173
Cytotoxic oedema	10067276
Dialysis disequilibrium syndrome	10059256
Idiopathic intracranial hypertension	10078904
Intracranial pressure increased	10022773
Papilloedema	10033712
Vasogenic cerebral oedema	10067275

MedDRA version 21.0.

135 Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
11-beta-hydroxylase deficiency	10000002
17,20-desmolase deficiency	10000013
17-alpha-hydroxylase deficiency	10000014
18q minus syndrome	10068533
2-Hydroxyglutaric aciduria	10078971
20,22-desmolase deficiency	10000020
21-hydroxylase deficiency	10000021
3-hydroxyacetyl-coenzyme A dehydrogenase deficiency	10072273
5-alpha-reductase deficiency	10000029
ABO haemolytic disease of newborn	10000205
Aase syndrome	10063429
Abdominal transposition	10000098
Abdominal wall anomaly	10000101
Abnormal palmar/plantar creases	10000162
Acardia	10075721
Accelerated idioventricular rhythm	10049003
Accessory auricle	10000361
Accessory breast	10049786
Accessory cardiac pathway	10067618
Accessory carpal bone	10000362
Accessory kidney	10048781
Accessory liver lobe	10052752
Accessory muscle	10000364
Accessory navicular syndrome	10062626
Accessory salivary gland	10000368
Accessory spleen	10068059
Acetylcholinesterase deficiency	10071435
Achromotrichia congenital	10049864
Acquired C1 inhibitor deficiency	10081035
Acquired amegakaryocytic thrombocytopenia	10076747
Acquired hepatocerebral degeneration	10080860
Acral peeling skin syndrome	10078538
Acrodermatitis enteropathica	10000596
Acrodysostosis	10079856
Acrokeratosis verruciformis	10069445
Activated PI3 kinase delta syndrome	10078281
Acute focal bacterial nephritis	10071736
Acute generalised exanthematous pustulosis	10048799
Acute graft versus host disease in liver	10066263
Acute hepatic failure	10000804
Acute kidney injury	10069339
Acute motor axonal neuropathy	10076658
Acute motor-sensory axonal neuropathy	10076657
Acute on chronic liver failure	10077305
Acute phosphate nephropathy	10069688
Acute yellow liver atrophy	10070815
Adactyly	10049207
Adams-Oliver syndrome	10079369
Adams-Stokes syndrome	10001115
Adenine phosphoribosyl transferase deficiency	10072609
Adenomatous polyposis coli	10056981
Adrenal insufficiency neonatal	10001368
Adrenogenital syndrome	10061630
Adrenoleukodystrophy	10051260
Adult polyglucosan body disease	10077946
Aglossia	10001501
Agonal rhythm	10054015
Agranulocytosis	10001507
Aicardi's syndrome	10054935
Alagille syndrome	10053870
Albinism	10001557
Albright's disease	10052032
Alcoholic pancreatitis	10056977

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Alcoholic pancreopathy	10076384
Alkaptonuria	10001689
Allan-Herndon-Dudley syndrome	10078821
Allergic hepatitis	10071198
Alloimmune hepatitis	10080576
Alpers' disease	10062943
Alpha-1 anti-trypsin deficiency	10001806
Alport's syndrome	10001843
Alstroem syndrome	10068783
Alternating hemiplegia of childhood	10077948
Alveolar capillary dysplasia	10077023
Amblyopia congenital	10001908
Amegakaryocytic thrombocytopenia	10076744
Aminoaciduria	10001939
Amniotic band syndrome	10064100
Amyotrophic lateral sclerosis gene carrier	10052653
Anal atresia	10002120
Anaphylactic reaction	10002198
Anaphylactic shock	10002199
Anaphylactic transfusion reaction	10067113
Anaphylactoid reaction	10002216
Anaphylactoid shock	10063119
Androgen insensitivity syndrome	10056292
Anencephaly	10002320
Angelman's syndrome	10049004
Angioedema	10002424
Angiotensin converting enzyme inhibitor foetopathy	10051098
Aniridia	10002532
Ankyloglossia congenital	10049244
Annular pancreas	10071757
Anodontia	10002583
Anomalous arrangement of pancreaticobiliary duct	10064902
Anomalous atrioventricular excitation	10002611
Anomalous pulmonary venous connection	10058079
Anomaly of external ear congenital	10062339
Anomaly of middle ear congenital	10060957
Anomaly of orbit, congenital	10002633
Anophthalmos	10002640
Anorchism	10002641
Anorectal agenesis	10056271
Anotia	10002654
Anterior chamber cleavage syndrome	10059199
Anterior displaced anus	10071651
Antithrombin III deficiency	10002832
Anuria	10002847
Aorta hypoplasia	10049209
Aortic valve atresia	10066801
Aorticopulmonary septal defect	10063732
Apert's syndrome	10002943
Aphakia congenital	10002947
Aplasia	10002961
Aplasia cutis congenita	10002963
Aplastic anaemia	10002967
Apparent mineralocorticoid excess	10080229
Arachnodactyly	10063847
Arcuate foramen	10067850
Arginase deficiency	10062695
Argininosuccinate lyase deficiency	10058299
Argininosuccinate synthetase deficiency	10058298
Arnold-Chiari malformation	10003101
Arrhythmia	10003119
Arrhythmia neonatal	10003124
Arrhythmia supraventricular	10003130

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Arrhythmogenic right ventricular dysplasia	10058093
Arterial tortuosity syndrome	10080250
Arteriovenous malformation	10003193
Ascites	10003445
Ash leaf macule	10076367
Aspartate-glutamate-transporter deficiency	10079140
Aspartylglucosaminuria	10068220
Asphyxiating thoracic dystrophy	10057621
Aspiration bone marrow abnormal	10003506
Asplenia	10053622
Asterixis	10003547
Asymptomatic gene carrier	10061662
Ataxia telangiectasia	10003594
Atrial conduction time prolongation	10064191
Atrial fibrillation	10003658
Atrial flutter	10003662
Atrial parasystole	10071666
Atrial septal defect	10003664
Atrial tachycardia	10003668
Atrioventricular block	10003671
Atrioventricular block complete	10003673
Atrioventricular block first degree	10003674
Atrioventricular block second degree	10003677
Atrioventricular conduction time shortened	10068180
Atrioventricular dissociation	10069571
Atrioventricular node dispersion	10077893
Atrioventricular septal defect	10063836
Auditory neuropathy spectrum disorder	10072198
Autoimmune aplastic anaemia	10071576
Autoimmune hepatitis	10003827
Autoimmune lymphoproliferative syndrome	10069521
Autoimmune nephritis	10077087
Autoimmune pancreatitis	10069002
Autosomal chromosome anomaly	10060975
Azotaemia	10003885
Azygos lobe	10069490
B-lymphocyte abnormalities	10053775
B-lymphocyte count abnormal	10078589
B-lymphocyte count decreased	10051313
Bacterascites	10068547
Baltic myoclonic epilepsy	10054895
Band neutrophil count decreased	10057950
Band neutrophil percentage decreased	10059130
Bannayan-Riley-Ruvalcaba syndrome	10080314
Baraitser Rodeck Garner syndrome	10076038
Barakat syndrome	10075281
Barth syndrome	10078537
Bartter's syndrome	10050839
Basal cell naevus syndrome	10062804
Baseline foetal heart rate variability disorder	10074638
Basophil count abnormal	10060978
Basophil count decreased	10004167
Basophil percentage decreased	10052219
Basophilopenia	10075813
Becker's muscular dystrophy	10059117
Beckwith-Wiedemann syndrome	10050344
Benign congenital hypotonia	10051900
Benign familial haematuria	10060876
Benign familial neonatal convulsions	10067866
Benign familial pemphigus	10004265
Berdon's syndrome	10064596
Beta ketothiolase deficiency	10067728
Bezold-Jarisch reflex	10076999

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Bickerstaff's encephalitis	10076985
Bicuspid aortic valve	10004552
Bicuspid pulmonary valve	10063730
Bicytopenia	10058956
Bifascicular block	10057393
Biliary cirrhosis	10004659
Biliary fibrosis	10004664
Biliary hamartoma	10074610
Bilirubin excretion disorder	10061009
Biopsy bone marrow abnormal	10004738
Biotinidase deficiency	10071434
Birt-Hogg-Dube syndrome	10067736
Birth mark	10004950
Bladder agenesis	10056655
Blau syndrome	10071755
Blepharophimosis congenital	10049241
Blindness congenital	10005176
Bloch-Sulzberger syndrome	10077624
Blood count abnormal	10064198
Blood disorder	10061590
Blood incompatibility haemolytic anaemia of newborn	10056369
Bloom syndrome	10073032
Bone marrow disorder	10061729
Bone marrow failure	10065553
Bone marrow infiltration	10075173
Bone marrow myelogram abnormal	10057528
Bone marrow necrosis	10058822
Bone marrow toxicity	10051779
Brachycephaly	10053682
Brachydactyly	10072883
Bradyarrhythmia	10049765
Bradycardia	10006093
Bradycardia foetal	10006094
Bradycardia neonatal	10056471
Brain malformation	10048409
Branchial cleft sinus	10006162
Branchial cyst	10006164
Branchio-oto-renal syndrome	10071135
Branchiogenic syndrome	10058169
Breast malformation	10006271
Bronchogenic cyst	10064585
Brugada syndrome	10059027
Bruton's agammaglobulinaemia	10060360
Bulbospinal muscular atrophy congenital	10068597
Bundle branch block	10006578
Bundle branch block bilateral	10006579
Bundle branch block left	10006580
Bundle branch block right	10006582
Buried penis syndrome	10067131
C3 glomerulopathy	10077827
CANDLE syndrome	10073960
CHARGE syndrome	10064063
Camptodactyly congenital	10049028
Camptomelia	10078297
Canavan disease	10067608
Cancer gene carrier	10052648
Carbamoyl phosphate synthetase deficiency	10058297
Carbohydrate metabolism disorder	10061023
Carcinogenic effect in offspring	10007268
Cardiac arrest	10007515
Cardiac arrest neonatal	10007516
Cardiac death	10049993
Cardiac fibrillation	10061592

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Cardiac flutter	10052840
Cardiac lymphangioma	10055010
Cardiac malposition	10007585
Cardiac septal defect	10064021
Cardiac telemetry abnormal	10053450
Cardio-respiratory arrest	10007617
Cardio-respiratory arrest neonatal	10007618
Carney complex	10076601
Carnitine palmitoyltransferase deficiency	10050215
Carnitine-acylcarnitine translocase deficiency	10078729
Carpus curvus	10007700
Cartilage-hair hypoplasia	10069596
Cataract congenital	10007747
Caudal regression syndrome	10059387
Central bradycardia	10078310
Central core disease	10057620
Central nervous system dermoid tumour	10007942
Cerebellar dysplasia	10072942
Cerebellar hypoplasia	10008033
Cerebral arteriovenous malformation haemorrhagic	10008086
Cerebral atrophy congenital	10052236
Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy	10065551
Cerebral dysgenesis	10056467
Cerebral palsy	10008129
Cerebrohepatorenal syndrome	10053684
Cerebrovascular arteriovenous malformation	10056371
Cervical auricle	10008227
Cervical rib	10008299
Chediak-Higashi syndrome	10008415
Chiari network	10069393
Chimerism	10068051
Choanal atresia	10008587
Choanal stenosis	10074053
Cholaemia	10048611
Cholangiectasis congenital	10053630
Cholangitis	10008604
Choledochal cyst	10008625
Cholestasis	10008635
Cholestatic liver injury	10067969
Cholestatic pruritus	10064190
Chondrodystrophy	10008723
Chondroectodermal dysplasia	10008724
Chordee	10008746
Chorioretinal degeneration congenital	10008763
Choroidal coloboma	10057402
Chromosomal deletion	10061764
Chromosomal mutation	10061765
Chronic autoimmune glomerulonephritis	10073016
Chronic graft versus host disease in liver	10072160
Chronic granulomatous disease	10008906
Chronic hepatic failure	10057573
Chronic hepatitis	10008909
Chronic infantile neurological cutaneous and articular syndrome	10064568
Chronic inflammatory demyelinating polyradiculoneuropathy	10057645
Chronotropic incompetence	10068627
Circulatory collapse	10009192
Circumoral oedema	10052250
Citrate transporter deficiency	10077947
Cleft lip	10009259
Cleft lip and palate	10009260
Cleft palate	10009269
Cleft uvula	10053507

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Cleidocranial dysostosis	10075994
Clinodactyly	10058668
Cloacal exstrophy	10067424
Clostridial infection	10061043
Clostridial sepsis	10078496
Clostridium bacteraemia	10058852
Clostridium colitis	10058305
Clostridium difficile colitis	10009657
Clostridium difficile infection	10054236
Clostridium test positive	10070027
Coagulation factor mutation	10065442
Coarctation of the aorta	10009807
Cobb syndrome	10068841
Cockayne's syndrome	10009835
Cohen syndrome	10049066
Collodion baby	10009926
Coloboma	10009934
Colour blindness	10010050
Coma hepatic	10010075
Combined immunodeficiency	10010099
Complement deficiency disease	10075551
Conduction disorder	10010276
Congenital Eustachian tube anomaly	10062331
Congenital HIV infection	10010504
Congenital Horner's syndrome	10074554
Congenital Zika syndrome	10081044
Congenital abdominal hernia	10067183
Congenital absence of bile ducts	10010317
Congenital absence of cranial vault	10010318
Congenital absence of vertebra	10010320
Congenital acrochordon	10050730
Congenital adrenal gland hypoplasia	10049057
Congenital amputation	10079701
Congenital anaemia	10010329
Congenital androgen deficiency	10063469
Congenital anomalies of ear ossicles	10010341
Congenital anomaly	10010356
Congenital anomaly in offspring	10063726
Congenital anomaly of adrenal gland	10062341
Congenital anomaly of inner ear	10062340
Congenital anosmia	10079876
Congenital aortic anomaly	10061052
Congenital aortic atresia	10010368
Congenital aortic dilatation	10058150
Congenital aortic stenosis	10010369
Congenital aortic valve incompetence	10010370
Congenital aortic valve stenosis	10010371
Congenital aplastic anaemia	10053138
Congenital aqueductal stenosis	10066084
Congenital arterial malformation	10062325
Congenital arteriovenous fistula	10010374
Congenital astigmatism	10074992
Congenital aural fistula	10054215
Congenital benign neoplasm	10073493
Congenital bladder anomaly	10061053
Congenital bladder diverticulum	10010381
Congenital bladder neck obstruction	10010382
Congenital bowing of long bones	10054064
Congenital brain damage	10010390
Congenital bronchiectasis	10010391
Congenital bronchomalacia	10010392
Congenital calyceal diverticulum	10057510
Congenital cardiovascular anomaly	10061054

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Congenital carnitine deficiency	10062698
Congenital central diabetes insipidus	10073008
Congenital central hypoventilation syndrome	10066131
Congenital central nervous system anomaly	10010411
Congenital cerebellar agenesis	10048784
Congenital cerebral cyst	10054954
Congenital cerebral haemangioma	10048924
Congenital cerebrovascular anomaly	10062327
Congenital choroid plexus cyst	10048785
Congenital choroidal anomaly	10057886
Congenital chylothorax	10078770
Congenital clavicular agenesis	10010416
Congenital claw toe	10010417
Congenital coagulopathy	10063563
Congenital condyloma	10066944
Congenital corneal anomaly	10061059
Congenital coronary artery malformation	10061060
Congenital cranial nerve paralysis	10069774
Congenital cutis laxa	10057042
Congenital cyst	10062328
Congenital cystic disease of liver	10010427
Congenital cystic kidney disease	10010428
Congenital cystic lung	10010429
Congenital cytomegalovirus infection	10010430
Congenital deformity of clavicle	10010434
Congenital dermal sinus	10048728
Congenital diaphragmatic anomaly	10061061
Congenital diaphragmatic eventration	10010438
Congenital diaphragmatic hernia	10010439
Congenital disorder of glycosylation	10075892
Congenital dysfibrinogenaemia	10051123
Congenital dyskeratosis	10062759
Congenital ectodermal dysplasia	10010452
Congenital ectopic bladder	10010453
Congenital ectopic pancreas	10056987
Congenital elevation of scapula	10010455
Congenital emphysema	10010456
Congenital endocrine anomaly	10062329
Congenital epiblepharon	10056531
Congenital epiglottal anomaly	10062330
Congenital eye disorder	10059159
Congenital eye naevus	10051050
Congenital eyelid malformation	10061146
Congenital facial nerve hypoplasia	10049449
Congenital fallopian tube anomaly	10061062
Congenital fibrosarcoma	10065859
Congenital flaccid paralysis	10010474
Congenital flat feet	10010475
Congenital floppy infant	10053153
Congenital foot malformation	10062332
Congenital gastric anomaly	10061063
Congenital gastrointestinal vessel anomaly	10062342
Congenital generalised lipodystrophy	10053547
Congenital genital malformation	10062333
Congenital genital malformation female	10010481
Congenital genital malformation male	10059492
Congenital genitourinary abnormality	10062334
Congenital great vessel anomaly	10061080
Congenital haematological disorder	10072107
Congenital hair disorder	10061064
Congenital hand malformation	10062335
Congenital hearing disorder	10010493
Congenital heart valve disorder	10064086

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Congenital heart valve incompetence	10077594
Congenital hemiparesis	10071359
Congenital hepatic fibrosis	10056533
Congenital hepatitis B infection	10010496
Congenital hepatobiliary anomaly	10061065
Congenital hepatomegaly	10051130
Congenital herpes simplex infection	10019949
Congenital hiatus hernia	10010501
Congenital high airway obstruction syndrome	10074187
Congenital hydrocele renalis	10051147
Congenital hydrocephalus	10010506
Congenital hydronephrosis	10050975
Congenital hypercoagulation	10070954
Congenital hyperextension of knee	10048954
Congenital hyperextension of spine	10048953
Congenital hyperthyroidism	10062264
Congenital hypertrichosis	10010507
Congenital hypogammaglobulinaemia	10060747
Congenital hypoparathyroidism	10051315
Congenital hypoplasia of depressor angularis oris muscle	10080879
Congenital hypothyroidism	10010510
Congenital infection	10062343
Congenital inguinal hernia	10068321
Congenital intestinal malformation	10061067
Congenital intestinal obstruction	10073207
Congenital intrinsic factor deficiency	10070440
Congenital iris anomaly	10057411
Congenital jaw malformation	10062336
Congenital joint malformation	10062337
Congenital knee deformity	10061068
Congenital knee dislocation	10010520
Congenital kyphoscoliosis	10048890
Congenital labia pudendi adhesions	10050268
Congenital lacrimal gland anomaly	10010523
Congenital lacrimal passage anomaly	10062338
Congenital large intestinal atresia	10010526
Congenital laryngeal stridor	10010527
Congenital lenticonus	10064660
Congenital limb hyperextension	10049011
Congenital lip fistula	10010532
Congenital lymphoedema	10010535
Congenital malaria	10010538
Congenital malignant neoplasm	10073492
Congenital megacolon	10010539
Congenital megaureter	10010540
Congenital melanocytic naevus	10072036
Congenital melanosis	10010541
Congenital methaemoglobinaemia	10010543
Congenital midline defect	10079687
Congenital mitochondrial cytopathy	10057954
Congenital mitral valve incompetence	10010547
Congenital mitral valve stenosis	10010548
Congenital monorchidism	10069505
Congenital multiplex arthrogryposis	10051643
Congenital muscle absence	10010550
Congenital musculoskeletal anomaly	10062344
Congenital myopathy	10062547
Congenital myopia	10069153
Congenital naevus	10067248
Congenital nail disorder	10010557
Congenital neoplasm	10078557
Congenital nephrogenic diabetes insipidus	10068304
Congenital nephrotic syndrome	10060737

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Congenital neurological degeneration	10010558
Congenital neurological disorder	10062345
Congenital neuropathy	10062346
Congenital night blindness	10010559
Congenital nipple anomaly	10080356
Congenital nipple inversion	10080355
Congenital nose malformation	10062347
Congenital nystagmus	10010562
Congenital oculomotor apraxia	10053877
Congenital oesophageal anomaly	10061069
Congenital oesophageal stenosis	10010564
Congenital oesophageal web	10010565
Congenital optic nerve anomaly	10061528
Congenital oral malformation	10061070
Congenital osteodystrophy	10010582
Congenital ovarian anomaly	10061071
Congenital oxalosis	10068593
Congenital pancreatic anomaly	10061072
Congenital perforated nasal septum	10010588
Congenital pharyngeal anomaly	10061073
Congenital pigmentation disorder	10010593
Congenital pneumonia	10010594
Congenital poikiloderma	10052465
Congenital pseudarthrosis	10061573
Congenital pulmonary artery anomaly	10061074
Congenital pulmonary hypertension	10050701
Congenital pulmonary valve atresia	10052644
Congenital pulmonary valve disorder	10061075
Congenital pyelocaliectasis	10049938
Congenital renal cyst	10010607
Congenital renal disorder	10066875
Congenital retinoblastoma	10073470
Congenital rubella infection	10010619
Congenital salivary gland anomaly	10010620
Congenital scleral disorder	10061530
Congenital scoliosis	10050694
Congenital scrotal hypertrophy	10048800
Congenital skin dimples	10072978
Congenital skin disorder	10067769
Congenital small intestinal atresia	10010626
Congenital spinal cord anomaly	10061076
Congenital spinal fusion	10010629
Congenital spinal stenosis	10077379
Congenital spondylolisthesis	10010633
Congenital spondylolysis	10010634
Congenital syphilis	10010641
Congenital syphilitic encephalitis	10010643
Congenital syphilitic meningitis	10010644
Congenital syphilitic osteochondritis	10054002
Congenital teratoma	10052012
Congenital thrombocyte disorder	10058896
Congenital thrombocytopenia	10077833
Congenital thymus absence	10048801
Congenital thyroid disorder	10076602
Congenital tongue anomaly	10061077
Congenital torticollis	10010650
Congenital toxoplasmosis	10010652
Congenital tracheomalacia	10010654
Congenital trichomegaly	10073654
Congenital tricuspid valve atresia	10049767
Congenital tricuspid valve incompetence	10067887
Congenital tricuspid valve stenosis	10010656
Congenital tuberculosis	10010657

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Congenital umbilical hernia	10010658
Congenital ureteric anomaly	10061078
Congenital ureterocele	10056434
Congenital ureterovesical junction anomaly	10068133
Congenital urethral anomaly	10062349
Congenital urinary tract obstruction	10010663
Congenital uterine anomaly	10061079
Congenital vaginal cyst	10063457
Congenital varicella infection	10010668
Congenital varicocele	10074459
Congenital vas deferens absence	10010670
Congenital vesicoureteric reflux	10010672
Congenital visual acuity reduced	10059157
Congenital vitreous anomaly	10061085
Congenital white blood cell disorder	10061086
Conjoined twins	10010688
Conjunctivitis gonococcal neonatal	10010749
Constricted ear deformity	10071233
Continuous haemodiafiltration	10066338
Cor biloculare	10010967
Cor triatriatum	10010972
Corneal dystrophy	10011005
Corneal opacity congenital	10011037
Cornelia de Lange syndrome	10077707
Corrected transposition of great vessels	10011120
Cortical dysplasia	10070666
Costello syndrome	10067380
Cowden's disease	10051906
Craniofacial deformity	10074180
Craniofacial dysostosis	10066946
Craniolacunia	10072116
Craniorachischisis	10011321
Craniosynostosis	10049889
Craniotabes	10065419
Cri du Chat syndrome	10011385
Crigler-Najjar syndrome	10011386
Cryopyrin associated periodic syndrome	10068850
Cryptogenic cirrhosis	10063075
Cryptophthalmos	10011497
Cryptorchism	10011498
Cullen's sign	10059029
Currarino syndrome	10079857
Cutaneous vasculitis	10011686
Cutaneovisceral angiomatosis with thrombocytopenia	10069098
Cyclic neutropenia	10053176
Cyclopia	10057648
Cystathionine beta-synthase deficiency	10071093
Cystic angiomatosis	10079371
Cystic eyeball, congenital	10011761
Cystic fibrosis	10011762
Cystic fibrosis carrier	10052656
Cystic fibrosis gastrointestinal disease	10079428
Cystic fibrosis hepatic disease	10068289
Cystic fibrosis lung	10011763
Cystic fibrosis pancreatic	10011766
Cystic fibrosis related diabetes	10068271
Cystic lymphangioma	10058949
Cystinosis	10011777
Cystinuria	10011778
Cytogenetic abnormality	10067477
Cytomegalovirus nephritis	10079095
Cytomegalovirus pancreatitis	10049566
Cytopenia	10066274

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
DNA mismatch repair protein gene mutation	10078672
DOOR syndrome	10080835
Dacryostenosis congenital	10011850
Dandy-Walker syndrome	10048411
Deaf mutism	10011875
Deafness congenital	10011882
Defect conduction intraventricular	10012118
Deficiency of bile secretion	10071634
Deficiency of the interleukin-1 receptor antagonist	10072224
Deficiency of the interleukin-36 receptor antagonist	10079451
Delayed foetal renal development	10079753
Delta-beta thalassaemia	10012236
Demyelinating polyneuropathy	10061811
Dent's disease	10069199
Dentatorubral-pallidoluysian atrophy	10075298
Dentinogenesis imperfecta	10054013
Dentofacial anomaly	10012331
Denys-Drash syndrome	10070179
Dermatitis bullous	10012441
Dermatitis exfoliative	10012455
Dermatitis exfoliative generalised	10012456
Dermatofibrosis lenticularis disseminata	10056878
Dermatoglyphic anomaly	10061455
Dermoid cyst	10012522
Developmental glaucoma	10012565
Developmental hip dysplasia	10073767
Dextrocardia	10012592
DiGeorge's syndrome	10012979
Diabetic foetopathy	10059116
Diabetic hepatopathy	10071265
Dialysis	10061105
Dialysis membrane reaction	10076665
Diaphragmatic aplasia	10012711
Diastematomyelia	10012750
Diencephalic syndrome of infancy	10012774
Diethylstilboestrol syndrome	10012780
Differential white blood cell count abnormal	10012785
Dihydropyrimidine dehydrogenase deficiency	10052622
Dilatation intrahepatic duct congenital	10013003
Disorder of sex development	10070597
Disseminated intravascular coagulation	10013442
Distichiasis	10066128
Diverticulitis Meckel's	10013542
Diverticulum of pharynx, congenital	10013568
Dolichocolon	10063917
Dopa-responsive dystonia	10080034
Double cortex syndrome	10073490
Double heterozygous sickling disorders	10013609
Double outlet left ventricle	10080133
Double outlet right ventricle	10013611
Double ureter	10013613
Dowling-Degos disease	10068651
Drug reaction with eosinophilia and systemic symptoms	10073508
Drug-induced liver injury	10072268
Duane's syndrome	10013799
Dubin-Johnson syndrome	10013800
Dubowitz syndrome	10059589
Duchenne muscular dystrophy	10013801
Duchenne muscular dystrophy gene carrier	10052655
Ductus arteriosus premature closure	10049996
Ductus arteriosus stenosis foetal	10013808
Ductus venosus agenesis	10068665
Duodenal atresia	10013812

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Duodenal varices	10051010
Duplex appendix	10078212
Dyke-Davidoff-Masson syndrome	10080312
Dyschondrosteosis	10071437
Dyschromatosis	10080785
Dysgnathia	10074336
Dysmorphism	10066054
Dysmyelination	10067601
Dysplastic naevus syndrome	10013960
ECG P wave inverted	10057526
Eagle Barrett syndrome	10051025
Ear malformation	10014016
Early onset familial Alzheimer's disease	10078036
Early onset primary dystonia	10076668
Ebstein's anomaly	10014075
Ectopia cordis	10014144
Ectopic kidney	10063044
Ectopic ovary	10074217
Ectopic posterior pituitary gland	10077557
Ectopic thyroid	10069503
Ectopic ureter	10014172
Ectrodactyly	10079827
Ehlers-Danlos syndrome	10014316
Electrocardiogram P wave abnormal	10050384
Electrocardiogram PQ interval prolonged	10053656
Electrocardiogram PQ interval shortened	10075328
Electrocardiogram PR prolongation	10053657
Electrocardiogram PR shortened	10014374
Electrocardiogram QRS complex prolonged	10014380
Electrocardiogram QT prolonged	10014387
Electrocardiogram RR interval prolonged	10067652
Electrocardiogram U wave inversion	10062314
Electrocardiogram U wave present	10057913
Electrocardiogram U-wave abnormality	10055032
Electrocardiogram abnormal	10014363
Electrocardiogram ambulatory abnormal	10014369
Electrocardiogram change	10061116
Electrocardiogram delta waves abnormal	10014372
Electrocardiogram repolarisation abnormality	10052464
Elliptocytosis hereditary	10014490
Ellis-van Creveld syndrome	10076418
Emanuel syndrome	10079203
Encapsulating peritoneal sclerosis	10075012
Encephalocele	10014617
Encephalocutaneous angiomatosis	10057653
Endocardial fibroelastosis	10014663
Enteric duplication	10076653
Entropion congenital	10014923
Eosinopenia	10014940
Eosinophil count abnormal	10061125
Eosinophil count decreased	10014943
Eosinophil percentage decreased	10052221
Epidermal naevus	10014985
Epidermal naevus syndrome	10077952
Epidermal necrosis	10059284
Epidermolysis	10053177
Epidermolysis bullosa	10014989
Epilepsy congenital	10015039
Epispadias	10015088
Erythema multiforme	10015218
Erythroblastosis foetalis	10015251
Erythrokeratodermia variabilis	10049048
Essential fructosuria	10015487

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Exfoliative rash	10064579
Exomphalos	10015677
Exophthalmos congenital	10050696
External auditory canal atresia	10054875
Extrarenal pelvis	10072727
Extrasystoles	10015856
Eye anterior chamber congenital anomaly	10061051
Eyelid oedema	10015993
Eyelid ptosis congenital	10015996
Fabry's disease	10016016
Face oedema	10016029
Faciodigitogenital dysplasia	10067141
Facioscapulohumeral muscular dystrophy	10064087
Factor I deficiency	10016075
Factor II deficiency	10016076
Factor II mutation	10065003
Factor III deficiency	10052473
Factor IX deficiency	10016077
Factor V Leiden carrier	10075652
Factor V Leiden mutation	10058279
Factor V deficiency	10048930
Factor VII deficiency	10016079
Factor VIII deficiency	10016080
Factor X deficiency	10052474
Factor XI deficiency	10016082
Factor XII deficiency	10051806
Factor XIII deficiency	10016083
Fallot's pentalogy	10059205
Fallot's tetralogy	10016193
Fallot's trilogy	10064011
Familial acromegaly	10080509
Familial amyloidosis	10016202
Familial amyotrophic lateral sclerosis	10077024
Familial cold autoinflammatory syndrome	10064570
Familial haemophagocytic lymphohistiocytosis	10070904
Familial hemiplegic migraine	10067039
Familial high density lipoprotein deficiency	10079119
Familial hypertriglyceridaemia	10059183
Familial hypocalciuric hypercalcaemia	10068698
Familial infantile bilateral striatal necrosis	10077450
Familial isolated hyperparathyroidism	10080773
Familial mediterranean fever	10016207
Familial medullary thyroid cancer	10073153
Familial periodic paralysis	10016208
Familial polycythaemia	10016209
Familial renal glycosuria	10073689
Familial scaphocephaly syndrome	10072229
Familial tremor	10016212
Fanconi syndrome	10016219
Fatal familial insomnia	10072077
Fatty acid oxidation disorder	10077951
Febrile bone marrow aplasia	10053213
Febrile neutropenia	10016288
Femoral anteversion	10064516
Femoral retroversion	10064514
Femur-fibula-ulna complex	10068448
Fibrillary glomerulonephritis	10068279
Fibrodysplasia ossificans progressiva	10068715
Fibrous dysplasia of bone	10016664
Fibrous dysplasia of jaw	10070535
Fibula agenesis	10054882
Fissure of tongue, congenital	10016715
Floating-Harbor syndrome	10079943

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Focal segmental glomerulosclerosis	10067757
Foetal alcohol syndrome	10016845
Foetal anticonvulsant syndrome	10066485
Foetal arrhythmia	10016847
Foetal chromosome abnormality	10064041
Foetal cystic hygroma	10052011
Foetal heart rate acceleration abnormality	10074642
Foetal heart rate deceleration abnormality	10074636
Foetal heart rate disorder	10061158
Foetal malformation	10060919
Foetal megacystis	10073660
Foetal methotrexate syndrome	10071183
Foetal renal impairment	10078987
Foetal retinoid syndrome	10073720
Foetal tachyarrhythmia	10077575
Foetal warfarin syndrome	10051445
Foramen magnum stenosis	10064157
Fragile X carrier	10052657
Fragile X syndrome	10017324
Fraser syndrome	10080219
Frasier syndrome	10080313
Freeman-Sheldon syndrome	10073655
Frenulum breve	10072007
Friedreich's ataxia	10017374
Fryns syndrome	10075223
Full blood count abnormal	10017412
Full blood count decreased	10017413
GNE myopathy	10077945
Galactosaemia	10017604
Gallbladder agenesis	10079018
Gallbladder anomaly congenital	10061163
Gallbladder varices	10072319
Gastric variceal injection	10076237
Gastric variceal ligation	10076238
Gastric varices	10051012
Gastric varices haemorrhage	10057572
Gastroenteritis clostridial	10017898
Gastrointestinal arteriovenous malformation	10017932
Gastrointestinal disorder congenital	10061973
Gastrointestinal malformation	10061596
Gastroschisis	10018046
Gaucher's disease	10018048
Gaucher's disease type I	10075697
Gaucher's disease type II	10075698
Gaucher's disease type III	10075699
Gelatinous transformation of the bone marrow	10078097
Gene mutation	10064571
Generalised resistance to thyroid hormone	10018096
Genitalia external ambiguous	10018183
Gilbert's syndrome	10018267
Gitelman's syndrome	10062906
Gleich's syndrome	10066837
Glomerulonephritis	10018364
Glomerulonephritis acute	10018366
Glomerulonephritis chronic	10018367
Glomerulonephritis membranoproliferative	10018370
Glomerulonephritis membranous	10018372
Glomerulonephritis minimal lesion	10018374
Glomerulonephritis proliferative	10018376
Glomerulonephritis rapidly progressive	10018378
Glucose transporter type 1 deficiency syndrome	10078727
Glucose-6-phosphate dehydrogenase deficiency	10018444
Glucose-galactose malabsorption	10066388

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Glutathione synthetase deficiency	10079364
Glycogen storage disease type I	10018464
Glycogen storage disease type II	10053185
Glycogen storage disease type III	10053250
Glycogen storage disease type IV	10053249
Glycogen storage disease type V	10018462
Glycogen storage disease type VI	10053240
Glycogen storage disease type VII	10053241
Glycogen storage disease type VIII	10053242
Glycogen storage disorder	10061990
Gnathoschisis	10068845
Goitre congenital	10018499
Gollop-Wolfgang complex	10079731
Gonadal dysgenesis	10018504
Goodpasture's syndrome	10018620
Gorham's disease	10071283
Graft versus host disease in liver	10064676
Granulocyte count decreased	10018681
Granulocytes abnormal	10018685
Granulocytes maturation arrest	10050443
Granulocytopenia	10018687
Granulocytopenia neonatal	10018688
Granulomatosis with polyangiitis	10072579
Granulomatous liver disease	10018704
Gray matter heterotopia	10080533
Greig's syndrome	10053878
Grey Turner's sign	10075426
Guillain-Barre syndrome	10018767
HIV associated nephropathy	10070737
Haemangioma congenital	10018818
Haemangioma of retina	10018822
Haematotoxicity	10061188
Haemochromatosis trait	10073217
Haemodialysis	10018875
Haemofiltration	10053090
Haemoglobin C disease	10018883
Haemoglobin C trait	10055021
Haemoglobin D disease	10055019
Haemoglobin D trait	10055020
Haemoglobin E disease	10053215
Haemoglobin E trait	10063740
Haemoglobin E-thalassaemia disease	10062917
Haemoglobinopathy	10060892
Haemophilia	10061992
Haemophilia A with anti factor VIII	10056492
Haemophilia A without inhibitors	10056493
Haemophilia B with anti factor IX	10056494
Haemophilia B without inhibitors	10056495
Haemophilia carrier	10051658
Haemorrhagic arteriovenous malformation	10064595
Haemorrhagic necrotic pancreatitis	10076058
Hamartoma	10061193
Hamartoma vascular	10019106
Hand-foot-genital syndrome	10072361
Harlequin foetus	10019163
Hartnup disease	10019165
Heart alternation	10058155
Heart block congenital	10019263
Heart disease congenital	10019273
Heart rate abnormal	10019300
Heart rate decreased	10019301
Heart rate increased	10019303
Heart rate irregular	10019304

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Hemihypertrophy	10019463
Hemimegalencephaly	10078100
Hemivertebra	10019477
Henoch-Schonlein purpura nephritis	10069440
Hepatectomy	10061997
Hepatic arteriovenous malformation	10019633
Hepatic atrophy	10019637
Hepatic calcification	10065274
Hepatic cirrhosis	10019641
Hepatic encephalopathy	10019660
Hepatic encephalopathy prophylaxis	10066599
Hepatic failure	10019663
Hepatic fibrosis	10019668
Hepatic hamartoma	10079685
Hepatic hydrothorax	10067365
Hepatic infiltration eosinophilic	10064668
Hepatic lesion	10061998
Hepatic lymphocytic infiltration	10079686
Hepatic necrosis	10019692
Hepatic steato-fibrosis	10077215
Hepatic steatosis	10019708
Hepatitis	10019717
Hepatitis acute	10019727
Hepatitis cholestatic	10019754
Hepatitis chronic active	10019755
Hepatitis chronic persistent	10019759
Hepatitis fulminant	10019772
Hepatitis toxic	10019795
Hepatitis virus-associated nephropathy	10068610
Hepato-lenticular degeneration	10019819
Hepatobiliary disease	10062000
Hepatocellular foamy cell syndrome	10053244
Hepatocellular injury	10019837
Hepatopulmonary syndrome	10052274
Hepatorenal failure	10019845
Hepatorenal syndrome	10019846
Hepatotoxicity	10019851
Hereditary angioedema	10019860
Hereditary angioedema with C1 esterase inhibitor deficiency	10080955
Hereditary angioedema with normal C1 esterase inhibitor	10080953
Hereditary areflexic dystasia	10063449
Hereditary cerebral degeneration	10061204
Hereditary choroidal dystrophy	10019864
Hereditary disorder	10061205
Hereditary fructose intolerance	10019878
Hereditary haemochromatosis	10057873
Hereditary haemolytic anaemia	10060893
Hereditary haemorrhagic telangiectasia	10019883
Hereditary hypophosphataemic rickets	10077943
Hereditary leiomyomatosis renal cell carcinoma	10067944
Hereditary motor and sensory neuropathy	10077306
Hereditary motor neurone disease	10071328
Hereditary multiple osteochondromas	10079019
Hereditary neuropathic amyloidosis	10019889
Hereditary neuropathy with liability to pressure palsies	10069382
Hereditary non-polyposis colorectal cancer syndrome	10051922
Hereditary optic atrophy	10019895
Hereditary palmoplantar keratoderma	10072537
Hereditary pancreatitis	10056976
Hereditary papillary renal carcinoma	10067943
Hereditary renal microhaematuria	10080385
Hereditary retinal dystrophy	10019899
Hereditary sideroblastic anaemia	10019902

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Hereditary spastic paraplegia	10019903
Hereditary spherocytosis	10019904
Hereditary stomatocytosis	10053589
Hermansky-Pudlak syndrome	10071775
Hermaphroditism	10019906
Hernia congenital	10019912
Heterochromia iridis	10066799
Heterotaxia	10067265
Hexokinase deficiency anaemia	10020022
High arched palate	10020046
Hollow visceral myopathy	10060811
Holoprosencephaly	10056304
Holt-Oram syndrome	10050469
Homocystinaemia	10048707
Homocystinuria	10020365
Hooded prepuce	10072135
Huntington's disease	10070668
Hydranencephaly	10073472
Hydrocele	10020488
Hydronephrosis	10020524
Hydroureter	10020533
Hydroxyprolinaemia	10053148
Hyper IgD syndrome	10072010
Hyper IgE syndrome	10051040
Hyper IgM syndrome	10066130
Hyperbilirubinaemia	10020578
Hyperexplexia	10058271
Hyperglycinaemia	10080883
Hyperinsulinism syndrome	10077858
Hypermethioninaemia	10051245
Hypermethioniuria	10051231
Hyperprolinaemia	10058509
Hypersplenism congenital	10049282
Hypertelorism of orbit	10020771
Hyperthermia malignant	10020844
Hypertrophic cardiomyopathy	10020871
Hypocalvaria	10073670
Hypochondroplasia	10020967
Hypodontia	10055001
Hypomelanosis of Ito	10075301
Hyponatriuria	10077515
Hypophosphatasia	10049933
Hypopituitarism foetal	10021068
Hypoplastic left heart syndrome	10021076
Hypoplastic nasal cartilage	10074970
Hypoplastic right heart syndrome	10064962
Hypospadias	10021093
Hypotelorism of orbit	10057855
Hypothalamic hamartoma	10078217
Hypoxanthine-guanine phosphoribosyl transferase deficiency	10075774
IPEX syndrome	10080631
Ichthyosis	10021198
Icterus index increased	10021209
Idiopathic angioedema	10073257
Idiopathic neutropenia	10051645
IgA nephropathy	10021263
IgM nephropathy	10077209
Ileal atresia	10021298
Immune-mediated hepatitis	10078962
Immunodeficiency congenital	10021450
Immunotactoid glomerulonephritis	10067871
Imperforate hymen	10021529
Imperforate oesophagus	10021530

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Inborn error in primary bile acid synthesis	10070882
Inborn error of bilirubin metabolism	10062017
Inborn error of lipid metabolism	10072272
Inborn error of metabolism	10062018
Infantile cortical hyperostosis	10073206
Infantile genetic agranulocytosis	10052210
Infantile septic granulomatosis	10048708
Inferior vena cava syndrome	10070911
Inherited cardiac conduction disorder	10070294
Iniencephaly	10022034
Interferon gamma receptor deficiency	10057605
Interruption of aortic arch	10022599
Intestinal angioedema	10076229
Intestinal atresia	10062022
Intestinal malrotation	10064024
Intestinal neuronal dysplasia	10073659
Intestinal sepsis	10075622
Intestinal transposition	10022712
Intestinal varices	10071502
Intestinal varices haemorrhage	10078058
Intracranial arterial fenestration	10077285
Intracranial lipoma	10072288
Iris coloboma	10052642
Ischaemic hepatitis	10023025
Ischaemic pancreatitis	10066127
Jaundice	10023126
Jaundice cholestatic	10023129
Jaundice hepatocellular	10023136
Johanson-Blizzard syndrome	10074947
Joubert syndrome	10078574
Junctional ectopic tachycardia	10074640
Juvenile Paget's disease	10078977
Kabuki make-up syndrome	10063935
Kaufman-McKusick syndrome	10052312
Kearns-Sayre syndrome	10048804
Kenny-Caffey syndrome	10073228
Keratitis-ichthyosis-deafness syndrome	10048786
Keratolysis exfoliativa congenital	10052290
Keratosis follicular	10023369
Kidney duplex	10023416
Kidney malformation	10023430
Kidney malrotation	10067877
Kimmerle's anomaly	10076416
Kinematic imbalances due to suboccipital strain	10062992
Kleefstra syndrome	10079365
Klinefelter's syndrome	10023463
Klippel-Feil syndrome	10023464
Klippel-Trenaunay syndrome	10051452
Kounis syndrome	10069167
Krabbe's disease	10023492
Kyphosis congenital	10048576
LDLR mutation	10075640
Labial tie	10076772
Lacrimal punctum agenesis	10023636
Laevocardia	10071015
Lafora's myoclonic epilepsy	10054030
Lamin A/C gene mutation	10075979
Langer-Giedion syndrome	10050638
Laron syndrome	10075492
Larsen syndrome	10073856
Laryngeal cleft	10069115
Laryngeal oedema	10023845
Laryngeal web	10023871

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Laryngo-onycho-cutaneous syndrome	10062987
Laryngocele	10023885
Laryngomalacia	10060786
Laryngotracheal oedema	10023893
Laurence-Moon-Bardet-Biedl syndrome	10056715
Leber's congenital amaurosis	10070667
Lecithin-cholesterol acyltransferase deficiency	10077917
Left ventricle outflow tract obstruction	10065930
Left ventricular false tendon	10079017
Left-to-right cardiac shunt	10077834
Lenegre's disease	10071710
Lens abnormality, congenital	10024202
Leukodystrophy	10024381
Leukopenia	10024384
Leukopenia neonatal	10050504
Li-Fraumeni syndrome	10066795
Lichen spinulosus	10024436
Liddle's syndrome	10052313
Limb hypoplasia congenital	10048575
Limb malformation	10024500
Limb reduction defect	10024503
Lip oedema	10024558
Lip swelling	10024570
Lipid proteinosis	10051661
Lipidosis	10024585
Lipodermoid tumour	10073484
Lipomeningocele	10050084
Lissencephaly	10048911
Liver and small intestine transplant	10052280
Liver dialysis	10076640
Liver disorder	10024670
Liver injury	10067125
Liver operation	10062040
Liver sarcoidosis	10068664
Liver transplant	10024714
Long QT syndrome	10024803
Long QT syndrome congenital	10057926
Long-chain acyl-coenzyme A dehydrogenase deficiency	10072653
Loss of consciousness	10024855
Low set ears	10024929
Lown-Ganong-Levine syndrome	10024984
Lowry-Wood syndrome	10062600
Lumbarisation	10063410
Lupoid hepatic cirrhosis	10025129
Lupus hepatitis	10067737
Lupus nephritis	10025140
Lupus pancreatitis	10067750
Lymphangiectasia intestinal congenital	10054722
Lymphocyte count abnormal	10025252
Lymphocyte count decreased	10025256
Lymphocyte percentage abnormal	10063337
Lymphocyte percentage decreased	10052231
Lymphocytopenia neonatal	10025279
Lymphopenia	10025327
Lysinuric protein intolerance	10058300
Lysosomal acid lipase deficiency	10077267
MELAS syndrome	10053872
MLASA syndrome	10078801
MYH9-related disease	10079437
Macrocephaly	10050183
Macrocheilia	10025378
Macrocornea	10059253
Macrodactyly	10025386

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Macrogenia	10025387
Macroglossia	10025391
Macrognathia	10052658
Macrostomia	10025395
Macrotia	10025396
Macular dystrophy congenital	10025412
Majeed's syndrome	10072223
Malformation biliary	10025523
Malformation venous	10025532
Mandibulofacial dysostosis	10051456
Maple syrup disease	10026817
Marcus Gunn syndrome	10064583
Marfan's syndrome	10026829
Maxillonasal dysplasia	10075843
Mayer-Rokitansky-Kuster-Hauser syndrome	10065148
Medium-chain acyl-coenzyme A dehydrogenase deficiency	10072654
Megakaryocytes decreased	10027119
Meier-Gorlin syndrome	10070612
Melkersson-Rosenthal syndrome	10027166
Membranous lipodystrophy	10065127
Meningocele	10027266
Meningomyelocele	10027287
Menkes' syndrome	10027294
Mesangioproliferative glomerulonephritis	10066453
Mesenteric fibrosis	10027398
Mesoblastic nephroma	10070665
Mesonephric duct cyst	10027405
Metabolic myopathy	10068836
Metachromatic leukodystrophy	10067609
Metamyelocyte count decreased	10050984
Metaphyseal dysplasia	10066147
Metatarsus primus varus	10027489
Methylenetetrahydrofolate reductase deficiency	10070309
Methylenetetrahydrofolate reductase gene mutation	10074753
Methylmalonic aciduria	10059521
Mevalonate kinase deficiency	10072221
Mevalonic aciduria	10072219
Microcephaly	10027534
Microcheilia	10027535
Microcolon	10073456
Microcornea	10057414
Microencephaly	10068320
Microgenia	10027541
Microglossia	10027542
Micrognathia	10027543
Microorchidism	10080650
Micropenis	10071706
Microphthalmos	10027548
Microscopic polyangiitis	10063344
Microstomia	10027553
Microtia	10027555
Microvillous inclusion disease	10068494
Miller Fisher syndrome	10049567
Minimal hepatic encephalopathy	10076204
Mismatch repair cancer syndrome	10077888
Mitochondrial DNA deletion	10051403
Mitochondrial DNA depletion	10059396
Mitochondrial DNA duplication	10052640
Mitochondrial DNA mutation	10052641
Mitochondrial encephalomyopathy	10058799
Mitochondrial enzyme deficiency	10067729
Mitochondrial hepatopathy	10062938
Mitochondrial myopathy	10027710

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Mitochondrial neurogastrointestinal encephalopathy	10065271
Mitral valve atresia	10066800
Mitral valve hypoplasia	10049211
Mittendorf dot	10076031
Mixed liver injury	10066758
Mobile caecum syndrome	10074307
Moebius II syndrome	10027802
Molybdenum cofactor deficiency	10069687
Monoblast count decreased	10058772
Monocyte count abnormal	10061293
Monocyte count decreased	10027878
Monocyte percentage decreased	10052229
Monocytopenia	10027905
Monopodia	10049214
Morning glory syndrome	10027974
Morton's syndrome	10079320
Mosaicism	10068052
Mount-Reback syndrome	10065658
Mouth swelling	10075203
Muckle-Wells syndrome	10064569
Mucolipidosis	10072939
Mucolipidosis type I	10072927
Mucolipidosis type II	10072928
Mucolipidosis type III	10072929
Mucolipidosis type IV	10072930
Mucopolysaccharidosis	10028093
Mucopolysaccharidosis I	10056886
Mucopolysaccharidosis II	10056889
Mucopolysaccharidosis III	10056890
Mucopolysaccharidosis IV	10028095
Mucopolysaccharidosis V	10056891
Mucopolysaccharidosis VI	10056892
Mucopolysaccharidosis VII	10056893
Muir-Torre syndrome	10063042
Multiple carboxylase deficiency	10028176
Multiple cardiac defects	10028178
Multiple congenital abnormalities	10028182
Multiple cutaneous and uterine leiomyomatosis	10077859
Multiple endocrine neoplasia	10051747
Multiple endocrine neoplasia Type 1	10073150
Multiple endocrine neoplasia Type 2	10073149
Multiple endocrine neoplasia Type 2A	10073148
Multiple endocrine neoplasia Type 2B	10073151
Multiple epiphyseal dysplasia	10028197
Multiple gastrointestinal atresias	10028210
Multiple lentigines syndrome	10062901
Multiple organ dysfunction syndrome	10077361
Muscular dystrophy	10028356
Mutagenic effect	10028400
Myeloblast count decreased	10050961
Myeloblast percentage decreased	10052225
Myelocyte count decreased	10050986
Myelocyte percentage decreased	10052227
Myelodysplastic syndrome	10028533
Myelodysplastic syndrome transformation	10067387
Myelofibrosis	10028537
Myeloid maturation arrest	10028560
Myeloid metaplasia	10028561
Myeloperoxidase deficiency	10074767
Myocardial bridging	10052289
Myoclonic epilepsy and ragged-red fibres	10069825
Myotonia congenita	10028655
Myotonic dystrophy	10068871

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
N-acetylglutamate synthase deficiency	10071092
Naevus anaemicus	10069365
Naevus flammeus	10067193
Naevus spider congenital	10050896
Nail aplasia	10079732
Nail-patella syndrome	10063431
Nasopharyngeal atresia	10069701
Neonatal alloimmune thrombocytopenia	10075149
Neonatal anuria	10049778
Neonatal haemochromatosis	10078355
Neonatal leukaemia	10028958
Neonatal lupus erythematosus	10057887
Neonatal tachycardia	10049775
Nephritic syndrome	10065673
Nephritis	10029117
Nephritis allergic	10029120
Nephritis haemorrhagic	10029132
Nephritis radiation	10029140
Nephropathy toxic	10029155
Nephrotic syndrome	10029164
Netherton's syndrome	10062909
Neural tube defect	10052046
Neurofibromatosis	10029268
Neuroleptic malignant syndrome	10029282
Neuronal ceroid lipofuscinosis	10074607
Neuronal migration disorder	10076677
Neuropathy, ataxia, retinitis pigmentosa syndrome	10062940
Neutropenia	10029354
Neutropenia neonatal	10029358
Neutropenic colitis	10062959
Neutropenic infection	10059482
Neutropenic sepsis	10049151
Neutrophil count abnormal	10061313
Neutrophil count decreased	10029366
Neutrophil percentage decreased	10052223
Niemann-Pick disease	10029403
Nijmegen breakage syndrome	10067857
Nodal arrhythmia	10029458
Nodal rhythm	10029470
Nodular regenerative hyperplasia	10051081
Non-alcoholic fatty liver	10029530
Non-alcoholic steatohepatitis	10053219
Non-cirrhotic portal hypertension	10077259
Non-compaction cardiomyopathy	10079253
Nonreassuring foetal heart rate pattern	10074641
Noonan syndrome	10029748
Norrie's disease	10069760
Obstructive pancreatitis	10079822
Ocular albinism	10065276
Ocular icterus	10058117
Oculoauriculovertebral dysplasia	10051934
Oculocerebrorenal syndrome	10051707
Oculodentodigital dysplasia	10063691
Oculomucocutaneous syndrome	10030081
Oculopharyngeal dystrophy	10052181
Oculorespiratory syndrome	10067317
Odontogenic cyst	10063413
Oedema due to hepatic disease	10049631
Oedema mouth	10030110
Oedematous pancreatitis	10052400
Oesophageal atresia	10030146
Oesophageal cyst	10079063
Oesophageal varices haemorrhage	10030210

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Olfacto genital dysplasia	10053142
Olfactory nerve agenesis	10072941
Oliguria	10030302
Olmsted syndrome	10068842
Omenn syndrome	10069097
Opitz-G/BBB syndrome	10079435
Optic disc pit	10079967
Optic nerve hypoplasia	10062942
Oral-facial-digital syndrome type II	10078419
Ornithine transcarbamoylase deficiency	10052450
Oropharyngeal oedema	10078783
Oropharyngeal swelling	10031118
Oroticaciduria congenital	10052773
Os trigonum	10069805
Osteogenesis imperfecta	10031243
Osteopathia striata	10073776
Osteopetrosis	10031280
Osteopoikilosis	10031281
Osteoporosis-pseudoglioma syndrome	10052452
Ota's naevus	10051713
Otocephaly	10058118
Ovarian agenesis	10033120
Ovarian hypoplasia	10079495
Oxycephaly	10080833
PHACES syndrome	10068032
Pacemaker generated arrhythmia	10053486
Pacemaker syndrome	10051994
Pachydermoperiostosis	10051686
Pachygyria	10048910
Pachyonychia congenita	10080088
Pallister-Killian syndrome	10080297
Palpitations	10033557
Pancreas divisum	10069419
Pancreas infection	10051741
Pancreatic abscess	10048984
Pancreatic haemorrhage	10033625
Pancreatic necrosis	10058096
Pancreatic phlegmon	10056975
Pancreatic pseudocyst	10033635
Pancreatic pseudocyst drainage	10033636
Pancreatitis	10033645
Pancreatitis acute	10033647
Pancreatitis bacterial	10065191
Pancreatitis chronic	10033649
Pancreatitis fungal	10065190
Pancreatitis haemorrhagic	10033650
Pancreatitis helminthic	10065189
Pancreatitis mumps	10033653
Pancreatitis necrotising	10033654
Pancreatitis relapsing	10033657
Pancreatitis viral	10065192
Pancreatorenal syndrome	10056277
Pancytopenia	10033661
Panmyelopathy	10050026
Parachute mitral valve	10064192
Paranasal sinus aplasia	10074401
Paraneoplastic glomerulonephritis	10076749
Paraneoplastic nephrotic syndrome	10075626
Parasystole	10033929
Parenteral nutrition associated liver disease	10074151
Parkes-Weber syndrome	10075554
Paroxysmal arrhythmia	10050106
Paroxysmal atrioventricular block	10077503

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Patent ductus arteriosus	10034130
Pearson's syndrome	10062941
Pectus carinatum	10034203
Pectus excavatum	10034204
Pelizaeus-Merzbacher disease	10067610
Pelvi-ureteric obstruction	10034232
Pelvic fibrosis	10034244
Pelvic kidney	10034259
Pendred syndrome	10080398
Penile torsion	10070235
Penoscrotal fusion	10064951
Penoscrotal transposition	10067287
Perinephritis	10072058
Periodontal congenital anomaly	10057476
Periorbital oedema	10034545
Peripancreatic varices	10073215
Peritoneal dialysis	10034660
Perry syndrome	10079207
Persistent cloaca	10069442
Persistent foetal circulation	10034708
Persistent left superior vena cava	10064193
Persistent pupillary membrane	10070872
Persistent urogenital sinus	10059800
Peutz-Jeghers syndrome	10034764
Phakomatosis	10048734
Phalangeal agenesis	10054879
Phalangeal hypoplasia	10049212
Pharyngeal oedema	10034829
Phenylketonuria	10034872
Phimosis	10034878
Phytosterolaemia	10063985
Pierre Robin syndrome	10035009
Pilonidal cyst congenital	10054019
Plagiocephaly	10048586
Plasma cell disorder	10062081
Plasma cells absent	10035230
Plasmablast count decreased	10058774
Platelet count decreased	10035528
Platelet glycoprotein gene mutation	10071024
Platelet maturation arrest	10035537
Platelet production decreased	10035540
Platelet toxicity	10059440
Platonychia	10072590
Platybasia	10057115
Platyspondylia	10068629
Poland's syndrome	10036007
Polycystic liver disease	10048834
Polydactyly	10036063
Polymicrogyria	10073489
Popliteal pterygium syndrome	10079892
Porencephaly	10036172
Porokeratosis	10036175
Porphyria	10036181
Porphyria acute	10036182
Porphyria non-acute	10036186
Porphyrin metabolism disorder	10061356
Porphyrinuria	10036193
Portal fibrosis	10074726
Portal hypertension	10036200
Portal hypertensive colopathy	10079446
Portal hypertensive enteropathy	10068923
Portal hypertensive gastropathy	10050897
Portal tract inflammation	10075331

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Portal vein cavernous transformation	10073979
Portal vein dilatation	10073209
Portal venous system anomaly	10076609
Portopulmonary hypertension	10067281
Post infection glomerulonephritis	10074480
Post streptococcal glomerulonephritis	10036303
Postauricular fistula	10036329
Posterior segment of eye anomaly congenital	10053202
Potter's syndrome	10036462
Prader-Willi syndrome	10036476
Preauricular cyst	10036509
Preduodenal portal vein	10059798
Prerenal failure	10072370
Preternatural anus	10064917
Primary biliary cholangitis	10080429
Primary cerebellar degeneration	10036686
Primary ciliary dyskinesia	10069713
Primary familial brain calcification	10078822
Primary familial hypomagnesaemia	10076626
Primary hypercholesterolaemia	10077965
Primary immunodeficiency syndrome	10064859
Primary insulin like growth factor-1 deficiency	10071079
Primary myelofibrosis	10077161
Procedural shock	10080894
Progeria	10036794
Progressive cerebellar degeneration	10036801
Progressive external ophthalmoplegia	10036802
Progressive familial intrahepatic cholestasis	10076033
Prominent epicanthal folds	10065273
Promyelocyte count decreased	10050987
Protein C deficiency	10051298
Protein S deficiency	10051292
Proteus syndrome	10074067
Protuberant ear	10071232
Proximal focal femoral deficiency	10078473
Pseudocholinesterase deficiency	10062674
Pseudohermaphroditism	10037122
Pseudohermaphroditism female	10037123
Pseudohermaphroditism male	10037124
Pseudohypoaldosteronism	10080593
Pseudohypoparathyroidism	10037126
Pseudomembranous colitis	10037128
Pseudotruncus arteriosus	10050053
Pseudoxanthoma elasticum	10037150
Pterygium colli	10051972
Pulmonary aplasia	10037322
Pulmonary arteriovenous fistula	10037332
Pulmonary artery atresia	10037337
Pulmonary artery stenosis congenital	10037339
Pulmonary hypoplasia	10037407
Pulmonary lymphangiectasia	10073661
Pulmonary malformation	10037419
Pulmonary renal syndrome	10068513
Pulmonary sequestration	10059160
Pulmonary valve stenosis congenital	10037451
Pulseless electrical activity	10058151
Pure white cell aplasia	10068043
Pyloric stenosis	10037621
Pyogenic sterile arthritis pyoderma gangrenosum and acne syndrome	10072222
Pyruvate carboxylase deficiency	10077944
Pyruvate kinase deficiency anaemia	10037682
Radiation hepatitis	10051015
Radiation leukopenia	10067354

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Radiation pancreatitis	10080726
Radioulnar synostosis	10037798
Rathke's cleft cyst	10058969
Rebound tachycardia	10067207
Rectal atresia	10038031
Red blood cell enzymes abnormal	10049191
Refsum's disease	10038275
Regenerative siderotic hepatic nodule	10080679
Renal and liver transplant	10052279
Renal aplasia	10064655
Renal arteriovenous malformation	10038368
Renal dysplasia	10038433
Renal failure	10038435
Renal failure neonatal	10038447
Renal fusion anomaly	10068033
Renal hypoplasia	10049102
Renal impairment	10062237
Renal impairment neonatal	10049776
Renal malposition	10072019
Renal vessel congenital anomaly	10038552
Reperfusion arrhythmia	10058156
Reproductive tract hypoplasia, male	10057858
Respiratory sinus arrhythmia magnitude abnormal	10079117
Respiratory sinus arrhythmia magnitude decreased	10079116
Respiratory sinus arrhythmia magnitude increased	10079115
Respiratory tract malformation	10038733
Retinal anomaly congenital	10038821
Retinal arteriovenous malformation	10038824
Retinal coloboma	10052643
Retinitis pigmentosa	10038914
Retinopathy congenital	10050706
Retinoschisis congenital	10038938
Retrograde p-waves	10071187
Retrograde portal vein flow	10067338
Retroperitoneal fibrosis	10038979
Retroperitonitis	10078424
Rett syndrome	10077709
Reye's syndrome	10039012
Reynold's syndrome	10070953
Rhesus haemolytic disease of newborn	10039037
Rhythm idioventricular	10039111
Rib hypoplasia	10048893
Rib synostosis	10076624
Right aortic arch	10067407
Right ventricle outflow tract obstruction	10064195
Right ventricular false tendon	10080132
Right-to-left cardiac shunt	10076605
Riley-Day syndrome	10039179
Rippling muscle disease	10069417
Rotor's syndrome	10039234
Rubinstein-Taybi syndrome	10039281
Sacral hypoplasia	10056659
Sacralisation	10064932
Sarcosinaemia	10059299
Scan bone marrow abnormal	10053504
Scaphocephaly	10049426
Schimke immunoosseous dysplasia	10048699
Schinzel-Giedion syndrome	10063540
Schizencephaly	10073487
Scimitar syndrome	10051951
Sclerotylosis	10070504
Sebaceous naevus	10039785
Sensory neuropathy hereditary	10040037

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Septate hymen	10068484
Septo-optic dysplasia	10067159
Septum pellucidum agenesis	10062267
Serotonin syndrome	10040108
Sertoli-cell-only syndrome	10066833
Severe myoclonic epilepsy of infancy	10073677
Sex chromosome abnormality	10061513
Shawl scrotum	10080319
Shigella sepsis	10074481
Shock	10040560
Shock symptom	10040581
Shone complex	10066802
Short-chain acyl-coenzyme A dehydrogenase deficiency	10072655
Shwachman-Diamond syndrome	10067940
Sickle cell anaemia	10040641
Sickle cell disease	10040644
Sickle cell trait	10040650
Silver-Russell syndrome	10062282
Single umbilical artery	10049807
Sinoatrial block	10040736
Sinus arrest	10040738
Sinus arrhythmia	10040739
Sinus bradycardia	10040741
Sinus node dysfunction	10075889
Sinus tachycardia	10040752
Sirenomelia	10072457
Sjogren-Larsson syndrome	10048676
Skeletal dysplasia	10072610
Skin hypoplasia	10040869
Skin malformation	10040888
Skin necrosis	10040893
Skull malformation	10062348
Smith-Lemli-Opitz syndrome	10078573
Sotos' syndrome	10064387
Special senses congenital anomaly	10041420
Spherophakia	10041513
Spina bifida	10041524
Spina bifida cystica	10071011
Spina bifida occulta	10041525
Spinal muscular atrophy	10041582
Spinal vessel congenital anomaly	10041603
Spine malformation	10041611
Spinocerebellar ataxia	10057660
Spleen malformation	10062350
Splenic hamartoma	10076586
Splenic varices	10067823
Splenic varices haemorrhage	10068662
Spondyloepiphyseal dysplasia	10062920
Stargardt's disease	10062766
Steatocystoma multiplex	10048905
Steatohepatitis	10076331
Stevens-Johnson syndrome	10042033
Stickler's syndrome	10063402
Sticky platelet syndrome	10068788
Strabismus congenital	10042161
Sturge-Weber syndrome	10042265
Subacute hepatic failure	10056956
Sucrase-isomaltase deficiency	10066387
Sudden cardiac death	10049418
Sudden death	10042434
Supernumerary nipple	10042571
Supernumerary vertebra	10077919
Supraventricular extrasystoles	10042602

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Supraventricular tachyarrhythmia	10065342
Supraventricular tachycardia	10042604
Swelling face	10042682
Swollen tongue	10042727
Syncope	10042772
Syndactyly	10042778
Synostosis	10042856
Syringomyelia	10042928
T-lymphocyte count abnormal	10057284
T-lymphocyte count decreased	10051318
Tachyarrhythmia	10049447
Tachycardia	10043071
Tachycardia foetal	10043074
Tachycardia paroxysmal	10043079
Talipes	10043101
Tangier disease	10051875
Tay-Sachs disease	10043147
Telangiectasia congenital	10061575
Teratogenicity	10043275
Testicular dysplasia	10059271
Testotoxicosis	10063654
Tetrahydrobiopterin deficiency	10069116
Thalassaemia	10043388
Thalassaemia alpha	10043390
Thalassaemia beta	10043391
Thalassaemia sickle cell	10043395
Thalidomide embryopathy	10071249
Thanatophoric dwarfism	10049808
Thrombocytopenia	10043554
Thrombocytopenia-absent radius syndrome	10071719
Thymus hypoplasia	10052645
Thyroglossal cyst	10051320
Thyroglossal fistula	10062601
Thyroid hemiagenesis	10077609
Thyroid malformation	10062125
Tibial agenesis	10079730
Tibial torsion	10064515
Tilted disc syndrome	10079368
Timothy syndrome	10079205
Tongue oedema	10043967
Tooth discolouration congenital	10044033
Tooth hypoplasia	10044041
Tooth malformation hereditary	10044047
Tornwaldt cyst	10078492
Torsade de pointes	10044066
Tourette's disorder	10044126
Toxic epidermal necrolysis	10044223
Toxic skin eruption	10057970
Tracheal atresia	10054955
Tracheal web	10077940
Tracheo-oesophageal fistula	10044310
Transitional vertebrae	10074306
Transposition of the great vessels	10044443
Traumatic pancreatitis	10074894
Trichorhinophalangeal syndrome	10051956
Trifascicular block	10044644
Trifunctional protein deficiency	10077949
Trimethylaminuria	10068233
Triple A syndrome	10073592
Trisomy 11	10044685
Trisomy 12	10063092
Trisomy 13	10044686
Trisomy 14	10071762

MedDRA version 21.0.

Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Trisomy 15	10062757
Trisomy 17	10053925
Trisomy 18	10053884
Trisomy 21	10044688
Trisomy 22	10044689
Trisomy 4p	10080079
Trisomy 8	10053871
Trisomy 9	10071547
Truncus arteriosus persistent	10044703
Tuberous sclerosis complex	10080584
Tubulointerstitial nephritis	10048302
Tubulointerstitial nephritis and uveitis syndrome	10069034
Tumour necrosis factor receptor-associated periodic syndrome	10067774
Turner's syndrome	10045181
Twin reversed arterial perfusion sequence malformation	10073455
Type I hyperlipidaemia	10060749
Type I hypersensitivity	10045240
Type II hyperlipidaemia	10045254
Type III hyperlipidaemia	10060751
Type IIa hyperlipidaemia	10045261
Type IIb hyperlipidaemia	10045263
Type IV hyperlipidaemia	10060753
Type V hyperlipidaemia	10060755
Tyrosinaemia	10063443
Uhl's anomaly	10048951
Umbilical artery hypoplasia	10045445
Umbilical malformation	10045469
Univentricular heart	10045545
Urachal abnormality	10066125
Urea cycle disorder	10080020
Ureteric atresia	10078351
Ureteric compression	10076715
Ureteric dilatation	10046399
Ureteric obstruction	10046406
Ureteric stenosis	10046411
Urethral atresia	10064895
Urethral valves	10046479
Urinary tract malformation	10046580
Urinary tract obstruction	10061574
Usher's syndrome	10063396
Uterine aplasia	10067704
Uterine cervix hypoplasia	10063120
Uterine hypoplasia	10063146
Uvula aplasia	10053506
VACTERL syndrome	10066022
Vaginal atresia	10046879
Vaginal hypoplasia	10053843
Vaginal septum	10064513
Varices oesophageal	10056091
Varicose veins of abdominal wall	10072284
Vascular malformation	10074979
Vein of Galen aneurysmal malformation	10077889
Velo-cardio-facial syndrome	10066430
Venolymphatic malformation	10079880
Venous angioma of brain	10053485
Ventricular arrhythmia	10047281
Ventricular asystole	10047284
Ventricular dyssynchrony	10071186
Ventricular extrasystoles	10047289
Ventricular fibrillation	10047290
Ventricular flutter	10047294
Ventricular hypoplasia	10047296
Ventricular parasystole	10058184

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Listing of preferred terms used for NNMQ - Rare events

Preferred Term Text	Preferred Term ID
Ventricular pre-excitation	10049761
Ventricular septal defect	10047298
Ventricular tachyarrhythmia	10065341
Ventricular tachycardia	10047302
Vertebral artery hypoplasia	10066907
Vertical talus	10066242
Very long-chain acyl-coenzyme A dehydrogenase deficiency	10072656
Vestibulocerebellar syndrome	10080748
Virilism foetal	10047487
Vitello-intestinal duct remnant	10066969
Von Hippel-Lindau disease	10047716
Von Willebrand's disease	10047715
Von Willebrand's disease gene carrier	10080844
Waardenburg syndrome	10069203
Wagner's disease	10063383
Wandering pacemaker	10047818
Weill-Marchesani syndrome	10064963
Welander distal myopathy	10078052
Werner's syndrome	10049429
White blood cell analysis abnormal	10073323
White blood cell count abnormal	10047940
White blood cell count decreased	10047942
White blood cell disorder	10061414
White nipple sign	10078438
Wildervanck syndrome	10069402
Williams syndrome	10049644
Winchester syndrome	10078901
Wiskott-Aldrich syndrome	10047992
Withdrawal arrhythmia	10047997
Wolf-Hirschhorn syndrome	10050361
Wolff-Parkinson-White syndrome	10048015
Wolff-Parkinson-White syndrome congenital	10049291
Wolfram syndrome	10078338
Wyburn Mason's syndrome	10048661
X-linked chromosomal disorder	10056554
X-linked lymphoproliferative syndrome	10068348
XXX syndrome	10076910
XXXY syndrome	10048228
XXYY syndrome	10048230
XYY syndrome	10056894
Xeroderma pigmentosum	10048220
Y-linked chromosomal disorder	10056555
Yellow skin	10048245
Young's syndrome	10063689
Zika virus associated Guillain Barre syndrome	10081046
Zika virus associated birth defect	10081047
Zika virus associated microencephaly	10081048
Zika virus associated ocular birth defect	10081045

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136 Listing of preferred terms used for NNMQ - Adrenocortical insufficiency (secondary)

Preferred Term Text	Preferred Term ID
Addison's disease	10001130
Adrenal androgen deficiency	10075902
Adrenal atrophy	10001324
Adrenal insufficiency	10001367
Adrenal insufficiency neonatal	10001368
Adrenal suppression	10001382
Adrenocortical insufficiency acute	10001389
Adrenocortical insufficiency neonatal	10001391
Adrenogenital syndrome	10061630
Congenital adrenal gland hypoplasia	10049057
Cortisol deficiency	10078563
Glucocorticoid deficiency	10072079
Hypoaldosteronism	10020944
Mineralocorticoid deficiency	10072080
Primary adrenal insufficiency	10052381
Pseudohypoaldosteronism	10080593
Secondary adrenocortical insufficiency	10039807
Steroid withdrawal syndrome	10042028
Triple A syndrome	10073592

MedDRA version 21.0.

137 Summary of baseline characteristics by treatment - 4054 - full analysis set

	placebo	Norditropin	somapacitan	total
Number of Subjects	61	119	226	300
Age (years), N	61	119	226	300
Mean (SD)	45.0 (15.7)	45.7 (15.3)	44.5 (14.9)	45.1 (15.0)
Median	46.0	46.0	43.5	44.5
Min ; Max	23.0 ; 76.0	23.0 ; 77.0	23.0 ; 75.0	23.0 ; 77.0
Agegroup, N (%)	61 (100.0)	119 (100.0)	226 (100.0)	300 (100.0)
18 - 64 years	51 (83.6)	101 (84.9)	197 (87.2)	259 (86.3)
>= 65 years	10 (16.4)	18 (15.1)	29 (12.8)	41 (13.7)
Sex, N (%)	61 (100.0)	119 (100.0)	226 (100.0)	300 (100.0)
Female	32 (52.5)	61 (51.3)	119 (52.7)	155 (51.7)
Male	29 (47.5)	58 (48.7)	107 (47.3)	145 (48.3)
Ethnicity, N (%)	61 (100.0)	119 (100.0)	226 (100.0)	300 (100.0)
Hispanic Or Latino	4 (6.6)	8 (6.7)	15 (6.6)	18 (6.0)
Not Hispanic Or Latino	57 (93.4)	109 (91.6)	209 (92.5)	280 (93.3)
NA	0	2 (1.7)	2 (0.9)	2 (0.7)
Race, N (%)	61 (100.0)	119 (100.0)	226 (100.0)	300 (100.0)
Asian	16 (26.2)	36 (30.3)	64 (28.3)	86 (28.7)
White	42 (68.9)	76 (63.9)	152 (67.3)	200 (66.7)
Black Or African American	2 (3.3)	3 (2.5)	4 (1.8)	7 (2.3)
Native Hawaiian Or Other Pacific Islander	0	0	1 (0.4)	1 (0.3)
Other	1 (1.6)	2 (1.7)	3 (1.3)	4 (1.3)
NA	0	2 (1.7)	2 (0.9)	2 (0.7)
Country, N (%)	61 (100.0)	119 (100.0)	226 (100.0)	300 (100.0)
Australia	7 (11.5)	10 (8.4)	26 (11.5)	30 (10.0)
Germany	2 (3.3)	3 (2.5)	5 (2.2)	8 (2.7)
India	6 (9.8)	11 (9.2)	19 (8.4)	28 (9.3)
Japan	10 (16.4)	18 (15.1)	36 (15.9)	46 (15.3)
Latvia	2 (3.3)	1 (0.8)	2 (0.9)	3 (1.0)
Lithuania	4 (6.6)	3 (2.5)	7 (3.1)	8 (2.7)
Malaysia	0	3 (2.5)	5 (2.2)	7 (2.3)
Poland	1 (1.6)	2 (1.7)	8 (3.5)	11 (3.7)
Romania	2 (3.3)	14 (11.8)	21 (9.3)	28 (9.3)
Russian Federation	5 (8.2)	6 (5.0)	15 (6.6)	18 (6.0)
South Africa	1 (1.6)	4 (3.4)	7 (3.1)	9 (3.0)
Sweden	0	2 (1.7)	2 (0.9)	2 (0.7)
Turkey	3 (4.9)	1 (0.8)	7 (3.1)	8 (2.7)
Ukraine	4 (6.6)	1 (0.8)	6 (2.7)	8 (2.7)
United Kingdom	0	6 (5.0)	4 (1.8)	7 (2.3)
United States	14 (23.0)	34 (28.6)	56 (24.8)	79 (26.3)
Height (m), N	61	119	226	300
Mean (SD)	1.63 (0.10)	1.64 (0.14)	1.64 (0.11)	1.64 (0.12)
Median	1.64	1.64	1.64	1.64
Min ; Max	1.39 ; 1.83	1.07 ; 1.93	1.30 ; 1.91	1.07 ; 1.93
Body Weight (kg), N	61	119	226	300
Mean (SD)	69.8 (19.7)	76.0 (22.7)	74.2 (21.7)	74.8 (21.5)
Median	69.0	74.1	70.6	72.4
Min ; Max	38.0 ; 115	22.5 ; 141	36.0 ; 141	22.5 ; 141
BMI (kg/m^2), N	61	119	226	300
Mean (SD)	26.1 (6.4)	27.7 (6.2)	27.3 (6.4)	27.4 (6.3)

N: Number of subjects, %: Percentage of subjects, SD: Standard deviation
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.

Summary of baseline characteristics by treatment - 4054 - full analysis set

	placebo	Norditropin	somapacitan	total
Median	25.4	26.8	26.4	26.7
Min ; Max	13.3 ; 44.3	17.0 ; 45.0	13.3 ; 47.2	13.3 ; 47.2
Waist circumference (cm), N	61	119	226	300
Mean (SD)	88.2 (14.5)	94.3 (16.6)	92.2 (15.5)	92.9 (15.7)
Median	87.7	94.6	90.8	92.8
Min ; Max	60.0 ; 123	45.3 ; 153	60.0 ; 153	45.3 ; 153
GHD Onset, N (%)	61 (100.0)	119 (100.0)	226 (100.0)	300 (100.0)
Childhood-Idiopathic	13 (21.3)	21 (17.6)	43 (19.0)	55 (18.3)
Childhood-Organic	7 (11.5)	12 (10.1)	27 (11.9)	36 (12.0)
Adulthood	41 (67.2)	86 (72.3)	156 (69.0)	209 (69.7)
Diabetes Mellitus, N (%)	61 (100.0)	119 (100.0)	226 (100.0)	300 (100.0)
Diabetic	3 (4.9)	6 (5.0)	11 (4.9)	16 (5.3)
Non-Diabetic	58 (95.1)	113 (95.0)	215 (95.1)	284 (94.7)

N: Number of subjects, %: Percentage of subjects, SD: Standard deviation
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.

138 Summary of exposure by treatment - 4054 entire trial - safety analysis set

	placebo	Norditropin	somapacitan
	once weekly	once daily	once weekly
Number of exposed subjects	61	119	226
Days of exposure*			
Mean (SD)	228 (36.1)	378 (193.8)	467 (147.2)
Median	238	243	378
Min; Max	28; 252	1; 619	7; 623
Treatment dose** (mg)			
Mean (SD)	2.20 (0.74)	0.33 (0.19)	2.59 (1.43)
Median	2.00	0.25	2.25
Min; Max	1.00; 3.50	0.10; 1.10	0.50; 8.00
Treatment dose** (mg/kg)			
Mean (SD)	0.034 (0.016)	0.005 (0.005)	0.040 (0.028)
Median	0.032	0.004	0.030
Min; Max	0.014; 0.080	0.001; 0.044	0.007; 0.171
Total Exposure*** (years)	38.2	123.2	288.8

SD: Standard deviation
* Exposure days are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan.
** Stable dose at last titration visit. For subjects in 4054 receiving same treatment in main and extension period, only first titration period is included.
*** Including titration period.

139 Adverse Events - 4054 entire trial - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All adverse events	46 (75.4)	182	456.8	98 (82.4)	611	467.8	179 (79.2)	1119	372.3	254 (84.7)	1912	406.0
Serious adverse events	5 (8.2)	7	17.6	14 (11.8)	19	14.5	21 (9.3)	42	14.0	37 (12.3)	68	14.4
Medical events of special interest	0			0			0			0		
Severity												
Mild	41 (67.2)	144	361.5	86 (72.3)	395	302.4	164 (72.6)	827	275.2	232 (77.3)	1366	290.0
Moderate	17 (27.9)	32	80.3	54 (45.4)	201	153.9	75 (33.2)	253	84.2	128 (42.7)	486	103.2
Severe	4 (6.6)	6	15.1	10 (8.4)	15	11.5	21 (9.3)	39	13.0	34 (11.3)	60	12.7
Causality												
Unlikely	45 (73.8)	163	409.2	93 (78.2)	523	400.4	170 (75.2)	913	303.8	243 (81.0)	1599	339.5
Possible	9 (14.8)	13	32.6	29 (24.4)	61	46.7	50 (22.1)	157	52.2	81 (27.0)	231	49.0
Probable	4 (6.6)	6	15.1	15 (12.6)	27	20.7	26 (11.5)	49	16.3	41 (13.7)	82	17.4
Outcome												
Recovered/Resolved	43 (70.5)	160	401.6	91 (76.5)	502	384.4	167 (73.9)	937	311.8	242 (80.7)	1599	339.5
Recovering/Resolving	1 (1.6)	2	5.0	8 (6.7)	12	9.2	10 (4.4)	15	5.0	19 (6.3)	29	6.2
Recovered/Resolved With Sequelae	1 (1.6)	1	2.5	3 (2.5)	4	3.1	3 (1.3)	3	1.0	6 (2.0)	8	1.7
Not Recovered/Not Resolved	13 (21.3)	18	45.2	42 (35.3)	88	67.4	75 (33.2)	160	53.2	116 (38.7)	266	56.5
Fatal	1 (1.6)	1	2.5	2 (1.7)	2	1.5	2 (0.9)	4	1.3	5 (1.7)	7	1.5

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Adverse Events - 4054 entire trial - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Unknown	0			1	(0.8)	3 2.3	0			1	(0.3)	3 0.6
Action												
Drug Interrupted	3	(4.9)	5 12.6	6	(5.0)	10 7.7	3	(1.3)	6 2.0	12	(4.0)	21 4.5
Drug Withdrawn	1	(1.6)	1 2.5	4	(3.4)	4 3.1	5	(2.2)	6 2.0	10	(3.3)	11 2.3
Dose Reduced	0			5	(4.2)	7 5.4	8	(3.5)	10 3.3	13	(4.3)	17 3.6
Dose Not Changed	45	(73.8)	170 426.7	95	(79.8)	571 437.2	178	(78.8)	1049 349.0	250	(83.3)	1790 380.1
Not Applicable	3	(4.9)	6 15.1	10	(8.4)	19 14.5	21	(9.3)	48 16.0	34	(11.3)	73 15.5
Treatment discontinuations due to adverse events*	1	(1.6)	1 2.5	5	(4.2)	5 3.8	5	(2.2)	6 2.0	11	(3.7)	12 2.5

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

140 Serious adverse events - 4054 entire trial - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All serious adverse events	5	(8.2)	7 17.6	14	(11.8)	19 14.5	21	(9.3)	42 14.0	37	(12.3)	68 14.4
Medical events of special interest	0			0			0			0		
Severity												
Mild	1	(1.6)	1 2.5	1	(0.8)	1 0.8	3	(1.3)	3 1.0	4	(1.3)	5 1.1
Moderate	1	(1.6)	1 2.5	7	(5.9)	7 5.4	9	(4.0)	13 4.3	16	(5.3)	21 4.5
Severe	3	(4.9)	5 12.6	8	(6.7)	11 8.4	12	(5.3)	26 8.7	22	(7.3)	42 8.9
Causality												
Unlikely	5	(8.2)	7 17.6	14	(11.8)	18 13.8	20	(8.8)	41 13.6	36	(12.0)	66 14.0
Possible	0			0			1	(0.4)	1 0.3	1	(0.3)	1 0.2
Probable	0			1	(0.8)	1 0.8	0			1	(0.3)	1 0.2
Outcome												
Recovered/Resolved	3	(4.9)	5 12.6	11	(9.2)	16 12.3	16	(7.1)	35 11.6	28	(9.3)	56 11.9
Recovered/Resolved With Sequelae	1	(1.6)	1 2.5	0			0			1	(0.3)	1 0.2
Not Recovered/Not Resolved	0			1	(0.8)	1 0.8	3	(1.3)	3 1.0	4	(1.3)	4 0.8
Fatal	1	(1.6)	1 2.5	2	(1.7)	2 1.5	2	(0.9)	4 1.3	5	(1.7)	7 1.5
Action												
Drug Interrupted	1	(1.6)	1 2.5	4	(3.4)	6 4.6	1	(0.4)	3 1.0	6	(2.0)	10 2.1
Drug Withdrawn	0			2	(1.7)	2 1.5	0			2	(0.7)	2 0.4

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Serious adverse events - 4054 entire trial - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Dose Reduced	0			1	(0.8)	1 0.8	0			1	(0.3)	1 0.2
Dose Not Changed	3	(4.9)	5 12.6	7	(5.9)	8 6.1	17	(7.5)	31 10.3	25	(8.3)	44 9.3
Not Applicable	1	(1.6)	1 2.5	2	(1.7)	2 1.5	4	(1.8)	8 2.7	7	(2.3)	11 2.3
Treatment discontinuations due to adverse events*	0			3	(2.5)	3 2.3	0			3	(1.0)	3 0.6

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

141 Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All adverse events	46 (75.4)	182	456.8	98 (82.4)	611	467.8	179 (79.2)	1119	372.3	254 (84.7)	1912	406.0
Infections and infestations	36 (59.0)	50	125.5	63 (52.9)	124	94.9	116 (51.3)	256	85.2	179 (59.7)	430	91.3
Nasopharyngitis	9 (14.8)	12	30.1	25 (21.0)	33	25.3	50 (22.1)	70	23.3	74 (24.7)	115	24.4
Upper respiratory tract infection	7 (11.5)	7	17.6	11 (9.2)	16	12.3	22 (9.7)	25	8.3	35 (11.7)	48	10.2
Gastroenteritis	2 (3.3)	2	5.0	3 (2.5)	4	3.1	12 (5.3)	16	5.3	17 (5.7)	22	4.7
Influenza	2 (3.3)	3	7.5	2 (1.7)	3	2.3	13 (5.8)	16	5.3	16 (5.3)	22	4.7
Urinary tract infection	1 (1.6)	1	2.5	3 (2.5)	4	3.1	12 (5.3)	17	5.7	15 (5.0)	22	4.7
Sinusitis	3 (4.9)	6	15.1	4 (3.4)	4	3.1	7 (3.1)	9	3.0	13 (4.3)	19	4.0
Bronchitis	3 (4.9)	3	7.5	3 (2.5)	3	2.3	7 (3.1)	7	2.3	12 (4.0)	13	2.8
Tonsillitis	1 (1.6)	1	2.5	4 (3.4)	5	3.8	7 (3.1)	7	2.3	12 (4.0)	13	2.8
Ear infection	1 (1.6)	1	2.5	2 (1.7)	2	1.5	4 (1.8)	7	2.3	7 (2.3)	10	2.1
Herpes zoster	1 (1.6)	1	2.5	1 (0.8)	1	0.8	4 (1.8)	9	3.0	6 (2.0)	11	2.3
Pharyngitis	1 (1.6)	1	2.5	3 (2.5)	5	3.8	2 (0.9)	2	0.7	6 (2.0)	8	1.7
Respiratory tract infection	2 (3.3)	2	5.0	2 (1.7)	2	1.5	2 (0.9)	3	1.0	6 (2.0)	7	1.5
Respiratory tract infection viral	0			3 (2.5)	3	2.3	3 (1.3)	3	1.0	6 (2.0)	6	1.3
Tooth abscess	0			3 (2.5)	3	2.3	3 (1.3)	3	1.0	6 (2.0)	6	1.3
Viral infection	0			1 (0.8)	1	0.8	5 (2.2)	5	1.7	6 (2.0)	6	1.3
Gastroenteritis viral	2 (3.3)	2	5.0	2 (1.7)	2	1.5	1 (0.4)	1	0.3	5 (1.7)	5	1.1
Lower respiratory tract infection	0			1 (0.8)	2	1.5	4 (1.8)	4	1.3	5 (1.7)	6	1.3
Viral upper respiratory tract infection	1 (1.6)	1	2.5	1 (0.8)	1	0.8	3 (1.3)	3	1.0	5 (1.7)	5	1.1
Cystitis	2 (3.3)	2	5.0	0			2 (0.9)	3	1.0	4 (1.3)	5	1.1
Fungal infection	0			2 (1.7)	2	1.5	2 (0.9)	2	0.7	4 (1.3)	4	0.8
Pharyngitis streptococcal	0			0			4 (1.8)	5	1.7	4 (1.3)	5	1.1
Cellulitis	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Oral herpes	0			0			3 (1.3)	4	1.3	3 (1.0)	4	0.8
Pulpitis dental	0			3 (2.5)	3	2.3	0			3 (1.0)	3	0.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Rhinitis	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Tooth infection	0			2 (1.7)	3	2.3	1 (0.4)	2	0.7	3 (1.0)	5	1.1
Appendicitis	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Bronchitis viral	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Clostridium difficile infection	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Laryngitis	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Otitis media	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Pneumonia	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Tinea infection	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Acarodermatitis	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Candida infection	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Diverticulitis	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Escherichia infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eye infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Folliculitis	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Gastrointestinal infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Gingivitis	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Helicobacter infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Herpes simplex	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Herpes virus infection	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Hordeolum	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Meningitis viral	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Molluscum contagiosum	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Onychomycosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ophthalmic herpes zoster	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Oral candidiasis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Otitis externa	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Paronychia	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Parotitis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Periodontitis	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Periporitis staphylogenes	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pilonidal cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pneumonia bacterial	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Pneumonia viral	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Post procedural infection	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Pulmonary tuberculosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pyoderma	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Rotavirus infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Sepsis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Tinea capitis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Tinea cruris	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Tinea pedis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Upper respiratory tract infection bacterial	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Urosepsis	0			1 (0.8)	2	1.5	0			1 (0.3)	2	0.4
Vaginal infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Vulvovaginal candidiasis	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Wound infection	0			1 (0.8)	2	1.5	0			1 (0.3)	2	0.4
Gastrointestinal disorders	13 (21.3)	24	60.2	34 (28.6)	60	45.9	62 (27.4)	129	42.9	101 (33.7)	213	45.2
Diarrhoea	5 (8.2)	8	20.1	8 (6.7)	8	6.1	17 (7.5)	26	8.7	29 (9.7)	42	8.9
Vomiting	1 (1.6)	2	5.0	5 (4.2)	7	5.4	13 (5.8)	16	5.3	19 (6.3)	25	5.3
Nausea	1 (1.6)	1	2.5	6 (5.0)	8	6.1	7 (3.1)	16	5.3	13 (4.3)	25	5.3
Abdominal pain	1 (1.6)	1	2.5	3 (2.5)	4	3.1	6 (2.7)	9	3.0	10 (3.3)	14	3.0
Dyspepsia	1 (1.6)	2	5.0	4 (3.4)	4	3.1	4 (1.8)	5	1.7	9 (3.0)	11	2.3
Toothache	1 (1.6)	1	2.5	4 (3.4)	4	3.1	4 (1.8)	6	2.0	9 (3.0)	11	2.3
Abdominal pain upper	1 (1.6)	1	2.5	2 (1.7)	2	1.5	4 (1.8)	7	2.3	7 (2.3)	10	2.1
Dental caries	0			3 (2.5)	4	3.1	4 (1.8)	4	1.3	7 (2.3)	8	1.7
Abdominal tenderness	0			3 (2.5)	3	2.3	1 (0.4)	1	0.3	4 (1.3)	4	0.8
Constipation	0			3 (2.5)	3	2.3	2 (0.9)	3	1.0	4 (1.3)	6	1.3
Gastritis	1 (1.6)	1	2.5	0			3 (1.3)	3	1.0	4 (1.3)	4	0.8
Gastrooesophageal reflux disease	1 (1.6)	1	2.5	0			3 (1.3)	3	1.0	4 (1.3)	4	0.8
Abdominal distension	0			0			3 (1.3)	4	1.3	3 (1.0)	4	0.8
Food poisoning	1 (1.6)	1	2.5	1 (0.8)	1	0.8	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Stomatitis	0			1 (0.8)	1	0.8	2 (0.9)	2	0.7	3 (1.0)	3	0.6
Abdominal discomfort	1 (1.6)	1	2.5	1 (0.8)	1	0.8	0			2 (0.7)	2	0.4

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Epigastric discomfort	0			0			2 (0.9)	5	1.7	2 (0.7)	5	1.1
Flatulence	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Lip swelling	1 (1.6)	1	2.5	0			1 (0.4)	1	0.3	2 (0.7)	2	0.4
Pancreatitis acute	1 (1.6)	1	2.5	1 (0.8)	1	0.8	0			2 (0.7)	2	0.4
Abdominal hernia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Abdominal pain lower	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Abdominal wall mass	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ascites	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Chronic gastritis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Colitis	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Colitis ulcerative	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Dental cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Dry mouth	0			0			1 (0.4)	2	0.7	1 (0.3)	2	0.4
Duodenal ulcer	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Enteritis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Faeces discoloured	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Gastric polyps	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Gastrointestinal disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Haemorrhoids	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Hiatus hernia	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Inguinal hernia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Irritable bowel syndrome	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Large intestine polyp	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Mouth ulceration	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Oesophagitis	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Oesophagitis ulcerative	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Rectal polyp	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Retching	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Spigelian hernia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Musculoskeletal and connective tissue disorders	10 (16.4)	14	35.1	37 (31.1)	67	51.3	60 (26.5)	100	33.3	97 (32.3)	181	38.4
Arthralgia	1 (1.6)	1	2.5	14 (11.8)	15	11.5	15 (6.6)	16	5.3	29 (9.7)	32	6.8

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Back pain	2 (3.3)	2	5.0	4 (3.4)	4	3.1	16 (7.1)	18	6.0	22 (7.3)	24	5.1
Myalgia	3 (4.9)	3	7.5	6 (5.0)	6	4.6	6 (2.7)	8	2.7	15 (5.0)	17	3.6
Pain in extremity	1 (1.6)	1	2.5	6 (5.0)	8	6.1	6 (2.7)	6	2.0	13 (4.3)	15	3.2
Joint stiffness	0			3 (2.5)	3	2.3	2 (0.9)	2	0.7	5 (1.7)	5	1.1
Muscle spasms	1 (1.6)	2	5.0	0			4 (1.8)	4	1.3	5 (1.7)	6	1.3
Musculoskeletal pain	0			2 (1.7)	2	1.5	3 (1.3)	3	1.0	5 (1.7)	5	1.1
Osteoarthritis	0			2 (1.7)	3	2.3	3 (1.3)	3	1.0	5 (1.7)	6	1.3
Musculoskeletal stiffness	0			1 (0.8)	1	0.8	3 (1.3)	3	1.0	4 (1.3)	4	0.8
Neck pain	0			1 (0.8)	1	0.8	3 (1.3)	4	1.3	4 (1.3)	5	1.1
Bursitis	1 (1.6)	2	5.0	0			3 (1.3)	4	1.3	3 (1.0)	6	1.3
Joint swelling	0			3 (2.5)	4	3.1	0			3 (1.0)	4	0.8
Muscular weakness	0			1 (0.8)	1	0.8	2 (0.9)	5	1.7	3 (1.0)	6	1.3
Musculoskeletal chest pain	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Pain in jaw	0			1 (0.8)	1	0.8	2 (0.9)	3	1.0	3 (1.0)	4	0.8
Tendonitis	1 (1.6)	1	2.5	1 (0.8)	1	0.8	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Arthritis	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Intervertebral disc degeneration	0			0			2 (0.9)	3	1.0	2 (0.7)	3	0.6
Intervertebral disc protrusion	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Muscle twitching	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Rotator cuff syndrome	0			2 (1.7)	3	2.3	0			2 (0.7)	3	0.6
Tenosynovitis	1 (1.6)	1	2.5	1 (0.8)	2	1.5	0			2 (0.7)	3	0.6
Costochondritis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Exostosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Foot deformity	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Fracture pain	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Groin pain	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Joint effusion	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Joint noise	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Limb deformity	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Limb discomfort	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Lumbar spinal stenosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Muscle disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Muscle tightness	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Myositis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Neck deformity	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Nodal osteoarthritis	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Periarthritis	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Plantar fasciitis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Rheumatoid arthritis	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Soft tissue disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Soft tissue mass	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Spinal pain	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Nervous system disorders	14 (23.0)	26	65.3	23 (19.3)	99	75.8	59 (26.1)	142	47.2	87 (29.0)	267	56.7
Headache	10 (16.4)	15	37.7	15 (12.6)	73	55.9	32 (14.2)	94	31.3	51 (17.0)	182	38.6
Dizziness	1 (1.6)	1	2.5	6 (5.0)	9	6.9	13 (5.8)	17	5.7	19 (6.3)	27	5.7
Hypoaesthesia	1 (1.6)	1	2.5	3 (2.5)	4	3.1	4 (1.8)	4	1.3	8 (2.7)	9	1.9
Paraesthesia	2 (3.3)	2	5.0	1 (0.8)	1	0.8	4 (1.8)	5	1.7	7 (2.3)	8	1.7
Migraine	1 (1.6)	3	7.5	1 (0.8)	1	0.8	3 (1.3)	4	1.3	4 (1.3)	8	1.7
Somnolence	0			1 (0.8)	1	0.8	2 (0.9)	3	1.0	3 (1.0)	4	0.8
Dysgeusia	1 (1.6)	1	2.5	1 (0.8)	1	0.8	0			2 (0.7)	2	0.4
Hypersomnia	0			0			2 (0.9)	3	1.0	2 (0.7)	3	0.6
Intercostal neuralgia	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Lethargy	1 (1.6)	1	2.5	0			1 (0.4)	1	0.3	2 (0.7)	2	0.4
Syncope	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Tremor	1 (1.6)	1	2.5	1 (0.8)	2	1.5	0			2 (0.7)	3	0.6
Ataxia	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Burning sensation	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Carpal tunnel syndrome	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Depressed level of consciousness	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hydrocephalus	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Memory impairment	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Meralgia paraesthetica	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Neuralgia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Parosmia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Partial seizures	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Sciatica	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Seizure	0			1 (0.8)	3	2.3	0			1 (0.3)	3	0.6
Vestibular migraine	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
General disorders and administration site conditions	9 (14.8)	13	32.6	30 (25.2)	52	39.8	53 (23.5)	98	32.6	82 (27.3)	163	34.6
Fatigue	2 (3.3)	2	5.0	7 (5.9)	7	5.4	13 (5.8)	16	5.3	22 (7.3)	25	5.3
Oedema peripheral	0			6 (5.0)	9	6.9	12 (5.3)	24	8.0	18 (6.0)	33	7.0
Asthenia	1 (1.6)	1	2.5	3 (2.5)	4	3.1	5 (2.2)	6	2.0	9 (3.0)	11	2.3
Injection site bruising	2 (3.3)	3	7.5	6 (5.0)	6	4.6	1 (0.4)	1	0.3	9 (3.0)	10	2.1
Pyrexia	0			1 (0.8)	2	1.5	8 (3.5)	10	3.3	9 (3.0)	12	2.5
Peripheral swelling	1 (1.6)	1	2.5	3 (2.5)	3	2.3	4 (1.8)	4	1.3	8 (2.7)	8	1.7
Pain	0			3 (2.5)	3	2.3	3 (1.3)	4	1.3	6 (2.0)	7	1.5
Chest pain	1 (1.6)	1	2.5	2 (1.7)	2	1.5	2 (0.9)	2	0.7	5 (1.7)	5	1.1
Face oedema	1 (1.6)	1	2.5	1 (0.8)	1	0.8	3 (1.3)	3	1.0	4 (1.3)	5	1.1
Malaise	1 (1.6)	1	2.5	1 (0.8)	1	0.8	2 (0.9)	2	0.7	4 (1.3)	4	0.8
Feeling hot	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Influenza like illness	0			2 (1.7)	2	1.5	2 (0.9)	4	1.3	3 (1.0)	6	1.3
Injection site pain	1 (1.6)	1	2.5	1 (0.8)	1	0.8	1 (0.4)	2	0.7	3 (1.0)	4	0.8
Non-cardiac chest pain	0			0			3 (1.3)	3	1.0	3 (1.0)	3	0.6
Fat tissue decreased	0			1 (0.8)	1	0.8	1 (0.4)	3	1.0	2 (0.7)	4	0.8
Injection site reaction	0			1 (0.8)	1	0.8	1 (0.4)	3	1.0	2 (0.7)	4	0.8
Nodule	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Axillary pain	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Chest discomfort	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Chills	0			1 (0.8)	2	1.5	0			1 (0.3)	2	0.4
Cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Death	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Gait disturbance	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Hunger	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Injection site atrophy	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Injection site haematoma	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Injection site hypertrophy	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

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MedDRA version 21.0.

Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Oedema	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Oedema mucosal	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pre-existing condition improved	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Retention cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Swelling	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Vaccination site pain	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Skin and subcutaneous tissue disorders	12 (19.7)	16	40.2	20 (16.8)	30	23.0	40 (17.7)	57	19.0	67 (22.3)	103	21.9
Rash	2 (3.3)	2	5.0	6 (5.0)	8	6.1	5 (2.2)	5	1.7	13 (4.3)	15	3.2
Dry skin	2 (3.3)	2	5.0	0			5 (2.2)	5	1.7	7 (2.3)	7	1.5
Urticaria	0			2 (1.7)	2	1.5	5 (2.2)	6	2.0	7 (2.3)	8	1.7
Pruritus	0			4 (3.4)	4	3.1	2 (0.9)	3	1.0	6 (2.0)	7	1.5
Acne	0			0			3 (1.3)	4	1.3	3 (1.0)	4	0.8
Dermatitis	2 (3.3)	2	5.0	0			2 (0.9)	2	0.7	3 (1.0)	4	0.8
Dermatitis contact	1 (1.6)	1	2.5	1 (0.8)	1	0.8	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Eczema	2 (3.3)	2	5.0	1 (0.8)	1	0.8	1 (0.4)	2	0.7	3 (1.0)	5	1.1
Rash generalised	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Acanthosis	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Dermatitis atopic	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Ecchymosis	1 (1.6)	1	2.5	1 (0.8)	1	0.8	0			2 (0.7)	2	0.4
Haemorrhage subcutaneous	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Hyperkeratosis	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Lipodystrophy acquired	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Lipohypertrophy	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Miliaria	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Skin discolouration	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Alopecia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blister	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Dermatitis allergic	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Drug eruption	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eczema asteatotic	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Erythema	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Exfoliative rash	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Ingrowing nail	1 (1.6)	1	2.5	0			1 (0.4)	1	0.3	1 (0.3)	2	0.4
Onychoclasis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Papule	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Prurigo	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Pruritus generalised	1 (1.6)	2	5.0	0			0			1 (0.3)	2	0.4
Pustular psoriasis	0			0			1 (0.4)	2	0.7	1 (0.3)	2	0.4
Rash erythematous	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Rash macular	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Rash maculo-papular	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Rash papular	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Skin burning sensation	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Skin erosion	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Skin lesion	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Skin mass	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Skin ulcer	0			1 (0.8)	2	1.5	0			1 (0.3)	2	0.4
Skin warm	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Swelling face	0			0			1 (0.4)	2	0.7	1 (0.3)	2	0.4
Investigations	7 (11.5)	10	25.1	23 (19.3)	40	30.6	34 (15.0)	78	26.0	58 (19.3)	128	27.2
Blood creatine phosphokinase increased	0			0			9 (4.0)	11	3.7	9 (3.0)	11	2.3
Weight increased	0			1 (0.8)	1	0.8	6 (2.7)	7	2.3	7 (2.3)	8	1.7
Blood testosterone decreased	0			3 (2.5)	3	2.3	3 (1.3)	3	1.0	6 (2.0)	6	1.3
Thyroxine free decreased	1 (1.6)	1	2.5	1 (0.8)	1	0.8	3 (1.3)	4	1.3	5 (1.7)	6	1.3
Alanine aminotransferase increased	1 (1.6)	1	2.5	1 (0.8)	1	0.8	3 (1.3)	3	1.0	4 (1.3)	5	1.1
Blood uric acid increased	0			2 (1.7)	2	1.5	2 (0.9)	2	0.7	4 (1.3)	4	0.8
Cortisol decreased	0			0			4 (1.8)	4	1.3	4 (1.3)	4	0.8
Creatinine renal clearance decreased	0			1 (0.8)	1	0.8	3 (1.3)	3	1.0	4 (1.3)	4	0.8
Glycosylated haemoglobin increased	0			1 (0.8)	2	1.5	3 (1.3)	4	1.3	4 (1.3)	6	1.3
Aspartate aminotransferase increased	1 (1.6)	1	2.5	0			3 (1.3)	4	1.3	3 (1.0)	5	1.1

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Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hepatic enzyme increased	2 (3.3)	2	5.0	0			1 (0.4)	1	0.3	3 (1.0)	3	0.6
Intraocular pressure increased	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Blood alkaline phosphatase increased	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Blood glucose increased	0			1 (0.8)	3	2.3	1 (0.4)	1	0.3	2 (0.7)	4	0.8
Blood insulin increased	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Blood potassium decreased	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Blood thyroid stimulating hormone decreased	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Haematocrit increased	1 (1.6)	1	2.5	0			1 (0.4)	1	0.3	2 (0.7)	2	0.4
Liver function test abnormal	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Platelet count increased	0			1 (0.8)	2	1.5	1 (0.4)	1	0.3	2 (0.7)	3	0.6
Weight decreased	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
White blood cell count increased	1 (1.6)	1	2.5	0			1 (0.4)	1	0.3	2 (0.7)	2	0.4
Blood alkaline phosphatase decreased	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Blood bilirubin increased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blood cholesterol increased	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Blood creatinine decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blood creatinine increased	0			0			1 (0.4)	2	0.7	1 (0.3)	2	0.4
Blood insulin decreased	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Blood phosphorus increased	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Blood potassium increased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blood pressure decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blood pressure increased	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Blood testosterone increased	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Body temperature increased	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Cardiac murmur	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Cholangiogram	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Cortisol increased	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Creatinine renal clearance increased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Electrocardiogram PR prolongation	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Electrocardiogram QT prolonged	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Electrocardiogram T wave abnormal	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Electrocardiogram T wave inversion	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Electrocardiogram abnormal	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Gamma-glutamyltransferase increased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Glomerular filtration rate increased	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Heart rate increased	0			1 (0.8)	3	2.3	0			1 (0.3)	3	0.6
Lymph node palpable	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Normetanephrine urine increased	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Platelet count decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pulmonary function test decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Thyroid hormones decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Thyroxine decreased	0			0			1 (0.4)	3	1.0	1 (0.3)	3	0.6
Thyroxine increased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Tri-iodothyronine decreased	0			1 (0.8)	2	1.5	0			1 (0.3)	2	0.4
Urine analysis abnormal	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Vitamin D decreased	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Injury, poisoning and procedural complications	3 (4.9)	3	7.5	18 (15.1)	27	20.7	31 (13.7)	43	14.3	48 (16.0)	73	15.5
Contusion	1 (1.6)	1	2.5	4 (3.4)	6	4.6	3 (1.3)	4	1.3	8 (2.7)	11	2.3
Fall	0			3 (2.5)	4	3.1	3 (1.3)	4	1.3	6 (2.0)	8	1.7
Tooth fracture	1 (1.6)	1	2.5	2 (1.7)	2	1.5	3 (1.3)	3	1.0	6 (2.0)	6	1.3
Arthropod bite	0			2 (1.7)	2	1.5	2 (0.9)	2	0.7	3 (1.0)	4	0.8
Foot fracture	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Ligament sprain	0			1 (0.8)	1	0.8	2 (0.9)	2	0.7	3 (1.0)	3	0.6
Arthropod sting	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Chest injury	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Head injury	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Laceration	0			1 (0.8)	2	1.5	1 (0.4)	1	0.3	2 (0.7)	3	0.6
Limb injury	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Muscle strain	0			1 (0.8)	1	0.8	1 (0.4)	2	0.7	2 (0.7)	3	0.6

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Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Post procedural complication	0			1 (0.8)	1	0.8	1 (0.4)	2	0.7	2 (0.7)	3	0.6
Procedural pain	1 (1.6)	1	2.5	0			1 (0.4)	2	0.7	2 (0.7)	3	0.6
Spinal compression fracture	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Drug dispensing error	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Incorrect dose administered	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ligament rupture	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Multiple fractures	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Muscle injury	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Post-traumatic pain	0			0			1 (0.4)	3	1.0	1 (0.3)	3	0.6
Prescription drug used without a prescription	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Procedural dizziness	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Radius fracture	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Scratch	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Thermal burn	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Tibia fracture	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Toxicity to various agents	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Wrist fracture	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Respiratory, thoracic and mediastinal disorders	4 (6.6)	5	12.6	14 (11.8)	22	16.8	27 (11.9)	44	14.6	44 (14.7)	71	15.1
Cough	3 (4.9)	3	7.5	6 (5.0)	7	5.4	7 (3.1)	9	3.0	16 (5.3)	19	4.0
Oropharyngeal pain	2 (3.3)	2	5.0	1 (0.8)	1	0.8	10 (4.4)	10	3.3	12 (4.0)	13	2.8
Dyspnoea	0			3 (2.5)	3	2.3	1 (0.4)	1	0.3	3 (1.0)	4	0.8
Epistaxis	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Rhinitis allergic	0			2 (1.7)	3	2.3	1 (0.4)	1	0.3	3 (1.0)	4	0.8
Sleep apnoea syndrome	0			1 (0.8)	1	0.8	2 (0.9)	2	0.7	3 (1.0)	3	0.6
Asthma	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Nasal congestion	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Sinus congestion	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Upper respiratory tract congestion	0			1 (0.8)	1	0.8	1 (0.4)	2	0.7	2 (0.7)	3	0.6
Upper-airway cough syndrome	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Dyspnoea exertional	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Dyspnoea paroxysmal nocturnal	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Increased viscosity of upper respiratory secretion	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Paranasal sinus hypersecretion	0			0			1 (0.4)	2	0.7	1 (0.3)	2	0.4
Pharyngeal erythema	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pneumonia aspiration	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Respiratory disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Respiratory tract congestion	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Rhinorrhoea	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Sinus polyp	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Sneezing	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Snoring	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Upper respiratory tract inflammation	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Metabolism and nutrition disorders	5 (8.2)	6	15.1	9 (7.6)	10	7.7	22 (9.7)	29	9.6	36 (12.0)	45	9.6
Iron deficiency	0			0			4 (1.8)	4	1.3	4 (1.3)	4	0.8
Vitamin D deficiency	0			1 (0.8)	1	0.8	3 (1.3)	3	1.0	4 (1.3)	4	0.8
Gout	0			1 (0.8)	1	0.8	2 (0.9)	4	1.3	3 (1.0)	5	1.1
Hyperphosphataemia	0			0			3 (1.3)	3	1.0	3 (1.0)	3	0.6
Hypocalcaemia	1 (1.6)	1	2.5	0			2 (0.9)	2	0.7	3 (1.0)	3	0.6
Hypokalaemia	0			0			3 (1.3)	3	1.0	3 (1.0)	3	0.6
Diabetes mellitus	0			2 (1.7)	2	1.5	0			2 (0.7)	2	0.4
Dyslipidaemia	0			2 (1.7)	2	1.5	0			2 (0.7)	2	0.4
Fluid retention	0			0			2 (0.9)	3	1.0	2 (0.7)	3	0.6
Hypercholesterolaemia	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Hyperkalaemia	1 (1.6)	1	2.5	1 (0.8)	1	0.8	0			2 (0.7)	2	0.4
Hyperlipidaemia	1 (1.6)	1	2.5	0			1 (0.4)	1	0.3	2 (0.7)	2	0.4
Hypoglycaemia	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Decreased appetite	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Dehydration	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Hyperglycaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hypertriglyceridaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hyponatraemia	1 (1.6)	2	5.0	0			0			1 (0.3)	2	0.4
Obesity	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Vitamin B complex deficiency	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Vascular disorders	1 (1.6)	1	2.5	8 (6.7)	9	6.9	15 (6.6)	15	5.0	23 (7.7)	25	5.3
Hypertension	1 (1.6)	1	2.5	7 (5.9)	7	5.4	8 (3.5)	8	2.7	16 (5.3)	16	3.4
Hot flush	0			1 (0.8)	1	0.8	3 (1.3)	3	1.0	4 (1.3)	4	0.8
Hypotension	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Arteriosclerosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Orthostatic hypotension	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Vascular fragility	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eye disorders	2 (3.3)	2	5.0	9 (7.6)	12	9.2	11 (4.9)	13	4.3	21 (7.0)	27	5.7
Vision blurred	1 (1.6)	1	2.5	1 (0.8)	1	0.8	2 (0.9)	2	0.7	4 (1.3)	4	0.8
Visual impairment	0			4 (3.4)	4	3.1	0			4 (1.3)	4	0.8
Dry eye	0			0			3 (1.3)	3	1.0	3 (1.0)	3	0.6
Cataract	0			2 (1.7)	2	1.5	0			2 (0.7)	2	0.4
Conjunctival haemorrhage	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Age-related macular degeneration	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Conjunctivitis allergic	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Diplopia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eye irritation	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eye pruritus	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eyelid disorder	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Eyelid oedema	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Glaucoma	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Neovascular age-related macular degeneration	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Scleral disorder	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Visual acuity reduced	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Xerophthalmia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Psychiatric disorders	2 (3.3)	2	5.0	4 (3.4)	4	3.1	16 (7.1)	20	6.7	21 (7.0)	26	5.5

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Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Insomnia	0			1 (0.8)	1	0.8	5 (2.2)	5	1.7	6 (2.0)	6	1.3
Anxiety	1 (1.6)	1	2.5	0			3 (1.3)	6	2.0	4 (1.3)	7	1.5
Sleep disorder	1 (1.6)	1	2.5	0			3 (1.3)	3	1.0	4 (1.3)	4	0.8
Attention deficit/hyperactivity disorder	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Adjustment disorder with depressed mood	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Delirium	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Depression	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Emotional disorder	0			0			1 (0.4)	2	0.7	1 (0.3)	2	0.4
Mood swings	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Nervousness	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Endocrine disorders	2 (3.3)	2	5.0	6 (5.0)	7	5.4	11 (4.9)	12	4.0	18 (6.0)	21	4.5
Adrenocortical insufficiency acute	1 (1.6)	1	2.5	0			3 (1.3)	3	1.0	4 (1.3)	4	0.8
Hypothyroidism	1 (1.6)	1	2.5	2 (1.7)	2	1.5	1 (0.4)	1	0.3	4 (1.3)	4	0.8
Adrenal insufficiency	0			0			3 (1.3)	3	1.0	3 (1.0)	3	0.6
Secondary hypothyroidism	0			3 (2.5)	3	2.3	0			3 (1.0)	3	0.6
Diabetes insipidus	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Glucocorticoid deficiency	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Hyperthyroidism	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hypopituitarism	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Secondary adrenocortical insufficiency	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Thyroid disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Thyroid mass	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blood and lymphatic system disorders	0			5 (4.2)	7	5.4	12 (5.3)	15	5.0	17 (5.7)	22	4.7
Anaemia	0			2 (1.7)	2	1.5	7 (3.1)	7	2.3	9 (3.0)	9	1.9
Lymphadenopathy	0			0			3 (1.3)	6	2.0	3 (1.0)	6	1.3
Haemoconcentration	0			2 (1.7)	3	2.3	0			2 (0.7)	3	0.6
Iron deficiency anaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Polycythaemia	0			1 (0.8)	2	1.5	0			1 (0.3)	2	0.4

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Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Thrombocytopenia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ear and labyrinth disorders	0			7 (5.9)	9	6.9	11 (4.9)	12	4.0	16 (5.3)	21	4.5
Ear pain	0			5 (4.2)	6	4.6	3 (1.3)	3	1.0	7 (2.3)	9	1.9
Vertigo	0			1 (0.8)	1	0.8	4 (1.8)	4	1.3	5 (1.7)	5	1.1
Cerumen impaction	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ear discomfort	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Ear disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eustachian tube dysfunction	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
External ear pain	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Middle ear inflammation	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Tinnitus	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Renal and urinary disorders	1 (1.6)	1	2.5	9 (7.6)	11	8.4	6 (2.7)	7	2.3	16 (5.3)	19	4.0
Pollakiuria	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Haematuria	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Nocturia	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Renal cyst	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Bladder pain	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Calculus urinary	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Chronic kidney disease	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Dysuria	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Micturition disorder	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Nephrolithiasis	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Polyuria	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ureterolithiasis	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Urinary incontinence	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Urinary tract obstruction	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Cardiac disorders	1 (1.6)	1	2.5	4 (3.4)	4	3.1	10 (4.4)	17	5.7	15 (5.0)	22	4.7
Palpitations	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Tachycardia	0			0			3 (1.3)	3	1.0	3 (1.0)	3	0.6
Atrioventricular block first degree	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4

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Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Angina unstable	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Aortic valve incompetence	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Bradycardia	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Bundle branch block right	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Cardiac discomfort	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Cardiogenic shock	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Cardiomyopathy	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Cardiovascular disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Left ventricular dysfunction	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Mitral valve incompetence	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Myocardial ischaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Sinus arrhythmia	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Ventricular extrasystoles	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ventricular fibrillation	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Reproductive system and breast disorders	2 (3.3)	2	5.0	4 (3.4)	4	3.1	8 (3.5)	9	3.0	14 (4.7)	15	3.2
Dysmenorrhoea	2 (3.3)	2	5.0	1 (0.8)	1	0.8	1 (0.4)	1	0.3	4 (1.3)	4	0.8
Gynaecomastia	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Cervical dysplasia	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Menstruation delayed	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Menstruation irregular	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Nipple pain	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Prostatitis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Uterine polyp	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Vaginal discharge	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Vaginal haemorrhage	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Vulvovaginal pruritus	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Immune system disorders	2 (3.3)	2	5.0	3 (2.5)	3	2.3	6 (2.7)	7	2.3	11 (3.7)	12	2.5
Seasonal allergy	1 (1.6)	1	2.5	1 (0.8)	1	0.8	5 (2.2)	6	2.0	7 (2.3)	8	1.7
Allergy to plants	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Allergy to vaccine	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2

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Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Food allergy	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Multiple allergies	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			4 (3.4)	5	3.8	5 (2.2)	5	1.7	9 (3.0)	10	2.1
Lipoma	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Angiomyolipoma	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Basal cell carcinoma	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Bladder transitional cell carcinoma	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Melanocytic naevus	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Pituitary tumour	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pituitary tumour benign	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Plasma cell myeloma	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Soft tissue neoplasm	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Hepatobiliary disorders	0			2 (1.7)	3	2.3	5 (2.2)	5	1.7	7 (2.3)	8	1.7
Biliary colic	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Cholelithiasis	0			1 (0.8)	2	1.5	0			1 (0.3)	2	0.4
Hepatic cirrhosis	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Hepatic steatosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hepatomegaly	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Liver disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Surgical and medical procedures	1 (1.6)	1	2.5	2 (1.7)	2	1.5	2 (0.9)	4	1.3	5 (1.7)	7	1.5
Tooth extraction	1 (1.6)	1	2.5	1 (0.8)	1	0.8	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Arterial stent insertion	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Cholecystectomy	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Skin operation	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Umbilical hernia repair	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Congenital, familial and genetic disorders	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Myotonia congenita	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

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Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

Adverse events by system organ class and preferred term - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Rathke's cleft cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Product issues	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Device malfunction	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

142 Serious adverse events by system organ class, preferred term, and treatment group - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All serious adverse events	5 (8.2)	7	17.6	14 (11.8)	19	14.5	21 (9.3)	42	14.0	37 (12.3)	68	14.4
Infections and infestations	1 (1.6)	1	2.5	5 (4.2)	7	5.4	7 (3.1)	10	3.3	12 (4.0)	18	3.8
Appendicitis	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Gastroenteritis	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Gastroenteritis viral	1 (1.6)	1	2.5	0			1 (0.4)	1	0.3	2 (0.7)	2	0.4
Urinary tract infection	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Clostridium difficile infection	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Herpes simplex	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Influenza	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Pneumonia	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Pneumonia viral	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Sepsis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Urosepsis	0			1 (0.8)	2	1.5	0			1 (0.3)	2	0.4
Viral infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Viral upper respiratory tract infection	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Gastrointestinal disorders	2 (3.3)	3	7.5	1 (0.8)	2	1.5	4 (1.8)	5	1.7	7 (2.3)	10	2.1
Vomiting	1 (1.6)	1	2.5	0			2 (0.9)	2	0.7	3 (1.0)	3	0.6
Pancreatitis acute	1 (1.6)	1	2.5	1 (0.8)	1	0.8	0			2 (0.7)	2	0.4
Abdominal pain	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Dental cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Diarrhoea	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Inguinal hernia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Stomatitis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Endocrine disorders	1 (1.6)	1	2.5	1 (0.8)	1	0.8	4 (1.8)	4	1.3	6 (2.0)	6	1.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

Serious adverse events by system organ class, preferred term, and treatment group - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Adrenocortical insufficiency acute	1 (1.6)	1	2.5	0			2 (0.9)	2	0.7	3 (1.0)	3	0.6
Diabetes insipidus	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hypopituitarism	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Secondary adrenocortical insufficiency	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
General disorders and administration site conditions	0			0			5 (2.2)	5	1.7	5 (1.7)	5	1.1
Fatigue	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Death	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Non-cardiac chest pain	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pyrexia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Injury, poisoning and procedural complications	0			2 (1.7)	3	2.3	3 (1.3)	3	1.0	5 (1.7)	6	1.3
Drug dispensing error	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Fall	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Spinal compression fracture	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Tibia fracture	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Tooth fracture	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Toxicity to various agents	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Investigations	1 (1.6)	1	2.5	1 (0.8)	1	0.8	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Blood testosterone increased	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Cholangiogram	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Electrocardiogram T wave abnormal	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Respiratory, thoracic and mediastinal disorders	0			0			3 (1.3)	3	1.0	3 (1.0)	3	0.6
Dyspnoea exertional	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pneumonia aspiration	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Sleep apnoea syndrome	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

Serious adverse events by system organ class, preferred term, and treatment group - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Cardiac disorders	0			0			2 (0.9)	3	1.0	2 (0.7)	3	0.6
Cardiogenic shock	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ventricular extrasystoles	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ventricular fibrillation	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Bladder transitional cell carcinoma	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Plasma cell myeloma	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Renal and urinary disorders	0			2 (1.7)	2	1.5	0			2 (0.7)	2	0.4
Chronic kidney disease	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Nephrolithiasis	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Blood and lymphatic system disorders	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Haemoconcentration	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Metabolism and nutrition disorders	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Hyponatraemia	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Nervous system disorders	0			0			1 (0.4)	2	0.7	1 (0.3)	2	0.4
Depressed level of consciousness	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Headache	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Psychiatric disorders	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Delirium	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Skin and subcutaneous tissue disorders	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Dermatitis atopic	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Surgical and medical procedures	0			0			1 (0.4)	3	1.0	1 (0.3)	3	0.6
Arterial stent insertion	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

Serious adverse events by system organ class, preferred term, and treatment group - 4054 entire trial - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Cholecystectomy	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Umbilical hernia repair	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Vascular disorders	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hypertension	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

143 Most frequent adverse events (>=5%) by system organ class and preferred term - 4054 entire trial - safety analysis

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
Infections and infestations												
Nasopharyngitis	9 (14.8)	12	30.1	25 (21.0)	33	25.3	50 (22.1)	70	23.3	74 (24.7)	115	24.4
Upper respiratory tract infection	7 (11.5)	7	17.6	11 (9.2)	16	12.3	22 (9.7)	25	8.3	35 (11.7)	48	10.2
Gastroenteritis	2 (3.3)	2	5.0	3 (2.5)	4	3.1	12 (5.3)	16	5.3	17 (5.7)	22	4.7
Influenza	2 (3.3)	3	7.5	2 (1.7)	3	2.3	13 (5.8)	16	5.3	16 (5.3)	22	4.7
Urinary tract infection	1 (1.6)	1	2.5	3 (2.5)	4	3.1	12 (5.3)	17	5.7	15 (5.0)	22	4.7
Nervous system disorders												
Headache	10 (16.4)	15	37.7	15 (12.6)	73	55.9	32 (14.2)	94	31.3	51 (17.0)	182	38.6
Dizziness	1 (1.6)	1	2.5	6 (5.0)	9	6.9	13 (5.8)	17	5.7	19 (6.3)	27	5.7
Musculoskeletal and connective tissue disorders												
Arthralgia	1 (1.6)	1	2.5	14 (11.8)	15	11.5	15 (6.6)	16	5.3	29 (9.7)	32	6.8
Back pain	2 (3.3)	2	5.0	4 (3.4)	4	3.1	16 (7.1)	18	6.0	22 (7.3)	24	5.1
Myalgia	3 (4.9)	3	7.5	6 (5.0)	6	4.6	6 (2.7)	8	2.7	15 (5.0)	17	3.6
Pain in extremity	1 (1.6)	1	2.5	6 (5.0)	8	6.1	6 (2.7)	6	2.0	13 (4.3)	15	3.2
Gastrointestinal disorders												
Diarrhoea	5 (8.2)	8	20.1	8 (6.7)	8	6.1	17 (7.5)	26	8.7	29 (9.7)	42	8.9
Vomiting	1 (1.6)	2	5.0	5 (4.2)	7	5.4	13 (5.8)	16	5.3	19 (6.3)	25	5.3
Nausea	1 (1.6)	1	2.5	6 (5.0)	8	6.1	7 (3.1)	16	5.3	13 (4.3)	25	5.3
General disorders and administration site conditions												
Fatigue	2 (3.3)	2	5.0	7 (5.9)	7	5.4	13 (5.8)	16	5.3	22 (7.3)	25	5.3
Oedema peripheral	0			6 (5.0)	9	6.9	12 (5.3)	24	8.0	18 (6.0)	33	7.0
Injection site bruising	2 (3.3)	3	7.5	6 (5.0)	6	4.6	1 (0.4)	1	0.3	9 (3.0)	10	2.1

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

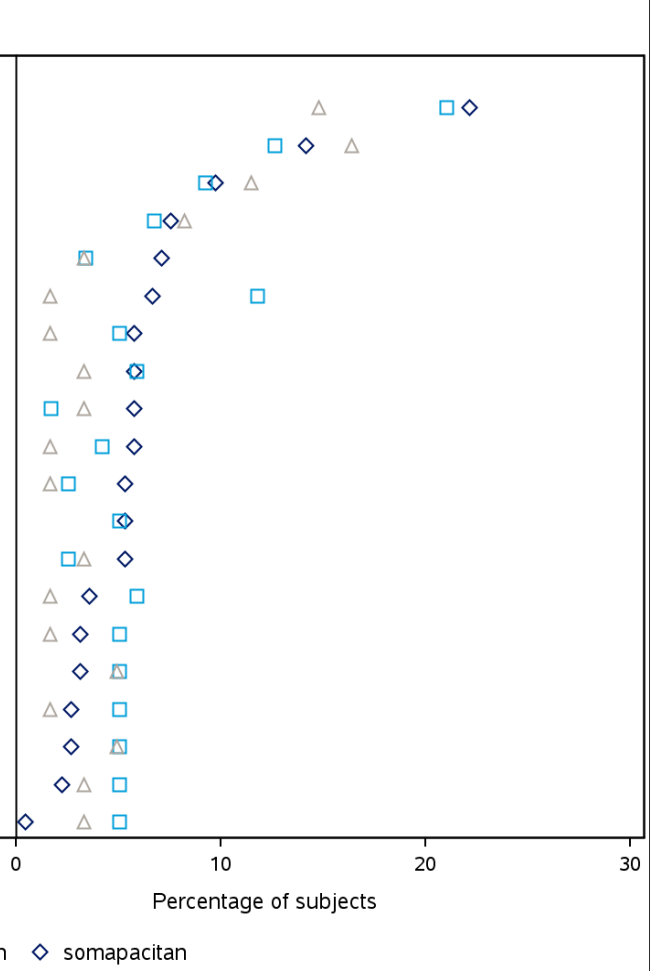
Most frequent adverse events (>=5%) by system organ class and preferred term - 4054 entire trial - safety analysis

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Respiratory, thoracic and mediastinal disorders												
Cough	3 (4.9)	3	7.5	6 (5.0)	7	5.4	7 (3.1)	9	3.0	16 (5.3)	19	4.0
Vascular disorders												
Hypertension	1 (1.6)	1	2.5	7 (5.9)	7	5.4	8 (3.5)	8	2.7	16 (5.3)	16	3.4
Skin and subcutaneous tissue disorders												
Rash	2 (3.3)	2	5.0	6 (5.0)	8	6.1	5 (2.2)	5	1.7	13 (4.3)	15	3.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

144 Most frequent adverse events by preferred term (>=5%) - 4054 entire trial - safety analysis set

-	placebo %	placebo R	Norditropin %	Norditropin R	somapacitan %	somapacitan R
Nasopharyngitis	14.8	30.1	21.0	25.3	22.1	23.3
Headache	16.4	37.7	12.6	55.9	14.2	31.3
Upper respiratory tract infection	11.5	17.6	9.2	12.3	9.7	8.3
Diarrhoea	8.2	20.1	6.7	6.1	7.5	8.7
Back pain	3.3	5.0	3.4	3.1	7.1	6.0
Arthralgia	1.6	2.5	11.8	11.5	6.6	5.3
Dizziness	1.6	2.5	5.0	6.9	5.8	5.7
Fatigue	3.3	5.0	5.9	5.4	5.8	5.3
Influenza	3.3	7.5	1.7	2.3	5.8	5.3
Vomiting	1.6	5.0	4.2	5.4	5.8	5.3
Urinary tract infection	1.6	2.5	2.5	3.1	5.3	5.7
Oedema peripheral			5.0	6.9	5.3	8.0
Gastroenteritis	3.3	5.0	2.5	3.1	5.3	5.3
Hypertension	1.6	2.5	5.9	5.4	3.5	2.7
Nausea	1.6	2.5	5.0	6.1	3.1	5.3
Cough	4.9	7.5	5.0	5.4	3.1	3.0
Pain in extremity	1.6	2.5	5.0	6.1	2.7	2.0
Myalgia	4.9	7.5	5.0	4.6	2.7	2.7
Rash	3.3	5.0	5.0	6.1	2.2	1.7
Injection site bruising	3.3	7.5	5.0	4.6	0.4	0.3



%: Percentage of exposed subjects having the event, R: Event rate per 100 patient years
MedDRA version 21.0.

145 Adverse events by system organ class and preferred term - Hypothyroidism - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All hypothyroidism events	1 (1.6)	1	2.5	5 (4.2)	5	3.8	1 (0.4)	1	0.3	7 (2.3)	7	1.5
Endocrine disorders	1 (1.6)	1	2.5	5 (4.2)	5	3.8	1 (0.4)	1	0.3	7 (2.3)	7	1.5
Hypothyroidism	1 (1.6)	1	2.5	2 (1.7)	2	1.5	1 (0.4)	1	0.3	4 (1.3)	4	0.8
Secondary hypothyroidism	0			3 (2.5)	3	2.3	0			3 (1.0)	3	0.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

146 Adverse events by system organ class and preferred term - Hypothyroidism - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All hypothyroidism events	3 (9.7)	3	19.7	1 (1.6)	1	3.2	4 (4.3)	4	8.7
Endocrine disorders	3 (9.7)	3	19.7	1 (1.6)	1	3.2	4 (4.3)	4	8.7
Hypothyroidism	2 (6.5)	2	13.1	1 (1.6)	1	3.2	3 (3.3)	3	6.5
Secondary hypothyroidism	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

147 Adverse events by system organ class and preferred term - Hypothyroidism - 4244 - safety analysis set

There are no data for this output

148 Adverse events by system organ class and preferred term - Pancreaitis - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All pancreaitis events	1 (1.6)	1	2.5	1 (0.8)	1	0.8	0			2 (0.7)	2	0.4
Gastrointestinal disorders	1 (1.6)	1	2.5	1 (0.8)	1	0.8	0			2 (0.7)	2	0.4
Pancreatitis acute	1 (1.6)	1	2.5	1 (0.8)	1	0.8	0			2 (0.7)	2	0.4

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

149 Adverse events by system organ class and preferred term - Pancreaitis - 4043 - safety analysis set

There are no data for this output

150 Adverse events by system organ class and preferred term - Pancreaitis - 4244 - safety analysis set

There are no data for this output

151 Adverse events by system organ class and preferred term - Peripheral oedema - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All peripheral oedema events	1 (1.6)	1	2.5	8 (6.7)	12	9.2	15 (6.6)	28	9.3	24 (8.0)	41	8.7
General disorders and administration site conditions	1 (1.6)	1	2.5	8 (6.7)	12	9.2	15 (6.6)	28	9.3	24 (8.0)	41	8.7
Oedema peripheral	0			6 (5.0)	9	6.9	12 (5.3)	24	8.0	18 (6.0)	33	7.0
Peripheral swelling	1 (1.6)	1	2.5	3 (2.5)	3	2.3	4 (1.8)	4	1.3	8 (2.7)	8	1.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

152 Adverse events by system organ class and preferred term - Peripheral oedema - 4043 - safety analysis set

There are no data for this output

153 Adverse events by system organ class and preferred term - Peripheral oedema - 4244 - safety analysis set

There are no data for this output

154 Adverse events by system organ class and preferred term - Fatigue/Asthenia - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All fatigue/asthenia events	4 (6.6)	4	10.0	11 (9.2)	12	9.2	20 (8.8)	24	8.0	35 (11.7)	40	8.5
General disorders and administration site conditions	4 (6.6)	4	10.0	11 (9.2)	12	9.2	20 (8.8)	24	8.0	35 (11.7)	40	8.5
Fatigue	2 (3.3)	2	5.0	7 (5.9)	7	5.4	13 (5.8)	16	5.3	22 (7.3)	25	5.3
Asthenia	1 (1.6)	1	2.5	3 (2.5)	4	3.1	5 (2.2)	6	2.0	9 (3.0)	11	2.3
Malaise	1 (1.6)	1	2.5	1 (0.8)	1	0.8	2 (0.9)	2	0.7	4 (1.3)	4	0.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

155 Adverse events by system organ class and preferred term - Fatigue/Asthenia - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All fatigue/asthenia events	7 (22.6)	7	45.9	12 (19.7)	14	45.3	19 (20.7)	21	45.5
General disorders and administration site conditions	7 (22.6)	7	45.9	12 (19.7)	14	45.3	19 (20.7)	21	45.5
Fatigue	5 (16.1)	5	32.8	6 (9.8)	7	22.6	11 (12.0)	12	26.0
Asthenia	1 (3.2)	1	6.6	4 (6.6)	5	16.2	5 (5.4)	6	13.0
Malaise	1 (3.2)	1	6.6	2 (3.3)	2	6.5	3 (3.3)	3	6.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

156 Adverse events by system organ class and preferred term - Fatigue/Asthenia - 4244 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	16			46			62		
Total patient years	15.2			46.4			61.5		
All fatigue/asthenia events	1 (6.3)	1	6.6	1 (2.2)	1	2.2	2 (3.2)	2	3.2
General disorders and administration site conditions	1 (6.3)	1	6.6	1 (2.2)	1	2.2	2 (3.2)	2	3.2
Fatigue	1 (6.3)	1	6.6	0			1 (1.6)	1	1.6
Malaise	0			1 (2.2)	1	2.2	1 (1.6)	1	1.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

157 Adverse events by system organ class and preferred term - Allergic reactions (non-anaphylactic reactions) - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All allergic reaction (non-anaphylactic reaction) events	9 (14.8)	10	25.1	18 (15.1)	23	17.6	24 (10.6)	30	10.0	46 (15.3)	63	13.4
Skin and subcutaneous tissue disorders	7 (11.5)	7	17.6	14 (11.8)	18	13.8	18 (8.0)	23	7.7	36 (12.0)	48	10.2
Rash	2 (3.3)	2	5.0	6 (5.0)	8	6.1	5 (2.2)	5	1.7	13 (4.3)	15	3.2
Urticaria	0			2 (1.7)	2	1.5	5 (2.2)	6	2.0	7 (2.3)	8	1.7
Dermatitis	2 (3.3)	2	5.0	0			2 (0.9)	2	0.7	3 (1.0)	4	0.8
Dermatitis contact	1 (1.6)	1	2.5	1 (0.8)	1	0.8	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Eczema	2 (3.3)	2	5.0	1 (0.8)	1	0.8	1 (0.4)	2	0.7	3 (1.0)	5	1.1
Rash generalised	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Dermatitis atopic	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Dermatitis allergic	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Drug eruption	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Exfoliative rash	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Rash erythematous	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Rash macular	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Rash maculo-papular	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Swelling face	0			0			1 (0.4)	2	0.7	1 (0.3)	2	0.4
General disorders and administration site conditions	1 (1.6)	1	2.5	1 (0.8)	1	0.8	3 (1.3)	3	1.0	4 (1.3)	5	1.1
Face oedema	1 (1.6)	1	2.5	1 (0.8)	1	0.8	3 (1.3)	3	1.0	4 (1.3)	5	1.1
Respiratory, thoracic and mediastinal disorders	0			2 (1.7)	3	2.3	1 (0.4)	1	0.3	3 (1.0)	4	0.8
Rhinitis allergic	0			2 (1.7)	3	2.3	1 (0.4)	1	0.3	3 (1.0)	4	0.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

Adverse events by system organ class and preferred term - Allergic reactions (non-anaphylactic reactions) - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Eye disorders	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Conjunctivitis allergic	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eyelid oedema	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Gastrointestinal disorders	1 (1.6)	1	2.5	0			1 (0.4)	1	0.3	2 (0.7)	2	0.4
Lip swelling	1 (1.6)	1	2.5	0			1 (0.4)	1	0.3	2 (0.7)	2	0.4
Immune system disorders	1 (1.6)	1	2.5	0			1 (0.4)	1	0.3	2 (0.7)	2	0.4
Allergy to vaccine	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Multiple allergies	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

158 Adverse events by system organ class and preferred term - Allergic reactions (non-anaphylactic reactions) - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All allergic reaction (non-anaphylactic reaction) events	2 (6.5)	2	13.1	1 (1.6)	1	3.2	3 (3.3)	3	6.5
Skin and subcutaneous tissue disorders	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Rash	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Eye disorders	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Eye swelling	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

159 Adverse events by system organ class and preferred term - Allergic reactions (non-anaphylactic reactions) - 4244 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	16			46			62		
Total patient years	15.2			46.4			61.5		
All allergic reaction (non-anaphylactic reaction) events	5 (31.3)	5	33.0	2 (4.3)	2	4.3	7 (11.3)	7	11.4
Skin and subcutaneous tissue disorders	4 (25.0)	4	26.4	1 (2.2)	1	2.2	5 (8.1)	5	8.1
Rash	3 (18.8)	3	19.8	0			3 (4.8)	3	4.9
Dermatitis atopic	0			1 (2.2)	1	2.2	1 (1.6)	1	1.6
Eczema	1 (6.3)	1	6.6	0			1 (1.6)	1	1.6
Respiratory, thoracic and mediastinal disorders	1 (6.3)	1	6.6	1 (2.2)	1	2.2	2 (3.2)	2	3.2
Rhinitis allergic	1 (6.3)	1	6.6	1 (2.2)	1	2.2	2 (3.2)	2	3.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

160 Adverse events by system organ class and preferred term - Injection site reactions - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All injection site reaction events	3 (4.9)	5	12.6	8 (6.7)	8	6.1	4 (1.8)	8	2.7	14 (4.7)	21	4.5
General disorders and administration site conditions	3 (4.9)	5	12.6	8 (6.7)	8	6.1	4 (1.8)	8	2.7	14 (4.7)	21	4.5
Injection site bruising	2 (3.3)	3	7.5	6 (5.0)	6	4.6	1 (0.4)	1	0.3	9 (3.0)	10	2.1
Injection site pain	1 (1.6)	1	2.5	1 (0.8)	1	0.8	1 (0.4)	2	0.7	3 (1.0)	4	0.8
Injection site reaction	0			1 (0.8)	1	0.8	1 (0.4)	3	1.0	2 (0.7)	4	0.8
Injection site atrophy	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Injection site haematoma	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Injection site hypertrophy	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

161 Adverse events by system organ class and preferred term - Injection site reactions - 4043 - safety analysis set

There are no data for this output

162 Adverse events by system organ class and preferred term - Injection site reactions - 4244 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	16			46			62		
Total patient years	15.2			46.4			61.5		
All injection site reaction events	1 (6.3)	1	6.6	1 (2.2)	1	2.2	2 (3.2)	2	3.2
General disorders and administration site conditions	1 (6.3)	1	6.6	1 (2.2)	1	2.2	2 (3.2)	2	3.2
Injection site haemorrhage	1 (6.3)	1	6.6	0			1 (1.6)	1	1.6
Injection site pain	0			1 (2.2)	1	2.2	1 (1.6)	1	1.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

163 Adverse events by system organ class and preferred term - Lipohypertrophy - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All lipohypertrophy events	0			0			5 (2.2)	5	1.7	5 (1.7)	5	1.1
Skin and subcutaneous tissue disorders	0			0			4 (1.8)	4	1.3	4 (1.3)	4	0.8
Lipodystrophy acquired	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Lipohypertrophy	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
General disorders and administration site conditions	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Injection site hypertrophy	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

164 Adverse events by system organ class and preferred term - Lipohypertrophy - 4043 - safety analysis set

There are no data for this output

165 Adverse events by system organ class and preferred term - Lipohypertrophy - 4244 - safety analysis set

There are no data for this output

166 Adverse events by system organ class and preferred term - Lipoatrophy - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All lipoatrophy events	0			1 (0.8)	1	0.8	2 (0.9)	4	1.3	3 (1.0)	5	1.1
General disorders and administration site conditions	0			1 (0.8)	1	0.8	2 (0.9)	4	1.3	3 (1.0)	5	1.1
Fat tissue decreased	0			1 (0.8)	1	0.8	1 (0.4)	3	1.0	2 (0.7)	4	0.8
Injection site atrophy	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

167 Adverse events by system organ class and preferred term - Lipoatrophy - 4043 - safety analysis set

There are no data for this output

168 Adverse events by system organ class and preferred term - Lipoatrophy - 4244 - safety analysis set

There are no data for this output

169 Adverse events by system organ class and preferred term - Blood alkaline phosphatase increased (bone) - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All blood alkaline phosphatase increased (bone) events	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Investigations	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Blood alkaline phosphatase increased	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

170 Adverse events by system organ class and preferred term - Blood alkaline phosphatase increased (bone) - 4043 - safety analysis set

There are no data for this output

171 Adverse events by system organ class and preferred term - Blood alkaline phosphatase increased (bone) - 4244 - safety analysis set

There are no data for this output

172 Adverse events by system organ class and preferred term - Drug specific antibodies present - 4054 - safety analysis set

There are no data for this output

173 Adverse events by system organ class and preferred term - Drug specific antibodies present - 4043 - safety analysis set

There are no data for this output

174 Adverse events by system organ class and preferred term - Drug specific antibodies present - 4244 - safety analysis set

There are no data for this output

175 Adverse events by system organ class and preferred term - High level group terms Cardiac and vascular investigations incl. arrhythmia - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All cardiac and vascular investigations and cardiac arrhythmia	2 (3.3)	2	5.0	6 (5.0)	8	6.1	9 (4.0)	11	3.7	17 (5.7)	21	4.5
Cardiac disorders	1 (1.6)	1	2.5	2 (1.7)	2	1.5	6 (2.7)	7	2.3	9 (3.0)	10	2.1
Tachycardia	0			0			3 (1.3)	3	1.0	3 (1.0)	3	0.6
Atrioventricular block first degree	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Bradycardia	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Bundle branch block right	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Sinus arrhythmia	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Ventricular extrasystoles	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ventricular fibrillation	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Investigations	1 (1.6)	1	2.5	4 (3.4)	6	4.6	4 (1.8)	4	1.3	9 (3.0)	11	2.3
Blood pressure decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Blood pressure increased	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Cardiac murmur	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Electrocardiogram PR prolongation	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Electrocardiogram QT prolonged	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Electrocardiogram T wave abnormal	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Electrocardiogram T wave inversion	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Electrocardiogram abnormal	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Heart rate increased	0			1 (0.8)	3	2.3	0			1 (0.3)	3	0.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

176 Adverse events by system organ class and preferred term - High level group terms Cardiac and vascular investigations incl. arrhythmia - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All cardiac and vascular investigations and cardiac arrhythmia	1 (3.2)	2	13.1	0			1 (1.1)	2	4.3
Cardiac disorders	1 (3.2)	2	13.1	0			1 (1.1)	2	4.3
Atrial flutter	1 (3.2)	2	13.1	0			1 (1.1)	2	4.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

177 Adverse events by system organ class and preferred term - High level group terms Cardiac and vascular investigations incl. arrhythmia - 4244 - safety analysis set

There are no data for this output

178 Adverse events by system organ class and preferred term - Weight increased - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All weight increased events	0			1 (0.8)	1	0.8	6 (2.7)	7	2.3	7 (2.3)	8	1.7
Investigations	0			1 (0.8)	1	0.8	6 (2.7)	7	2.3	7 (2.3)	8	1.7
Weight increased	0			1 (0.8)	1	0.8	6 (2.7)	7	2.3	7 (2.3)	8	1.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

179 Adverse events by system organ class and preferred term - Weight increased - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All weight increased events	1 (3.2)	1	6.6	3 (4.9)	3	9.7	4 (4.3)	4	8.7
Investigations	1 (3.2)	1	6.6	3 (4.9)	3	9.7	4 (4.3)	4	8.7
Weight increased	1 (3.2)	1	6.6	3 (4.9)	3	9.7	4 (4.3)	4	8.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

180 Adverse events by system organ class and preferred term - Weight increased - 4244 - safety analysis set

There are no data for this output

181 Adverse events by system organ class and preferred term - Hyperglycaemia - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All hyperglycemia events	0			1 (0.8)	5	3.8	4 (1.8)	6	2.0	5 (1.7)	11	2.3
Investigations	0			1 (0.8)	5	3.8	3 (1.3)	5	1.7	4 (1.3)	10	2.1
Glycosylated haemoglobin increased	0			1 (0.8)	2	1.5	3 (1.3)	4	1.3	4 (1.3)	6	1.3
Blood glucose increased	0			1 (0.8)	3	2.3	1 (0.4)	1	0.3	2 (0.7)	4	0.8
Metabolism and nutrition disorders	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Hyperglycaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

182 Adverse events by system organ class and preferred term - Hyperglycaemia - 4043 - safety analysis set

There are no data for this output

183 Adverse events by system organ class and preferred term - Hyperglycaemia - 4244 - safety analysis set

There are no data for this output

184 Adverse events by system organ class and preferred term - Type 2 diabetes - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All type 2 diabetes events	0			4 (3.4)	8	6.1	4 (1.8)	7	2.3	8 (2.7)	15	3.2
Investigations	0			2 (1.7)	6	4.6	3 (1.3)	6	2.0	5 (1.7)	12	2.5
Glycosylated haemoglobin increased	0			1 (0.8)	2	1.5	3 (1.3)	4	1.3	4 (1.3)	6	1.3
Blood glucose increased	0			1 (0.8)	3	2.3	1 (0.4)	1	0.3	2 (0.7)	4	0.8
Blood insulin increased	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Metabolism and nutrition disorders	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Diabetes mellitus	0			2 (1.7)	2	1.5	0			2 (0.7)	2	0.4
Hyperglycaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

185 Adverse events by system organ class and preferred term - Type 2 diabetes - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All type 2 diabetes events	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Investigations	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Blood insulin increased	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

186 Adverse events by system organ class and preferred term - Type 2 diabetes - 4244 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	16			46			62		
Total patient years	15.2			46.4			61.5		
All type 2 diabetes events	1 (6.3)	1	6.6	0			1 (1.6)	1	1.6
Metabolism and nutrition disorders	1 (6.3)	1	6.6	0			1 (1.6)	1	1.6
Diabetes mellitus	1 (6.3)	1	6.6	0			1 (1.6)	1	1.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

187 Adverse events by system organ class and preferred term - Arthralgia - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All athralgia events	1 (1.6)	1	2.5	14 (11.8)	15	11.5	15 (6.6)	16	5.3	29 (9.7)	32	6.8
Musculoskeletal and connective tissue disorders	1 (1.6)	1	2.5	14 (11.8)	15	11.5	15 (6.6)	16	5.3	29 (9.7)	32	6.8
Arthralgia	1 (1.6)	1	2.5	14 (11.8)	15	11.5	15 (6.6)	16	5.3	29 (9.7)	32	6.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

188 Adverse events by system organ class and preferred term - Arthralgia - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All athralgia events	2 (6.5)	2	13.1	5 (8.2)	5	16.2	7 (7.6)	7	15.2
Musculoskeletal and connective tissue disorders	2 (6.5)	2	13.1	5 (8.2)	5	16.2	7 (7.6)	7	15.2
Arthralgia	2 (6.5)	2	13.1	5 (8.2)	5	16.2	7 (7.6)	7	15.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

189 Adverse events by system organ class and preferred term - Arthralgia - 4244 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	16			46			62		
Total patient years	15.2			46.4			61.5		
All athralgia events	1 (6.3)	1	6.6	3 (6.5)	4	8.6	4 (6.5)	5	8.1
Musculoskeletal and connective tissue disorders	1 (6.3)	1	6.6	3 (6.5)	4	8.6	4 (6.5)	5	8.1
Arthralgia	1 (6.3)	1	6.6	3 (6.5)	4	8.6	4 (6.5)	5	8.1

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

190 Adverse events by system organ class and preferred term - Myalgia - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All myalgia events	3 (4.9)	3	7.5	6 (5.0)	6	4.6	6 (2.7)	8	2.7	15 (5.0)	17	3.6
Musculoskeletal and connective tissue disorders	3 (4.9)	3	7.5	6 (5.0)	6	4.6	6 (2.7)	8	2.7	15 (5.0)	17	3.6
Myalgia	3 (4.9)	3	7.5	6 (5.0)	6	4.6	6 (2.7)	8	2.7	15 (5.0)	17	3.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

191 Adverse events by system organ class and preferred term - Myalgia - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All myalgia events	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Musculoskeletal and connective tissue disorders	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Myalgia	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

192 Adverse events by system organ class and preferred term - Myalgia - 4244 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	16			46			62		
Total patient years	15.2			46.4			61.5		
All myalgia events	1 (6.3)	1	6.6	0			1 (1.6)	1	1.6
Musculoskeletal and connective tissue disorders	1 (6.3)	1	6.6	0			1 (1.6)	1	1.6
Myalgia	1 (6.3)	1	6.6	0			1 (1.6)	1	1.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

193 Adverse events by system organ class and preferred term - Scoliosis - 4054 - safety analysis set

There are no data for this output

194 Adverse events by system organ class and preferred term - Scoliosis - 4043 - safety analysis set

There are no data for this output

195 Adverse events by system organ class and preferred term - Scoliosis - 4244 - safety analysis set

There are no data for this output

196 Adverse events by system organ class and preferred term - All benign, malignant and unspecified neoplasms - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All benign, malignant and unspecified neoplasm events	0			4 (3.4)	5	3.8	5 (2.2)	5	1.7	9 (3.0)	10	2.1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			4 (3.4)	5	3.8	5 (2.2)	5	1.7	9 (3.0)	10	2.1
Lipoma	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Angiomyolipoma	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Basal cell carcinoma	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Bladder transitional cell carcinoma	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Melanocytic naevus	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Pituitary tumour	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pituitary tumour benign	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Plasma cell myeloma	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Soft tissue neoplasm	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

197 Adverse events by system organ class and preferred term - All benign, malignant and unspecified neoplasms - 4043 - safety analysis set

There are no data for this output

198 Adverse events by system organ class and preferred term - All benign, malignant and unspecified neoplasms - 4244 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	16			46			62		
Total patient years	15.2			46.4			61.5		
All benign, malignant and unspecified neoplasm events	0			2 (4.3)	2	4.3	2 (3.2)	2	3.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			2 (4.3)	2	4.3	2 (3.2)	2	3.2
Intraductal papillary mucinous neoplasm	0			1 (2.2)	1	2.2	1 (1.6)	1	1.6
Pituitary tumour benign	0			1 (2.2)	1	2.2	1 (1.6)	1	1.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

199 Adverse events by system organ class and preferred term - Headache - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All headache events	10 (16.4)	15	37.7	15 (12.6)	73	55.9	32 (14.2)	94	31.3	51 (17.0)	182	38.6
Nervous system disorders	10 (16.4)	15	37.7	15 (12.6)	73	55.9	32 (14.2)	94	31.3	51 (17.0)	182	38.6
Headache	10 (16.4)	15	37.7	15 (12.6)	73	55.9	32 (14.2)	94	31.3	51 (17.0)	182	38.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

200 Adverse events by system organ class and preferred term - Headache - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All headache events	6 (19.4)	10	65.5	7 (11.5)	11	35.6	13 (14.1)	21	45.5
Nervous system disorders	6 (19.4)	10	65.5	7 (11.5)	11	35.6	13 (14.1)	21	45.5
Headache	6 (19.4)	10	65.5	7 (11.5)	11	35.6	13 (14.1)	21	45.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

201 Adverse events by system organ class and preferred term - Headache - 4244 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	16			46			62		
Total patient years	15.2			46.4			61.5		
All headache events	1 (6.3)	2	13.2	4 (8.7)	4	8.6	5 (8.1)	6	9.7
Nervous system disorders	1 (6.3)	2	13.2	4 (8.7)	4	8.6	5 (8.1)	6	9.7
Headache	1 (6.3)	2	13.2	4 (8.7)	4	8.6	5 (8.1)	6	9.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

202 Adverse events by system organ class and preferred term - Paraesthesia - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All paraesthesia events	2 (3.3)	2	5.0	1 (0.8)	1	0.8	4 (1.8)	5	1.7	7 (2.3)	8	1.7
Nervous system disorders	2 (3.3)	2	5.0	1 (0.8)	1	0.8	4 (1.8)	5	1.7	7 (2.3)	8	1.7
Paraesthesia	2 (3.3)	2	5.0	1 (0.8)	1	0.8	4 (1.8)	5	1.7	7 (2.3)	8	1.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

203 Adverse events by system organ class and preferred term - Paraesthesia - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All paraesthesia events	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Nervous system disorders	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Paraesthesia	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:14:32 - t_ae_soc_by_trial.sas/t_ae_soc_paraesth_sas_4043.txt

204 Adverse events by system organ class and preferred term - Paraesthesia - 4244 - safety analysis set

There are no data for this output

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:15:07 - t_ae_soc_by_trial.sas/t_ae_soc_paraesth_sas_4244.txt

205 Adverse events by system organ class and preferred term - Stroke - 4054 - safety analysis set

There are no data for this output

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:15:43 - t_ae_soc_by_trial.sas/t_ae_soc_stroke_sas_4054.txt

206 Adverse events by system organ class and preferred term - Stroke - 4043 - safety analysis set

There are no data for this output

207 Adverse events by system organ class and preferred term - Stroke - 4244 - safety analysis set

There are no data for this output

208 Adverse events by system organ class and preferred term - Carpal tunnel syndrome - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All carpal tunnel syndrome events	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Nervous system disorders	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Carpal tunnel syndrome	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

209 Adverse events by system organ class and preferred term - Carpal tunnel syndrome - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All carpal tunnel syndrome events	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Nervous system disorders	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Carpal tunnel syndrome	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:14:35 - t_ae_soc_by_trial.sas/t_ae_soc_cts_sas_4043.txt

210 Adverse events by system organ class and preferred term - Carpal tunnel syndrome - 4244 - safety analysis set

There are no data for this output

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:15:09 - t_ae_soc_by_trial.sas/t_ae_soc_cts_sas_4244.txt

211 Adverse events by system organ class and preferred term - Benign intracranial hypertension - 4054 - safety analysis set

There are no data for this output

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:15:45 - t_ae_soc_by_trial.sas/t_ae_soc_bintrhyper_sas_4054.txt

212 Adverse events by system organ class and preferred term - Benign intracranial hypertension - 4043 - safety analysis set

There are no data for this output

213 Adverse events by system organ class and preferred term - Benign intracranial hypertension - 4244 - safety analysis set

There are no data for this output

214 Adverse events by system organ class and preferred term - Rare events - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All rare events	5 (8.2)	5	12.6	12 (10.1)	16	12.3	21 (9.3)	24	8.0	36 (12.0)	45	9.6
Cardiac disorders	1 (1.6)	1	2.5	4 (3.4)	4	3.1	6 (2.7)	8	2.7	11 (3.7)	13	2.8
Palpitations	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Tachycardia	0			0			3 (1.3)	3	1.0	3 (1.0)	3	0.6
Atrioventricular block first degree	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Bradycardia	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Bundle branch block right	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Sinus arrhythmia	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Ventricular extrasystoles	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ventricular fibrillation	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Gastrointestinal disorders	2 (3.3)	2	5.0	2 (1.7)	2	1.5	1 (0.4)	1	0.3	5 (1.7)	5	1.1
Lip swelling	1 (1.6)	1	2.5	0			1 (0.4)	1	0.3	2 (0.7)	2	0.4
Pancreatitis acute	1 (1.6)	1	2.5	1 (0.8)	1	0.8	0			2 (0.7)	2	0.4
Ascites	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Investigations	0			2 (1.7)	4	3.1	3 (1.3)	3	1.0	5 (1.7)	7	1.5
Electrocardiogram PR prolongation	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Electrocardiogram QT prolonged	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Electrocardiogram abnormal	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Heart rate increased	0			1 (0.8)	3	2.3	0			1 (0.3)	3	0.6
Platelet count decreased	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
General disorders and administration site conditions	1 (1.6)	1	2.5	1 (0.8)	1	0.8	3 (1.3)	3	1.0	4 (1.3)	5	1.1
Face oedema	1 (1.6)	1	2.5	1 (0.8)	1	0.8	3 (1.3)	3	1.0	4 (1.3)	5	1.1

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

Adverse events by system organ class and preferred term - Rare events - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hepatobiliary disorders	0			1 (0.8)	1	0.8	2 (0.9)	2	0.7	3 (1.0)	3	0.6
Hepatic cirrhosis	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Hepatic steatosis	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Liver disorder	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Congenital, familial and genetic disorders	0			0			2 (0.9)	2	0.7	2 (0.7)	2	0.4
Myotonia congenita	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Rathke's cleft cyst	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Infections and infestations	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Clostridium difficile infection	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Nervous system disorders	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Syncope	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Skin and subcutaneous tissue disorders	0			1 (0.8)	1	0.8	1 (0.4)	2	0.7	2 (0.7)	3	0.6
Exfoliative rash	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Swelling face	0			0			1 (0.4)	2	0.7	1 (0.3)	2	0.4
Blood and lymphatic system disorders	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Thrombocytopenia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Eye disorders	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Eyelid oedema	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Renal and urinary disorders	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Urinary tract obstruction	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

215 Adverse events by system organ class and preferred term - Rare events - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All rare events	1 (3.2)	2	13.1	0			1 (1.1)	2	4.3
Cardiac disorders	1 (3.2)	2	13.1	0			1 (1.1)	2	4.3
Atrial flutter	1 (3.2)	2	13.1	0			1 (1.1)	2	4.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

216 Adverse events by system organ class and preferred term - Rare events - 4244 - safety analysis set

There are no data for this output

217 Adverse events by system organ class and preferred term - Fatal outcome - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All fatal events	1 (1.6)	1	2.5	2 (1.7)	2	1.5	2 (0.9)	4	1.3	5 (1.7)	7	1.5
Infections and infestations	0			2 (1.7)	2	1.5	0			2 (0.7)	2	0.4
Influenza	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Pneumonia	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Cardiac disorders	0			0			1 (0.4)	2	0.7	1 (0.3)	2	0.4
Cardiogenic shock	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Ventricular fibrillation	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Endocrine disorders	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Adrenocortical insufficiency acute	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
General disorders and administration site conditions	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Death	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Respiratory, thoracic and mediastinal disorders	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2
Pneumonia aspiration	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

218 Adverse events by system organ class and preferred term - Fatal outcome - 4043 - safety analysis set

There are no data for this output

219 Adverse events by system organ class and preferred term - Fatal outcome - 4244 - safety analysis set

There are no data for this output

220 Adverse events by system organ class and preferred term - Hypersensitivity (Anaphylactic reactions) - 4054 - safety analysis set

There are no data for this output

221 Adverse events by system organ class and preferred term - Hypersensitivity (Anaphylactic reactions) - 4043 - safety analysis set

There are no data for this output

222 Adverse events by system organ class and preferred term - Hypersensitivity (Anaphylactic reactions) - 4244 - safety analysis set

There are no data for this output

223 Adverse events by system organ class and preferred term - Adrenocortical insufficiency (secondary) - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All adrenocortical insufficiency (secondary) events	1 (1.6)	1	2.5	2 (1.7)	2	1.5	6 (2.7)	6	2.0	9 (3.0)	9	1.9
Endocrine disorders	1 (1.6)	1	2.5	2 (1.7)	2	1.5	6 (2.7)	6	2.0	9 (3.0)	9	1.9
Adrenocortical insufficiency acute	1 (1.6)	1	2.5	0			3 (1.3)	3	1.0	4 (1.3)	4	0.8
Adrenal insufficiency	0			0			3 (1.3)	3	1.0	3 (1.0)	3	0.6
Glucocorticoid deficiency	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2
Secondary adrenocortical insufficiency	0			1 (0.8)	1	0.8	0			1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

224 Adverse events by system organ class and preferred term - Adrenocortical insufficiency (secondary) - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All adrenocortical insufficiency (secondary) events	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Endocrine disorders	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Adrenal insufficiency	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Adrenocortical insufficiency acute	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

225 Adverse events by system organ class and preferred term - Adrenocortical insufficiency (secondary) - 4244 - safety analysis set

There are no data for this output

226 Adverse events by system organ class and preferred term - metabolism disorders - glycaemic control - 4054 - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			226			300		
Total patient years	39.8			130.6			300.5			471.0		
All metabolism disorders - glyceamic control - events	1 (1.6)	1	2.5	4 (3.4)	8	6.1	4 (1.8)	7	2.3	9 (3.0)	16	3.4
Investigations	1 (1.6)	1	2.5	2 (1.7)	6	4.6	3 (1.3)	6	2.0	6 (2.0)	13	2.8
Glycosylated haemoglobin increased	0			1 (0.8)	2	1.5	3 (1.3)	4	1.3	4 (1.3)	6	1.3
Blood glucose increased	0			1 (0.8)	3	2.3	1 (0.4)	1	0.3	2 (0.7)	4	0.8
Blood insulin increased	0			1 (0.8)	1	0.8	1 (0.4)	1	0.3	2 (0.7)	2	0.4
Blood insulin decreased	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.2
Metabolism and nutrition disorders	0			2 (1.7)	2	1.5	1 (0.4)	1	0.3	3 (1.0)	3	0.6
Diabetes mellitus	0			2 (1.7)	2	1.5	0			2 (0.7)	2	0.4
Hyperglycaemia	0			0			1 (0.4)	1	0.3	1 (0.3)	1	0.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
Total number of exposed subjects does not equal the sum of exposed subjects in individual treatment due to trial design in 4054.
MedDRA version 21.0.

227 Adverse events by system organ class and preferred term - metabolism disorders - glycaemic control - 4043 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All metabolism disorders - glyceamic control - events	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Investigations	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Blood insulin increased	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

228 Adverse events by system organ class and preferred term - metabolism disorders - glycaemic control - 4244 - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	16			46			62		
Total patient years	15.2			46.4			61.5		
All metabolism disorders - glyceamic control - events	1 (6.3)	1	6.6	0			1 (1.6)	1	1.6
Metabolism and nutrition disorders	1 (6.3)	1	6.6	0			1 (1.6)	1	1.6
Diabetes mellitus	1 (6.3)	1	6.6	0			1 (1.6)	1	1.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

ソマプシタン（遺伝子組換え）

2.7.4.7 付録

2. 第 3 相試験結果に基づく解析帳票
（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

Table of contents

Page

1 Summary of exposure - 4054 main - Entire trial population - safety analysis set 3
2 Summary of exposure - 4054 main - Japanese subgroup - safety analysis set 4
3 Summary of exposure - 4054 extension - Entire trial population - safety analysis set 5
4 Summary of exposure - 4054 extension - Japanese subgroup - safety analysis set 7
5 Summary of exposure - 4043 - entire trial population - safety analysis set 9
6 Summary of exposure - 4043 - Japanese subgroup - safety analysis set 10
7 Summary of exposure at randomisation and titration visits (mg) - 4054 main trial - Japanese subgroup - safety analysis set 11
8 Summary of exposure at randomisation and titration visits (mg) - 4054 extension trial - Japanese subgroup - safety analysis set 13
9 Summary of exposure at randomisation and titration visits (mg) - 4043 - Japanese subgroup - safety analysis set 15
10 Subject exposure by 3 month periods - summary - Japanese subgroup - full analysis set 16
11 Adverse Events - 4054 main trial - entire trial population - safety analysis set 17
12 Adverse Events - 4054 main trial - Japanese subgroup - safety analysis set 19
13 Adverse Events - 4043 - entire trial population - safety analysis set 21
14 Adverse Events - 4043 - Japanese subgroup - safety analysis set 23
15 Adverse Events by system organ class and preferred term – 4054 main trial – entire trial population– safety analysis set 25
16 Adverse Events by system organ class and preferred term – 4054 main trial – Japanese subgroup – safety analysis set 38
17 Adverse Events by system organ class and preferred term – 4043 – entire trial population– safety analysis set 42
18 Adverse Events by system organ class and preferred term – 4043 – Japanese subgroup – safety analysis set 48
19 Possibly or probably related adverse events by system organ class and preferred term - 4054 main trial - entire trial population - safety analysis set 50
20 Possibly or probably related adverse events by system organ class and preferred term - 4054 main trial - Japanese subgroup - safety analysis set 54
21 Possibly or probably related adverse events by system organ class and preferred term - 4043 - entire trial population - safety analysis set 56
22 Possibly or probably related adverse events by system organ class and preferred term - 4043 - Japanese subgroup - safety analysis set 58
23 Adverse events with fatal outcome - 4054 - Japanese subgroup - listing safety analysis set 59
24 Adverse events with fatal outcome - 4043 - Japanese subgroup - listing safety analysis set 59
25 Serious adverse events - 4054 - Japanese subgroup - listing safety analysis set 60
26 Serious adverse events - 4043 - Japanese subgroup - listing safety analysis set 61
27 Adverse events leading to withdrawal from trial product - 4054 - Japanese subgroup - listing randomised subjects 62

28 Adverse events leading to withdrawal from trial product - 4043 - Japanese subgroup - listing randomised subjects 62
29 Adverse Events - Male - 4043 - entire trial population - safety analysis set 63
30 Adverse Events - Male - 4043 - Japanese subgroup - safety analysis set....65
31 Adverse Events - Female - 4043 - entire trial population - safety analysis set 66
32 Adverse Events - Female - 4043 - Japanese subgroup - safety analysis set 68
33 Adverse Events by system organ class and preferred term - Male - 4043 - entire trial population - safety analysis set 69
34 Adverse Events by system organ class and preferred term - Male - 4043 - Japanese subgroup - safety analysis set....73
35 Adverse Events by system organ class and preferred term - Female - 4043 - entire trial population - safety analysis set 74
36 Adverse Events by system organ class and preferred term - Female - 4043 - Japanese subgroup - safety analysis set 78
37 Adverse Events - Childhood onset - 4054 main trial - entire trial population - safety analysis set 80
38 Adverse Events - Childhood onset - 4054 main trial - Japanese subgroup - safety analysis set....82
39 Adverse Events - Adulthood onset - 4054 main trial - entire trial population - safety analysis set 83
40 Adverse Events - Adulthood onset - 4054 main trial - Japanese subgroup - safety analysis set 85
41 Adverse Events by system organ class and preferred term - Childhood onset - 4054 main trial - entire trial population - safety analysis set....87
42 Adverse Events by system organ class and preferred term - Childhood onset - 4054 main trial - Japanese subgroup - safety analysis set....93
43 Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - entire trial population - safety analysis set 95
44 Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - Japanese subgroup - safety analysis set....106
45 Adverse Events - age <65 years - 4054 main trial - entire trial population - safety analysis set 110
46 Adverse Events - age <65 years - 4054 main trial - Japanese subgroup - safety analysis set....112
47 Adverse Events - age >=65 years - 4054 main trial - entire trial population - safety analysis set 114
48 Adverse Events - age >=65 years - 4054 main trial - Japanese subgroup - safety analysis set 116
49 Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - entire trial population - safety analysis set....118
50 Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - Japanese subgroup - safety analysis set....129
51 Adverse Events by system organ class and preferred term - age >=65 years - 4054 main trial - entire trial population - safety analysis set....132
52 Adverse Events by system organ class and preferred term - age >=65 years - 4054 main trial - Japanese subgroup - safety analysis set....137

1 Summary of exposure - 4054 main - Entire trial population - safety analysis set

	placebo	Norditropin	somapacitan
	once weekly	once daily	once weekly
Number of exposed subjects	61	119	120
Days of exposure*			
Mean (SD)	228 (36.1)	226 (48.0)	232 (36.2)
Median	238	238	238
Min; Max	28; 252	1; 280	7; 259
Treatment dose** (mg)			
Mean (SD)	2.20 (0.74)	0.33 (0.19)	2.56 (1.48)
Median	2.00	0.25	2.00
Min; Max	1.00; 3.50	0.10; 1.10	0.50; 8.00
Treatment dose** (mg/kg)			
Mean (SD)	0.034 (0.016)	0.005 (0.005)	0.038 (0.028)
Median	0.032	0.004	0.029
Min; Max	0.014; 0.080	0.001; 0.044	0.007; 0.141
Total Exposure*** (years)	38.2	73.5	76.2

SD: Standard deviation

2 Summary of exposure - 4054 main - Japanese subgroup - safety analysis set

	placebo	Norditropin	somapacitan
	once weekly	once daily	once weekly
Number of exposed subjects	10	18	18
Days of exposure*			
Mean (SD)	238 (0.0)	237 (3.1)	238 (0.0)
Median	238	238	238
Min; Max	238; 238	225; 238	238; 238
Treatment dose** (mg)			
Mean (SD)	1.85 (0.85)	0.24 (0.10)	1.71 (1.09)
Median	1.50	0.20	1.50
Min; Max	1.00; 3.50	0.10; 0.45	0.50; 5.00
Treatment dose** (mg/kg)			
Mean (SD)	0.031 (0.013)	0.004 (0.002)	0.030 (0.024)
Median	0.028	0.004	0.026
Min; Max	0.015; 0.053	0.001; 0.009	0.007; 0.110
Total Exposure*** (years)	6.5	11.7	11.7

SD: Standard deviation

3 Summary of exposure - 4054 extension - Entire trial population - safety analysis set

	placebo/ somapacitan	somapacitan/ somapacitan	Norditropin/ Norditropin	Norditropin/ somapacitan	Norditropin/ -
Number of exposed subjects in main period	61	120	52	51	16
Number of exposed subjects in extension period	55	114	52	51	
Days of exposure in main*					
Mean (SD)	228 (36.1)	232 (36.2)	238 (4.8)	238 (3.7)	144 (98.8)
Median	238	238	238	238	156
Min; Max	28; 252	7; 259	233; 259	233; 252	1; 280
Treatment dose in main** (mg)					
Mean (SD)	2.20 (0.74)	2.56 (1.48)	0.31 (0.19)	0.34 (0.18)	0.44 (0.25)
Median	2.00	2.00	0.25	0.30	0.38
Min; Max	1.00; 3.50	0.50; 8.00	0.10; 1.10	0.10; 1.00	0.15; 1.00
Treatment dose in main** (mg/kg)					
Mean (SD)	0.034 (0.016)	0.038 (0.028)	0.004 (0.003)	0.005 (0.003)	0.010 (0.013)
Median	0.032	0.029	0.003	0.004	0.005
Min; Max	0.014; 0.080	0.007; 0.141	0.001; 0.015	0.001; 0.016	0.002; 0.044
Days of exposure in extension*					
Mean (SD)	357 (40.4)	355 (52.4)	349 (48.8)	343 (76.6)	
Median	364	364	364	364	
Min; Max	119; 378	21; 385	125; 372	49; 391	
Treatment dose in extension** (mg)					
Mean (SD)	2.61 (1.40)	2.35 (1.30)	0.28 (0.16)	2.66 (1.37)	
Median	2.50	2.00	0.25	2.25	
Min; Max	0.50; 7.50	0.10; 6.00	0.10; 0.80	1.00; 6.50	

SD: Standard deviation
*Exposure days are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan in the given period. Exposure days in complete trial is sum of main and extension.
** Stable dose at last titration visit 10 for main and visit 23 for extension. Weight measured at baseline.

Summary of exposure - 4054 extension - Entire trial population - safety analysis set

	placebo/ somapacitan	somapacitan/ somapacitan	Norditropin/ Norditropin	Norditropin/ somapacitan	Norditropin/ -
Treatment dose in extension** (mg/kg)					
Mean (SD)	0.043 (0.032)	0.034 (0.024)	0.004 (0.003)	0.041 (0.027)	
Median	0.031	0.026	0.003	0.031	
Min; Max	0.007; 0.171	0.001; 0.130	0.001; 0.011	0.010; 0.117	
Days of exposure complete trial*					
Mean (SD)	550 (145)	569 (122)	588 (49.4)	581 (76.6)	144 (98.8)
Median	602	602	601	601	156
Min; Max	28; 616	7; 623	363; 619	287; 637	1; 280
Sum of exposure in main* (years)	38.2	76.2	33.9	33.2	6.3
Sum of exposure in extension* (years)	53.7	110.9	49.7	47.9	
Total sum of exposure* (years)	91.9	187.1	83.7	81.2	6.3

SD: Standard deviation
*Exposure days are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan in the given period. Exposure days in complete trial is sum of main and extension.
** Stable dose at last titration visit 10 for main and visit 23 for extension. Weight measured at baseline.

4 Summary of exposure - 4054 extension - Japanese subgroup - safety analysis set

	placebo/ somapacitan	somapacitan/ somapacitan	Norditropin/ Norditropin	Norditropin/ somapacitan	Norditropin/ -
Number of exposed subjects in main period	10	18	9	8	1
Number of exposed subjects in extension period	10	18	9	8	
Days of exposure in main*					
Mean (SD)	238 (0.0)	238 (0.0)	238 (1.0)	238 (0.7)	225 (-)
Median	238	238	238	238	225
Min; Max	238; 238	238; 238	235; 238	236; 238	225; 225
Treatment dose in main** (mg)					
Mean (SD)	1.85 (0.85)	1.71 (1.09)	0.23 (0.10)	0.26 (0.12)	0.25 (-)
Median	1.50	1.50	0.20	0.23	0.25
Min; Max	1.00; 3.50	0.50; 5.00	0.15; 0.45	0.10; 0.45	0.25; 0.25
Treatment dose in main** (mg/kg)					
Mean (SD)	0.031 (0.013)	0.030 (0.024)	0.004 (0.002)	0.004 (0.002)	0.003 (-)
Median	0.028	0.026	0.003	0.004	0.003
Min; Max	0.015; 0.053	0.007; 0.110	0.002; 0.009	0.001; 0.009	0.003; 0.003
Days of exposure in extension*					
Mean (SD)	362 (6.7)	364 (0.2)	337 (79.6)	325 (111)	
Median	364	364	364	364	
Min; Max	343; 366	364; 365	125; 364	49; 364	
Treatment dose in extension** (mg)					
Mean (SD)	2.04 (1.07)	1.58 (0.94)	0.19 (0.07)	1.79 (0.70)	
Median	1.95	1.50	0.20	2.00	
Min; Max	1.00; 4.00	0.50; 4.50	0.10; 0.35	1.00; 3.00	

SD: Standard deviation
*Exposure days are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan in the given period. Exposure days in complete trial is sum of main and extension.
** Stable dose at last titration visit 10 for main and visit 23 for extension. Weight measured at baseline.

Summary of exposure - 4054 extension - Japanese subgroup - safety analysis set

	placebo/ somapacitan	somapacitan/ somapacitan	Norditropin/ Norditropin	Norditropin/ somapacitan	Norditropin/ -
Treatment dose in extension** (mg/kg)					
Mean (SD)	0.036 (0.022)	0.028 (0.021)	0.003 (0.002)	0.031 (0.014)	
Median	0.027	0.023	0.002	0.031	
Min; Max	0.015; 0.077	0.007; 0.099	0.001; 0.007	0.012; 0.047	
Days of exposure complete trial*					
Mean (SD)	600 (6.7)	602 (0.2)	575 (79.5)	562 (111)	225 (-)
Median	602	602	602	602	225
Min; Max	581; 604	602; 603	363; 602	287; 602	225; 225
Sum of exposure in main* (years)	6.5	11.7	5.9	5.2	0.6
Sum of exposure in extension* (years)	9.9	17.9	8.3	7.1	
Total sum of exposure* (years)	16.4	29.7	14.2	12.3	0.6

SD: Standard deviation
*Exposure days are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan in the given period. Exposure days in complete trial is sum of main and extension.
** Stable dose at last titration visit 10 for main and visit 23 for extension. Weight measured at baseline.

5 Summary of exposure - 4043 - entire trial population - safety analysis set

	Norditropin	somapacitan
	once daily	once weekly
Number of exposed subjects	31	61
Days of exposure*		
Mean (SD)	172 (34.5)	177 (28.6)
Median	182	182
Min; Max	10; 184	7; 196
Treatment dose** (mg)		
Mean (SD)	0.20 (0.14)	2.06 (1.64)
Median	0.18	1.50
Min; Max	0.05; 0.70	0.10; 8.00
Treatment dose** (mg/kg)		
Mean (SD)	0.003 (0.002)	0.027 (0.024)
Median	0.002	0.018
Min; Max	0.001; 0.009	0.001; 0.123
Total Exposure*** (years)	14.6	29.6

SD: Standard deviation
* Exposure days are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan.
** Stable dose at last titration visit 11 and weight measured at baseline.
*** Including titration period.

6 Summary of exposure - 4043 - Japanese subgroup - safety analysis set

	Norditropin	somapacitan
	once daily	once weekly
Number of exposed subjects	6	11
Days of exposure*		
Mean (SD)	182 (0.4)	179 (10.6)
Median	182	182
Min; Max	182; 183	147; 182
Treatment dose** (mg)		
Mean (SD)	0.13 (0.06)	2.47 (1.59)
Median	0.10	1.70
Min; Max	0.05; 0.20	0.50; 4.90
Treatment dose** (mg/kg)		
Mean (SD)	0.002 (0.001)	0.038 (0.027)
Median	0.002	0.024
Min; Max	0.001; 0.004	0.005; 0.083
Total Exposure*** (years)	3.0	5.4

SD: Standard deviation
* Exposure days are calculated as time from first date on randomised treatment to last date on randomised treatment for Norditropin and plus six days for somapacitan.
** Stable dose at last titration visit 11 and weight measured at baseline.
*** Including titration period.

7 Summary of exposure at randomisation and titration visits (mg) - 4054 main trial - Japanese subgroup - safety analysis set

	Placebo	Norditropin	Somapacitan
Number of exposed subjects	10	18	18
Visit 2 (Week 0) - Actual dose			
Number of subjects	10	18	18
Mean (SD)	1.25 (0.26)	0.18 (0.05)	1.44 (0.34)
Median	1.25	0.20	1.50
Min; Max	1.00; 1.50	0.10; 0.30	1.00; 2.00
Visit 4 (Week 2) - Actual dose			
Number of subjects	10	18	18
Mean (SD)	1.50 (0.33)	0.22 (0.07)	1.56 (0.63)
Median	1.50	0.20	1.50
Min; Max	1.00; 2.00	0.10; 0.40	1.00; 3.50
Visit 6 (Week 4) - Prescribed dose			
Number of subjects	10	18	18
Mean (SD)	1.65 (0.53)	0.23 (0.09)	1.65 (0.81)
Median	1.50	0.20	1.50
Min; Max	1.00; 2.50	0.10; 0.45	1.00; 4.00
Visit 8 (Week 6) - Prescribed dose			
Number of subjects	10	18	18
Mean (SD)	1.75 (0.68)	0.24 (0.10)	1.71 (0.98)
Median	1.50	0.20	1.50
Min; Max	1.00; 3.00	0.10; 0.45	0.50; 4.50
Visit 10 (Week 8) - Actual dose			
Number of subjects	10	18	18
Mean (SD)	1.85 (0.85)	0.24 (0.10)	1.71 (1.09)
Median	1.50	0.20	1.50
Min; Max	1.00; 3.50	0.10; 0.45	0.50; 5.00
Last dose taken according to diary (Week 34)*			
Number of subjects	10	18	18
Mean (SD)	1.85 (0.85)	0.23 (0.10)	1.71 (1.09)
Median	1.50	0.20	1.50

SD: Standard deviation
*Only subjects with dosing after visit 10.

Summary of exposure at randomisation and titration visits (mg) - 4054 main trial - Japanese subgroup - safety analysis set

	Placebo	Norditropin	Somapacitan
Min; Max	1.00; 3.50	0.10; 0.45	0.50; 5.00

SD: Standard deviation
*Only subjects with dosing after visit 10.

8 Summary of exposure at randomisation and titration visits (mg) - 4054 extension trial - Japanese subgroup - safety analysis set

	Placebo/ somapacitan	somapacitan/ somapacitan	Norditropin/ Norditropin	Norditropin/ somapacitan	Norditropin/ _
Number of exposed subjects	10	18	9	8	1
Visit 2 (Week 0) - Actual dose					
Number of subjects	10	18	9	8	1
Mean (SD)	1.25 (0.26)	1.44 (0.34)	0.19 (0.06)	0.16 (0.05)	0.20
Median	1.25	1.50	0.20	0.20	0.20
Min; Max	1.00; 1.50	1.00; 2.00	0.10; 0.30	0.10; 0.20	0.20; 0.20
Visit 4 (Week 2) - Actual dose					
Number of subjects	10	18	9	8	1
Mean (SD)	1.50 (0.33)	1.56 (0.63)	0.21 (0.06)	0.23 (0.09)	0.25
Median	1.50	1.50	0.20	0.20	0.25
Min; Max	1.00; 2.00	1.00; 3.50	0.15; 0.35	0.10; 0.40	0.25; 0.25
Visit 6 (Week 4) - Prescribed dose					
Number of subjects	10	18	9	8	1
Mean (SD)	1.65 (0.53)	1.65 (0.81)	0.22 (0.08)	0.25 (0.11)	0.25
Median	1.50	1.50	0.20	0.23	0.25
Min; Max	1.00; 2.50	1.00; 4.00	0.15; 0.40	0.10; 0.45	0.25; 0.25
Visit 8 (Week 6) - Prescribed dose					
Number of subjects	10	18	9	8	1
Mean (SD)	1.75 (0.68)	1.71 (0.98)	0.22 (0.08)	0.26 (0.12)	0.25
Median	1.50	1.50	0.20	0.23	0.25
Min; Max	1.00; 3.00	0.50; 4.50	0.15; 0.40	0.10; 0.45	0.25; 0.25
Visit 10 (Week 8) - Actual dose					
Number of subjects	10	18	9	8	1
Mean (SD)	1.85 (0.85)	1.71 (1.09)	0.23 (0.10)	0.26 (0.12)	0.25
Median	1.50	1.50	0.20	0.23	0.25
Min; Max	1.00; 3.50	0.50; 5.00	0.15; 0.45	0.10; 0.45	0.25; 0.25
Visit 15 (Week 35) - Actual dose					
Number of subjects	10	18	9	8	0
Mean (SD)	1.25 (0.26)	1.44 (0.34)	0.19 (0.06)	1.31 (0.26)	
Median	1.25	1.50	0.20	1.50	

SD: Standard deviation
*Only subjects with dosing after visit 23.

Summary of exposure at randomisation and titration visits (mg) - 4054 extension trial - Japanese subgroup - safety analysis set

	Placebo/ somapacitan	somapacitan/ somapacitan	Norditropin/ Norditropin	Norditropin/ somapacitan	Norditropin/ _
Min; Max	1.00; 1.50	1.00; 2.00	0.10; 0.30	1.00; 1.50	
Visit 17 (Week 37) - Actual dose					
Number of subjects	10	18	9	8	0
Mean (SD)	1.65 (0.58)	1.47 (0.53)	0.19 (0.05)	1.56 (0.42)	
Median	2.00	1.50	0.20	1.50	
Min; Max	1.00; 2.50	0.50; 3.00	0.15; 0.30	1.00; 2.00	
Visit 19 (Week 39) - Prescribed dose					
Number of subjects	10	18	9	8	0
Mean (SD)	1.90 (0.81)	1.50 (0.66)	0.19 (0.06)	1.69 (0.53)	
Median	2.25	1.50	0.20	1.75	
Min; Max	1.00; 3.00	0.50; 3.50	0.10; 0.30	1.00; 2.50	
Visit 21 (Week 41) - Prescribed dose					
Number of subjects	10	18	9	8	0
Mean (SD)	2.05 (0.98)	1.56 (0.78)	0.19 (0.06)	1.81 (0.65)	
Median	2.25	1.50	0.20	1.75	
Min; Max	1.00; 3.50	0.50; 4.00	0.10; 0.30	1.00; 2.50	
Visit 23 (Week 43) - Actual dose					
Number of subjects	10	18	9	7	0
Mean (SD)	2.04 (1.07)	1.58 (0.94)	0.19 (0.07)	1.79 (0.70)	
Median	1.95	1.50	0.20	2.00	
Min; Max	1.00; 4.00	0.50; 4.50	0.10; 0.35	1.00; 3.00	
Last dose taken according to diary (Week 86)*					
Number of subjects	10	18	9	7	0
Mean (SD)	2.02 (1.09)	1.58 (0.94)	0.19 (0.07)	1.79 (0.70)	
Median	1.95	1.50	0.20	2.00	
Min; Max	0.80; 4.00	0.50; 4.50	0.10; 0.35	1.00; 3.00	

SD: Standard deviation
*Only subjects with dosing after visit 23.

9 Summary of exposure at randomisation and titration visits (mg) - 4043 - Japanese subgroup - safety analysis set

	Norditropin	Somapacitan
Number of exposed subjects	6	11
Visit 3 (Week 0) - Actual dose		
Number of subjects	6	11
Mean (SD)	0.13 (0.05)	1.45 (0.42)
Median	0.10	1.50
Min; Max	0.10; 0.20	1.00; 2.00
Visit 5 (Week 2) - Actual dose		
Number of subjects	6	11
Mean (SD)	0.13 (0.05)	2.05 (0.94)
Median	0.10	1.70
Min; Max	0.10; 0.20	1.00; 3.50
Visit 7 (Week 4) - Prescribed dose		
Number of subjects	6	11
Mean (SD)	0.13 (0.06)	2.18 (1.12)
Median	0.10	1.70
Min; Max	0.05; 0.20	1.00; 4.20
Visit 9 (Week 6) - Prescribed dose		
Number of subjects	6	11
Mean (SD)	0.13 (0.06)	2.65 (1.71)
Median	0.10	1.70
Min; Max	0.05; 0.20	1.00; 6.00
Visit 11 (Week 8) - Actual dose		
Number of subjects	6	10
Mean (SD)	0.13 (0.06)	2.47 (1.59)
Median	0.10	1.70
Min; Max	0.05; 0.20	0.50; 4.90
Last dose taken according to diary (Week 25)*		
Number of subjects	6	10
Mean (SD)	0.13 (0.06)	2.47 (1.59)
Median	0.10	1.70

SD: Standard deviation
*Only subjects with dosing after visit 11.

Summary of exposure at randomisation and titration visits (mg) - 4043 - Japanese subgroup - safety analysis set

	Norditropin	Somapacitan
Min; Max	0.05; 0.20	0.50; 4.90

SD: Standard deviation
*Only subjects with dosing after visit 11.

10 Subject exposure by 3 month periods - summary - Japanese subgroup - full analysis set

	placebo N (%)	Norditropin N (%)	somapacitan N (%)
Number of subjects	10	40	93
Exposure period			
>0 months	10 (100.0)	40 (100.0)	93 (100.0)
>3 months	10 (100.0)	39 (97.5)	92 (98.9)
>6 months	10 (100.0)	39 (97.5)	91 (97.8)
>9 months	0	23 (57.5)	80 (86.0)
>12 months	0	23 (57.5)	79 (84.9)
>15 months	0	8 (20.0)	18 (19.4)
>18 months	0	8 (20.0)	18 (19.4)

N: Number of subjects, %: Percentage of subjects
Subjects from 4054 switching treatment after main trial period are included for each treatment.
Exposure to placebo was only done in 4054 and for no more than 35 weeks.
Month = 30 days.

11 Adverse Events - 4054 main trial - entire trial population - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	61			119			120			300		
Total patient years	39.8			77.5			79.9			197.2		
All adverse events	46 (75.4)	182	457.0	96 (80.7)	434	559.7	87 (72.5)	388	485.7	229 (76.3)	1004	509.0
Serious adverse events	5 (8.2)	7	17.6	11 (9.2)	13	16.8	7 (5.8)	12	15.0	23 (7.7)	32	16.2
Medical events of special interest	0			0			0			0		
Severity												
Mild	41 (67.2)	144	361.6	82 (68.9)	287	370.1	75 (62.5)	276	345.5	198 (66.0)	707	358.5
Moderate	17 (27.9)	32	80.4	42 (35.3)	137	176.7	34 (28.3)	101	126.4	93 (31.0)	270	136.9
Severe	4 (6.6)	6	15.1	9 (7.6)	10	12.9	7 (5.8)	11	13.8	20 (6.7)	27	13.7
Causality												
Unlikely	45 (73.8)	163	409.3	90 (75.6)	358	461.7	79 (65.8)	294	368.1	214 (71.3)	815	413.2
Possible	9 (14.8)	13	32.6	27 (22.7)	51	65.8	23 (19.2)	71	88.9	59 (19.7)	135	68.4
Probable	4 (6.6)	6	15.1	15 (12.6)	25	32.2	14 (11.7)	23	28.8	33 (11.0)	54	27.4
Outcome												
Recovered/Resolved	43 (70.5)	160	401.8	89 (74.8)	367	473.3	82 (68.3)	358	448.2	214 (71.3)	885	448.7
Recovering/Resolving	1 (1.6)	2	5.0	2 (1.7)	2	2.6	0			3 (1.0)	4	2.0
Recovered/Resolved With Sequelae	1 (1.6)	1	2.5	2 (1.7)	3	3.9	1 (0.8)	1	1.3	4 (1.3)	5	2.5
Not Recovered/Not Resolved	13 (21.3)	18	45.2	36 (30.3)	59	76.1	19 (15.8)	29	36.3	68 (22.7)	106	53.7
Fatal	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Unknown	0			1 (0.8)	3	3.9	0			1 (0.3)	3	1.5

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Adverse Events - 4054 main trial - entire trial population - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Action												
Drug Interrupted	3	(4.9)	5 12.6	5	(4.2)	8 10.3	0			8	(2.7)	13 6.6
Drug Withdrawn	1	(1.6)	1 2.5	4	(3.4)	4 5.2	0			5	(1.7)	5 2.5
Dose Reduced	0			5	(4.2)	6 7.7	2	(1.7)	3 3.8	7	(2.3)	9 4.6
Dose Not Changed	45	(73.8)	170 426.9	93	(78.2)	407 524.9	87	(72.5)	371 464.5	225	(75.0)	948 480.6
Not Applicable	3	(4.9)	6 15.1	6	(5.0)	9 11.6	6	(5.0)	14 17.5	15	(5.0)	29 14.7
Treatment discontinuations due to adverse events*	1	(1.6)	1 2.5	5	(4.2)	5 6.4	0			6	(2.0)	6 3.0

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

12 Adverse Events - 4054 main trial - Japanese subgroup - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	10			18			18			46		
Total patient years	6.7			12.1			12.1			31.0		
All adverse events	9 (90.0)	25	371.5	18 (100.0)	46	379.4	11 (61.1)	38	313.4	38 (82.6)	109	351.9
Serious adverse events	2 (20.0)	2	29.7	1 (5.6)	1	8.2	0			3 (6.5)	3	9.7
Medical events of special interest	0			0			0			0		
Severity												
Mild	8 (80.0)	23	341.8	16 (88.9)	41	338.2	11 (61.1)	36	297.0	35 (76.1)	100	322.8
Moderate	2 (20.0)	2	29.7	4 (22.2)	4	33.0	2 (11.1)	2	16.5	8 (17.4)	8	25.8
Severe	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Causality												
Unlikely	9 (90.0)	23	341.8	16 (88.9)	35	288.7	10 (55.6)	29	239.2	35 (76.1)	87	280.9
Possible	1 (10.0)	1	14.9	3 (16.7)	4	33.0	2 (11.1)	7	57.7	6 (13.0)	12	38.7
Probable	1 (10.0)	1	14.9	6 (33.3)	7	57.7	2 (11.1)	2	16.5	9 (19.6)	10	32.3
Outcome												
Recovered/Resolved	8 (80.0)	22	326.9	16 (88.9)	33	272.2	11 (61.1)	38	313.4	35 (76.1)	93	300.2
Recovering/Resolving	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Not Recovered/Not Resolved	3 (30.0)	3	44.6	7 (38.9)	12	99.0	0			10 (21.7)	15	48.4
Action												
Drug Interrupted	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Adverse Events - 4054 main trial - Japanese subgroup - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Drug Withdrawn	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Dose Reduced	0			2 (11.1)	3	24.7	1 (5.6)	1	8.2	3 (6.5)	4	12.9
Dose Not Changed	9 (90.0)	24	356.6	17 (94.4)	42	346.4	11 (61.1)	37	305.2	37 (80.4)	103	332.5
Treatment discontinuations due to adverse events*	0			2 (11.1)	2	16.5	0			2 (4.3)	2	6.5

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

13 Adverse Events - 4043 - entire trial population - safety analysis set

	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All adverse events	21 (67.7)	81	530.8	53 (86.9)	159	514.2	74 (80.4)	240	519.7
Serious adverse events	2 (6.5)	3	19.7	4 (6.6)	4	12.9	6 (6.5)	7	15.2
Medical events of special interest	0			0			0		
Severity									
Mild	18 (58.1)	58	380.1	44 (72.1)	119	384.8	62 (67.4)	177	383.3
Moderate	8 (25.8)	19	124.5	16 (26.2)	32	103.5	24 (26.1)	51	110.4
Severe	2 (6.5)	4	26.2	5 (8.2)	8	25.9	7 (7.6)	12	26.0
Causality									
Unlikely	21 (67.7)	68	445.6	46 (75.4)	130	420.4	67 (72.8)	198	428.7
Possible	3 (9.7)	5	32.8	9 (14.8)	15	48.5	12 (13.0)	20	43.3
Probable	4 (12.9)	8	52.4	8 (13.1)	14	45.3	12 (13.0)	22	47.6
Outcome									
Recovered/Resolved	20 (64.5)	57	373.5	46 (75.4)	109	352.5	66 (71.7)	166	359.4
Recovering/Resolving	4 (12.9)	6	39.3	9 (14.8)	10	32.3	13 (14.1)	16	34.6
Recovered/Resolved With Sequelae	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Not Recovered/Not Resolved	10 (32.3)	17	111.4	22 (36.1)	39	126.1	32 (34.8)	56	121.3
Unknown	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Action									
Drug Withdrawn	1 (3.2)	4	26.2	1 (1.6)	2	6.5	2 (2.2)	6	13.0
Dose Not Changed	20 (64.5)	74	484.9	52 (85.2)	146	472.2	72 (78.3)	220	476.4

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

Adverse Events - 4043 - entire trial population - safety analysis set

	Norditropin N	(%)	E	R	somapacitan N	(%)	E	R	total N	(%)	E	R
Not Applicable	3	(9.7)	3	19.7	9	(14.8)	11	35.6	12	(13.0)	14	30.3
Treatment discontinuations due to adverse events	1	(3.2)	4	26.2	1	(1.6)	2	6.5	2	(2.2)	6	13.0

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

14 Adverse Events - 4043 - Japanese subgroup - safety analysis set

	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	6			11			17		
Total patient years	3.1			5.7			8.8		
All adverse events	1 (16.7)	4	128.0	11 (100.0)	36	634.6	12 (70.6)	40	454.7
Serious adverse events	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Medical events of special interest	0			0			0		
Severity									
Mild	1 (16.7)	4	128.0	11 (100.0)	35	617.0	12 (70.6)	39	443.3
Moderate	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Causality									
Unlikely	1 (16.7)	4	128.0	11 (100.0)	31	546.5	12 (70.6)	35	397.9
Possible	0			1 (9.1)	2	35.3	1 (5.9)	2	22.7
Probable	0			1 (9.1)	3	52.9	1 (5.9)	3	34.1
Outcome									
Recovered/Resolved	1 (16.7)	4	128.0	11 (100.0)	28	493.6	12 (70.6)	32	363.8
Recovering/Resolving	0			2 (18.2)	2	35.3	2 (11.8)	2	22.7
Not Recovered/Not Resolved	0			4 (36.4)	6	105.8	4 (23.5)	6	68.2
Action									
Dose Not Changed	1 (16.7)	4	128.0	11 (100.0)	33	581.7	12 (70.6)	37	420.6
Not Applicable	0			2 (18.2)	3	52.9	2 (11.8)	3	34.1

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

Adverse Events - 4043 - Japanese subgroup - safety analysis set

	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Treatment discontinuations due to adverse events	0			0			0		

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

15 Adverse Events by system organ class and preferred term – 4054 main trial – entire trial population– safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			120			300		
Total patient years	39.8			77.5			79.9			197.2		
All adverse events	46 (75.4)	182	457.0	96 (80.7)	434	559.7	87 (72.5)	388	485.7	229 (76.3)	1004	509.0
Infections and infestations	36 (59.0)	50	125.6	53 (44.5)	80	103.2	51 (42.5)	92	115.2	140 (46.7)	222	112.6
Nasopharyngitis	9 (14.8)	12	30.1	20 (16.8)	25	32.2	23 (19.2)	29	36.3	52 (17.3)	66	33.5
Upper respiratory tract infection	7 (11.5)	7	17.6	9 (7.6)	10	12.9	6 (5.0)	7	8.8	22 (7.3)	24	12.2
Gastroenteritis	2 (3.3)	2	5.0	3 (2.5)	4	5.2	5 (4.2)	6	7.5	10 (3.3)	12	6.1
Bronchitis	3 (4.9)	3	7.5	3 (2.5)	3	3.9	1 (0.8)	1	1.3	7 (2.3)	7	3.5
Sinusitis	3 (4.9)	6	15.1	2 (1.7)	2	2.6	2 (1.7)	2	2.5	7 (2.3)	10	5.1
Tonsillitis	1 (1.6)	1	2.5	2 (1.7)	2	2.6	4 (3.3)	4	5.0	7 (2.3)	7	3.5
Urinary tract infection	1 (1.6)	1	2.5	1 (0.8)	1	1.3	5 (4.2)	5	6.3	7 (2.3)	7	3.5
Influenza	2 (3.3)	3	7.5	1 (0.8)	1	1.3	3 (2.5)	3	3.8	6 (2.0)	7	3.5
Ear infection	1 (1.6)	1	2.5	1 (0.8)	1	1.3	2 (1.7)	3	3.8	4 (1.3)	5	2.5
Gastroenteritis viral	2 (3.3)	2	5.0	1 (0.8)	1	1.3	1 (0.8)	1	1.3	4 (1.3)	4	2.0
Herpes zoster	1 (1.6)	1	2.5	1 (0.8)	1	1.3	2 (1.7)	5	6.3	4 (1.3)	7	3.5
Pharyngitis	1 (1.6)	1	2.5	3 (2.5)	3	3.9	0			4 (1.3)	4	2.0
Respiratory tract infection	2 (3.3)	2	5.0	2 (1.7)	2	2.6	0			4 (1.3)	4	2.0
Viral upper respiratory tract infection	1 (1.6)	1	2.5	1 (0.8)	1	1.3	2 (1.7)	2	2.5	4 (1.3)	4	2.0
Cystitis	2 (3.3)	2	5.0	0			1 (0.8)	2	2.5	3 (1.0)	4	2.0
Lower respiratory tract infection	0			1 (0.8)	2	2.6	2 (1.7)	2	2.5	3 (1.0)	4	2.0
Pulpitis dental	0			3 (2.5)	3	3.9	0			3 (1.0)	3	1.5
Respiratory tract infection viral	0			2 (1.7)	2	2.6	1 (0.8)	1	1.3	3 (1.0)	3	1.5
Tooth infection	0			2 (1.7)	2	2.6	1 (0.8)	1	1.3	3 (1.0)	3	1.5
Appendicitis	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Clostridium difficile infection	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Fungal infection	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Oral herpes	0			0			2 (1.7)	2	2.5	2 (0.7)	2	1.0
Rhinitis	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Candida infection	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - entire trial population- safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Cellulitis	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Diverticulitis	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Folliculitis	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Gingivitis	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Herpes simplex	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Herpes virus infection	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Hordeolum	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Laryngitis	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Molluscum contagiosum	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Onychomycosis	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Otitis media	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Paronychia	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Periodontitis	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Pharyngitis streptococcal	0			0			1 (0.8)	2	2.5	1 (0.3)	2	1.0
Pilonidal cyst	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Pneumonia bacterial	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Post procedural infection	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Pyoderma	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Sepsis	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Tinea infection	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Tooth abscess	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Upper respiratory tract infection bacterial	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Vaginal infection	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Viral infection	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Vulvovaginal candidiasis	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Musculoskeletal and connective tissue disorders	10 (16.4)	14	35.2	31 (26.1)	45	58.0	29 (24.2)	40	50.1	70 (23.3)	99	50.2
Arthralgia	1 (1.6)	1	2.5	11 (9.2)	11	14.2	8 (6.7)	8	10.0	20 (6.7)	20	10.1
Back pain	2 (3.3)	2	5.0	4 (3.4)	4	5.2	11 (9.2)	11	13.8	17 (5.7)	17	8.6
Pain in extremity	1 (1.6)	1	2.5	5 (4.2)	5	6.4	2 (1.7)	2	2.5	8 (2.7)	8	4.1
Myalgia	3 (4.9)	3	7.5	3 (2.5)	3	3.9	1 (0.8)	1	1.3	7 (2.3)	7	3.5
Joint stiffness	0			3 (2.5)	3	3.9	0			3 (1.0)	3	1.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - entire trial population- safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Muscular weakness	0			1 (0.8)	1	1.3	2 (1.7)	3	3.8	3 (1.0)	4	2.0
Tendonitis	1 (1.6)	1	2.5	1 (0.8)	1	1.3	1 (0.8)	1	1.3	3 (1.0)	3	1.5
Joint swelling	0			2 (1.7)	3	3.9	0			2 (0.7)	3	1.5
Muscle spasms	1 (1.6)	2	5.0	0			1 (0.8)	1	1.3	2 (0.7)	3	1.5
Musculoskeletal chest pain	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Musculoskeletal pain	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Neck pain	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Pain in jaw	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Rotator cuff syndrome	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Bursitis	1 (1.6)	2	5.0	0			0			1 (0.3)	2	1.0
Costochondritis	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Exostosis	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Foot deformity	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Intervertebral disc degeneration	0			0			1 (0.8)	2	2.5	1 (0.3)	2	1.0
Intervertebral disc protrusion	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Joint effusion	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Joint noise	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Limb deformity	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Limb discomfort	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Muscle twitching	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Musculoskeletal stiffness	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Myositis	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Nodal osteoarthritis	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Osteoarthritis	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Periarthritis	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Plantar fasciitis	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Spinal pain	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Tenosynovitis	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Gastrointestinal disorders	13 (21.3)	24	60.3	30 (25.2)	45	58.0	19 (15.8)	38	47.6	62 (20.7)	107	54.2
Diarrhoea	5 (8.2)	8	20.1	5 (4.2)	5	6.4	4 (3.3)	5	6.3	14 (4.7)	18	9.1
Nausea	1 (1.6)	1	2.5	6 (5.0)	8	10.3	2 (1.7)	2	2.5	9 (3.0)	11	5.6
Vomiting	1 (1.6)	2	5.0	4 (3.4)	5	6.4	4 (3.3)	4	5.0	9 (3.0)	11	5.6
Dyspepsia	1 (1.6)	2	5.0	4 (3.4)	4	5.2	2 (1.7)	2	2.5	7 (2.3)	8	4.1

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - entire trial population- safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Toothache	1 (1.6)	1	2.5	4 (3.4)	4	5.2	2 (1.7)	4	5.0	7 (2.3)	9	4.6
Abdominal pain	1 (1.6)	1	2.5	2 (1.7)	3	3.9	3 (2.5)	4	5.0	6 (2.0)	8	4.1
Abdominal pain upper	1 (1.6)	1	2.5	1 (0.8)	1	1.3	4 (3.3)	5	6.3	6 (2.0)	7	3.5
Dental caries	0			3 (2.5)	4	5.2	0			3 (1.0)	4	2.0
Abdominal discomfort	1 (1.6)	1	2.5	1 (0.8)	1	1.3	0			2 (0.7)	2	1.0
Abdominal distension	0			0			2 (1.7)	2	2.5	2 (0.7)	2	1.0
Abdominal tenderness	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Constipation	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Flatulence	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Food poisoning	1 (1.6)	1	2.5	1 (0.8)	1	1.3	0			2 (0.7)	2	1.0
Gastritis	1 (1.6)	1	2.5	0			1 (0.8)	1	1.3	2 (0.7)	2	1.0
Stomatitis	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Abdominal pain lower	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Ascites	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Dry mouth	0			0			1 (0.8)	2	2.5	1 (0.3)	2	1.0
Epigastric discomfort	0			0			1 (0.8)	3	3.8	1 (0.3)	3	1.5
Gastrooesophageal reflux disease	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Hiatus hernia	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Inguinal hernia	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Large intestine polyp	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Lip swelling	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Oesophagitis ulcerative	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Pancreatitis acute	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Rectal polyp	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
General disorders and administration site conditions	9 (14.8)	13	32.6	27 (22.7)	46	59.3	19 (15.8)	28	35.1	55 (18.3)	87	44.1
Fatigue	2 (3.3)	2	5.0	7 (5.9)	7	9.0	3 (2.5)	3	3.8	12 (4.0)	12	6.1
Oedema peripheral	0			6 (5.0)	8	10.3	5 (4.2)	7	8.8	11 (3.7)	15	7.6
Injection site bruising	2 (3.3)	3	7.5	6 (5.0)	6	7.7	1 (0.8)	1	1.3	9 (3.0)	10	5.1
Pain	0			3 (2.5)	3	3.9	1 (0.8)	1	1.3	4 (1.3)	4	2.0
Peripheral swelling	1 (1.6)	1	2.5	3 (2.5)	3	3.9	0			4 (1.3)	4	2.0
Pyrexia	0			1 (0.8)	2	2.6	3 (2.5)	4	5.0	4 (1.3)	6	3.0
Asthenia	1 (1.6)	1	2.5	1 (0.8)	1	1.3	1 (0.8)	1	1.3	3 (1.0)	3	1.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - entire trial population- safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Face oedema	1 (1.6)	1	2.5	1 (0.8)	1	1.3	1 (0.8)	1	1.3	3 (1.0)	3	1.5
Influenza like illness	0			2 (1.7)	2	2.6	1 (0.8)	2	2.5	3 (1.0)	4	2.0
Injection site pain	1 (1.6)	1	2.5	1 (0.8)	1	1.3	1 (0.8)	2	2.5	3 (1.0)	4	2.0
Malaise	1 (1.6)	1	2.5	1 (0.8)	1	1.3	1 (0.8)	1	1.3	3 (1.0)	3	1.5
Chest pain	1 (1.6)	1	2.5	1 (0.8)	1	1.3	0			2 (0.7)	2	1.0
Feeling hot	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Injection site reaction	0			1 (0.8)	1	1.3	1 (0.8)	2	2.5	2 (0.7)	3	1.5
Nodule	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Non-cardiac chest pain	0			0			2 (1.7)	2	2.5	2 (0.7)	2	1.0
Axillary pain	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Chest discomfort	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Chills	0			1 (0.8)	2	2.6	0			1 (0.3)	2	1.0
Fat tissue decreased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Gait disturbance	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Injection site haematoma	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Pre-existing condition improved	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Nervous system disorders	14 (23.0)	26	65.3	17 (14.3)	70	90.3	22 (18.3)	61	76.4	53 (17.7)	157	79.6
Headache	10 (16.4)	15	37.7	11 (9.2)	50	64.5	10 (8.3)	45	56.3	31 (10.3)	110	55.8
Dizziness	1 (1.6)	1	2.5	4 (3.4)	7	9.0	4 (3.3)	5	6.3	9 (3.0)	13	6.6
Paraesthesia	2 (3.3)	2	5.0	1 (0.8)	1	1.3	3 (2.5)	4	5.0	6 (2.0)	7	3.5
Hypoaesthesia	1 (1.6)	1	2.5	3 (2.5)	4	5.2	1 (0.8)	1	1.3	5 (1.7)	6	3.0
Migraine	1 (1.6)	3	7.5	1 (0.8)	1	1.3	1 (0.8)	1	1.3	3 (1.0)	5	2.5
Dysgeusia	1 (1.6)	1	2.5	1 (0.8)	1	1.3	0			2 (0.7)	2	1.0
Hypersomnia	0			0			2 (1.7)	3	3.8	2 (0.7)	3	1.5
Tremor	1 (1.6)	1	2.5	1 (0.8)	2	2.6	0			2 (0.7)	3	1.5
Burning sensation	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Lethargy	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Memory impairment	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Partial seizures	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Sciatica	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Seizure	0			1 (0.8)	2	2.6	0			1 (0.3)	2	1.0
Somnolence	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5

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MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - entire trial population- safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Skin and subcutaneous tissue disorders	12 (19.7)	16	40.2	13 (10.9)	18	23.2	20 (16.7)	24	30.0	45 (15.0)	58	29.4
Rash	2 (3.3)	2	5.0	3 (2.5)	4	5.2	3 (2.5)	3	3.8	8 (2.7)	9	4.6
Pruritus	0			4 (3.4)	4	5.2	1 (0.8)	1	1.3	5 (1.7)	5	2.5
Dry skin	2 (3.3)	2	5.0	0			2 (1.7)	2	2.5	4 (1.3)	4	2.0
Dermatitis contact	1 (1.6)	1	2.5	1 (0.8)	1	1.3	1 (0.8)	1	1.3	3 (1.0)	3	1.5
Dermatitis	2 (3.3)	2	5.0	0			0			2 (0.7)	2	1.0
Eczema	2 (3.3)	2	5.0	0			0			2 (0.7)	2	1.0
Haemorrhage subcutaneous	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Lipodystrophy acquired	0			0			2 (1.7)	2	2.5	2 (0.7)	2	1.0
Lipohypertrophy	0			0			2 (1.7)	2	2.5	2 (0.7)	2	1.0
Urticaria	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Acne	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Alopecia	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Dermatitis allergic	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Dermatitis atopic	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Ecchymosis	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Exfoliative rash	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Hyperkeratosis	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Ingrowing nail	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Onychoclasis	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Papule	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Prurigo	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Pruritus generalised	1 (1.6)	2	5.0	0			0			1 (0.3)	2	1.0
Pustular psoriasis	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Rash erythematous	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Rash generalised	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Rash macular	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Rash maculo-papular	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Rash papular	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Skin burning sensation	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Skin erosion	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Skin lesion	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Skin mass	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5

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MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - entire trial population- safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Skin ulcer	0			1 (0.8)	2	2.6	0			1 (0.3)	2	1.0
Investigations	7 (11.5)	10	25.1	17 (14.3)	29	37.4	14 (11.7)	28	35.1	38 (12.7)	67	34.0
Weight increased	0			1 (0.8)	1	1.3	4 (3.3)	4	5.0	5 (1.7)	5	2.5
Blood creatine phosphokinase increased	0			0			4 (3.3)	6	7.5	4 (1.3)	6	3.0
Alanine aminotransferase increased	1 (1.6)	1	2.5	1 (0.8)	1	1.3	1 (0.8)	1	1.3	3 (1.0)	3	1.5
Blood testosterone decreased	0			3 (2.5)	3	3.9	0			3 (1.0)	3	1.5
Hepatic enzyme increased	2 (3.3)	2	5.0	0			1 (0.8)	1	1.3	3 (1.0)	3	1.5
Thyroxine free decreased	1 (1.6)	1	2.5	1 (0.8)	1	1.3	1 (0.8)	2	2.5	3 (1.0)	4	2.0
Blood uric acid increased	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Creatinine renal clearance decreased	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Glycosylated haemoglobin increased	0			1 (0.8)	2	2.6	1 (0.8)	1	1.3	2 (0.7)	3	1.5
Intraocular pressure increased	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Aspartate aminotransferase increased	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Blood alkaline phosphatase increased	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Blood bilirubin increased	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Blood cholesterol increased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Blood creatinine increased	0			0			1 (0.8)	2	2.5	1 (0.3)	2	1.0
Blood glucose increased	0			1 (0.8)	2	2.6	0			1 (0.3)	2	1.0
Blood insulin decreased	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Blood potassium decreased	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Blood pressure increased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Blood testosterone increased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Blood thyroid stimulating hormone decreased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Body temperature increased	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Cortisol increased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Creatinine renal clearance increased	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Electrocardiogram PR prolongation	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5

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MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - entire trial population- safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Electrocardiogram T wave abnormal	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Electrocardiogram abnormal	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Gamma-glutamyltransferase increased	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Glomerular filtration rate increased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Haematocrit increased	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Heart rate increased	0			1 (0.8)	3	3.9	0			1 (0.3)	3	1.5
Lymph node palpable	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Normetanephrine urine increased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Platelet count increased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Thyroid hormones decreased	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Thyroxine decreased	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Tri-iodothyronine decreased	0			1 (0.8)	2	2.6	0			1 (0.3)	2	1.0
Weight decreased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
White blood cell count increased	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Injury, poisoning and procedural complications	3 (4.9)	3	7.5	15 (12.6)	19	24.5	9 (7.5)	12	15.0	27 (9.0)	34	17.2
Contusion	1 (1.6)	1	2.5	3 (2.5)	4	5.2	2 (1.7)	2	2.5	6 (2.0)	7	3.5
Fall	0			2 (1.7)	2	2.6	2 (1.7)	3	3.8	4 (1.3)	5	2.5
Tooth fracture	1 (1.6)	1	2.5	2 (1.7)	2	2.6	0			3 (1.0)	3	1.5
Arthropod bite	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Foot fracture	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Laceration	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Muscle strain	0			1 (0.8)	1	1.3	1 (0.8)	2	2.5	2 (0.7)	3	1.5
Arthropod sting	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Drug dispensing error	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Limb injury	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Post procedural complication	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Prescription drug used without a prescription	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Procedural pain	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Radius fracture	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Thermal burn	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5

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MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - entire trial population- safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Tibia fracture	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Wrist fracture	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Respiratory, thoracic and mediastinal disorders	4 (6.6)	5	12.6	13 (10.9)	19	24.5	10 (8.3)	15	18.8	27 (9.0)	39	19.8
Cough	3 (4.9)	3	7.5	5 (4.2)	6	7.7	3 (2.5)	3	3.8	11 (3.7)	12	6.1
Oropharyngeal pain	2 (3.3)	2	5.0	1 (0.8)	1	1.3	5 (4.2)	5	6.3	8 (2.7)	8	4.1
Dyspnoea	0			3 (2.5)	3	3.9	0			3 (1.0)	3	1.5
Asthma	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Epistaxis	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Rhinitis allergic	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Dyspnoea paroxysmal nocturnal	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Nasal congestion	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Paranasal sinus hypersecretion	0			0			1 (0.8)	2	2.5	1 (0.3)	2	1.0
Pharyngeal erythema	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Respiratory tract congestion	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Sinus congestion	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Sleep apnoea syndrome	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Snoring	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Upper respiratory tract congestion	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Metabolism and nutrition disorders	5 (8.2)	6	15.1	8 (6.7)	8	10.3	6 (5.0)	8	10.0	19 (6.3)	22	11.2
Gout	0			1 (0.8)	1	1.3	2 (1.7)	3	3.8	3 (1.0)	4	2.0
Diabetes mellitus	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Dyslipidaemia	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Hyperkalaemia	1 (1.6)	1	2.5	1 (0.8)	1	1.3	0			2 (0.7)	2	1.0
Dehydration	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Fluid retention	0			0			1 (0.8)	2	2.5	1 (0.3)	2	1.0
Hypercholesterolaemia	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Hyperlipidaemia	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Hypertriglyceridaemia	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Hypocalcaemia	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Hypoglycaemia	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Hyponatraemia	1 (1.6)	2	5.0	0			0			1 (0.3)	2	1.0

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Adverse Events by system organ class and preferred term - 4054 main trial - entire trial population- safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Obesity	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Vitamin D deficiency	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Endocrine disorders	2 (3.3)	2	5.0	4 (3.4)	5	6.4	6 (5.0)	6	7.5	12 (4.0)	13	6.6
Adrenal insufficiency	0			0			3 (2.5)	3	3.8	3 (1.0)	3	1.5
Hypothyroidism	1 (1.6)	1	2.5	1 (0.8)	1	1.3	1 (0.8)	1	1.3	3 (1.0)	3	1.5
Adrenocortical insufficiency acute	1 (1.6)	1	2.5	0			1 (0.8)	1	1.3	2 (0.7)	2	1.0
Secondary hypothyroidism	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Glucocorticoid deficiency	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Secondary adrenocortical insufficiency	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Thyroid mass	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Eye disorders	2 (3.3)	2	5.0	6 (5.0)	8	10.3	3 (2.5)	4	5.0	11 (3.7)	14	7.1
Vision blurred	1 (1.6)	1	2.5	1 (0.8)	1	1.3	1 (0.8)	1	1.3	3 (1.0)	3	1.5
Cataract	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Age-related macular degeneration	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Conjunctival haemorrhage	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Dry eye	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Eye pruritus	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Eyelid disorder	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Glaucoma	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Scleral disorder	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Visual acuity reduced	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Visual impairment	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Renal and urinary disorders	1 (1.6)	1	2.5	7 (5.9)	8	10.3	3 (2.5)	4	5.0	11 (3.7)	13	6.6
Pollakiuria	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Bladder pain	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Calculus urinary	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Chronic kidney disease	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Haematuria	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Micturition disorder	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Nephrolithiasis	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - entire trial population- safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Nocturia	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Polyuria	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Renal cyst	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Urinary incontinence	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Urinary tract obstruction	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Vascular disorders	1 (1.6)	1	2.5	5 (4.2)	6	7.7	5 (4.2)	5	6.3	11 (3.7)	12	6.1
Hypertension	1 (1.6)	1	2.5	4 (3.4)	4	5.2	4 (3.3)	4	5.0	9 (3.0)	9	4.6
Hot flush	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Orthostatic hypotension	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Psychiatric disorders	2 (3.3)	2	5.0	3 (2.5)	3	3.9	5 (4.2)	6	7.5	10 (3.3)	11	5.6
Sleep disorder	1 (1.6)	1	2.5	0			3 (2.5)	3	3.8	4 (1.3)	4	2.0
Anxiety	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Attention deficit/hyperactivity disorder	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Depression	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Emotional disorder	0			0			1 (0.8)	2	2.5	1 (0.3)	2	1.0
Insomnia	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Nervousness	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Blood and lymphatic system disorders	0			3 (2.5)	3	3.9	6 (5.0)	6	7.5	9 (3.0)	9	4.6
Anaemia	0			1 (0.8)	1	1.3	2 (1.7)	2	2.5	3 (1.0)	3	1.5
Lymphadenopathy	0			0			2 (1.7)	2	2.5	2 (0.7)	2	1.0
Haemoconcentration	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Iron deficiency anaemia	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Polycythaemia	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Thrombocytopenia	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Ear and labyrinth disorders	0			7 (5.9)	9	11.6	1 (0.8)	1	1.3	8 (2.7)	10	5.1
Ear pain	0			5 (4.2)	6	7.7	0			5 (1.7)	6	3.0
Vertigo	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Ear discomfort	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Tinnitus	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - entire trial population- safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Cardiac disorders	1 (1.6)	1	2.5	2 (1.7)	2	2.6	3 (2.5)	5	6.3	6 (2.0)	8	4.1
Aortic valve incompetence	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Bundle branch block right	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Cardiac discomfort	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Cardiovascular disorder	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Left ventricular dysfunction	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Mitral valve incompetence	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Palpitations	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Sinus arrhythmia	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Immune system disorders	2 (3.3)	2	5.0	2 (1.7)	2	2.6	2 (1.7)	2	2.5	6 (2.0)	6	3.0
Seasonal allergy	1 (1.6)	1	2.5	0			2 (1.7)	2	2.5	3 (1.0)	3	1.5
Allergy to plants	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Allergy to vaccine	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Food allergy	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Reproductive system and breast disorders	2 (3.3)	2	5.0	2 (1.7)	2	2.6	1 (0.8)	1	1.3	5 (1.7)	5	2.5
Dysmenorrhoea	2 (3.3)	2	5.0	0			0			2 (0.7)	2	1.0
Cervical dysplasia	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Nipple pain	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Vaginal discharge	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			3 (2.5)	3	3.9	0			3 (1.0)	3	1.5
Angiomyolipoma	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Melanocytic naevus	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Plasma cell myeloma	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Surgical and medical procedures	1 (1.6)	1	2.5	1 (0.8)	1	1.3	1 (0.8)	1	1.3	3 (1.0)	3	1.5
Tooth extraction	1 (1.6)	1	2.5	0			1 (0.8)	1	1.3	2 (0.7)	2	1.0
Skin operation	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Hepatobiliary disorders	0			2 (1.7)	3	3.9	0			2 (0.7)	3	1.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - entire trial population- safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Cholelithiasis	0			1 (0.8)	2	2.6	0			1 (0.3)	2	1.0
Hepatic cirrhosis	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Congenital, familial and genetic disorders	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Myotonia congenita	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Product issues	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Device malfunction	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

16 Adverse Events by system organ class and preferred term – 4054 main trial – Japanese subgroup – safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	10			18			18			46		
Total patient years	6.7			12.1			12.1			31.0		
All adverse events	9 (90.0)	25	371.5	18 (100.0)	46	379.4	11 (61.1)	38	313.4	38 (82.6)	109	351.9
Infections and infestations	7 (70.0)	9	133.7	11 (61.1)	15	123.7	7 (38.9)	14	115.5	25 (54.3)	38	122.7
Nasopharyngitis	4 (40.0)	5	74.3	9 (50.0)	10	82.5	6 (33.3)	9	74.2	19 (41.3)	24	77.5
Gastroenteritis	0			1 (5.6)	1	8.2	1 (5.6)	1	8.2	2 (4.3)	2	6.5
Tonsillitis	0			0			2 (11.1)	2	16.5	2 (4.3)	2	6.5
Upper respiratory tract infection	0			1 (5.6)	1	8.2	1 (5.6)	1	8.2	2 (4.3)	2	6.5
Cystitis	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Herpes zoster	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Laryngitis	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Molluscum contagiosum	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Periodontitis	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Pharyngitis	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Sinusitis	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Tinea infection	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Musculoskeletal and connective tissue disorders	2 (20.0)	2	29.7	8 (44.4)	9	74.2	3 (16.7)	4	33.0	13 (28.3)	15	48.4
Arthralgia	0			2 (11.1)	2	16.5	2 (11.1)	2	16.5	4 (8.7)	4	12.9
Pain in extremity	0			3 (16.7)	3	24.7	0			3 (6.5)	3	9.7
Back pain	0			1 (5.6)	1	8.2	1 (5.6)	1	8.2	2 (4.3)	2	6.5
Limb discomfort	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Muscular weakness	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Musculoskeletal chest pain	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Myalgia	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Nodal osteoarthritis	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Periarthritis	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
General disorders and administration site conditions	1 (10.0)	1	14.9	5 (27.8)	5	41.2	4 (22.2)	4	33.0	10 (21.7)	10	32.3
Oedema peripheral	0			2 (11.1)	2	16.5	2 (11.1)	2	16.5	4 (8.7)	4	12.9
Face oedema	0			1 (5.6)	1	8.2	1 (5.6)	1	8.2	2 (4.3)	2	6.5
Malaise	0			1 (5.6)	1	8.2	1 (5.6)	1	8.2	2 (4.3)	2	6.5
Asthenia	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Fat tissue decreased	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Gastrointestinal disorders	0			3 (16.7)	3	24.7	3 (16.7)	5	41.2	6 (13.0)	8	25.8
Dental caries	0			2 (11.1)	2	16.5	0			2 (4.3)	2	6.5
Vomiting	0			0			2 (11.1)	2	16.5	2 (4.3)	2	6.5
Abdominal pain upper	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Diarrhoea	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Dyspepsia	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Gastritis	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Investigations	3 (30.0)	6	89.2	2 (11.1)	3	24.7	1 (5.6)	1	8.2	6 (13.0)	10	32.3
Alanine aminotransferase increased	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Aspartate aminotransferase increased	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Blood creatine phosphokinase increased	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Blood insulin decreased	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Blood pressure increased	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Electrocardiogram T wave abnormal	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Hepatic enzyme increased	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Thyroxine free decreased	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Tri-iodothyronine decreased	0			1 (5.6)	2	16.5	0			1 (2.2)	2	6.5
Metabolism and nutrition disorders	4 (40.0)	5	74.3	2 (11.1)	2	16.5	0			6 (13.0)	7	22.6
Dehydration	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Diabetes mellitus	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Gout	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Hyperkalaemia	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hyperlipidaemia	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Hyponatraemia	1 (10.0)	2	29.7	0			0			1 (2.2)	2	6.5
Skin and subcutaneous tissue disorders	0			1 (5.6)	1	8.2	4 (22.2)	4	33.0	5 (10.9)	5	16.1
Haemorrhage subcutaneous	0			1 (5.6)	1	8.2	1 (5.6)	1	8.2	2 (4.3)	2	6.5
Dermatitis contact	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Rash	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Urticaria	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Nervous system disorders	0			2 (11.1)	2	16.5	2 (11.1)	4	33.0	4 (8.7)	6	19.4
Headache	0			2 (11.1)	2	16.5	1 (5.6)	1	8.2	3 (6.5)	3	9.7
Dizziness	0			0			1 (5.6)	2	16.5	1 (2.2)	2	6.5
Somnolence	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Injury, poisoning and procedural complications	1 (10.0)	1	14.9	0			1 (5.6)	1	8.2	2 (4.3)	2	6.5
Tooth fracture	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Wrist fracture	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Respiratory, thoracic and mediastinal disorders	0			1 (5.6)	2	16.5	1 (5.6)	1	8.2	2 (4.3)	3	9.7
Asthma	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Cough	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Rhinitis allergic	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Endocrine disorders	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Hypothyroidism	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Plasma cell myeloma	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Psychiatric disorders	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Insomnia	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Renal and urinary disorders	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Pollakiuria	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Vascular disorders	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Hypertension	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

17 Adverse Events by system organ class and preferred term – 4043 – entire trial population– safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All adverse events	21 (67.7)	81	530.8	53 (86.9)	159	514.2	74 (80.4)	240	519.7
Infections and infestations	12 (38.7)	18	117.9	23 (37.7)	30	97.0	35 (38.0)	48	103.9
Nasopharyngitis	8 (25.8)	11	72.1	12 (19.7)	13	42.0	20 (21.7)	24	52.0
Gastroenteritis	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Hordeolum	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Influenza	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Sinusitis	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Urinary tract infection	0			2 (3.3)	3	9.7	2 (2.2)	3	6.5
Abscess	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Bronchitis	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Conjunctivitis	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Device related sepsis	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Fungal infection	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Gastroenteritis viral	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Herpes zoster	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Lower respiratory tract infection	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Lung infection	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Otitis media	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Parotitis	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Upper respiratory tract infection	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Vulvovaginal mycotic infection	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
General disorders and administration site conditions	9 (29.0)	9	59.0	15 (24.6)	20	64.7	24 (26.1)	29	62.8
Fatigue	5 (16.1)	5	32.8	6 (9.8)	7	22.6	11 (12.0)	12	26.0
Asthenia	1 (3.2)	1	6.6	4 (6.6)	5	16.2	5 (5.4)	6	13.0
Malaise	1 (3.2)	1	6.6	2 (3.3)	2	6.5	3 (3.3)	3	6.5
Pain	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4043 - entire trial population- safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Pyrexia	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Inflammatory pain	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Influenza like illness	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Pre-existing condition improved	0			1 (1.6)	2	6.5	1 (1.1)	2	4.3
Nervous system disorders	10 (32.3)	17	111.4	13 (21.3)	19	61.4	23 (25.0)	36	78.0
Headache	6 (19.4)	10	65.5	7 (11.5)	11	35.6	13 (14.1)	21	45.5
Dizziness	3 (9.7)	3	19.7	1 (1.6)	1	3.2	4 (4.3)	4	8.7
Sciatica	0			4 (6.6)	4	12.9	4 (4.3)	4	8.7
Disturbance in attention	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Carpal tunnel syndrome	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Hypoaesthesia	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Hyposmia	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Paraesthesia	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Somnolence	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Gastrointestinal disorders	3 (9.7)	4	26.2	17 (27.9)	23	74.4	20 (21.7)	27	58.5
Abdominal pain	0			4 (6.6)	4	12.9	4 (4.3)	4	8.7
Abdominal pain upper	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Dental caries	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Diarrhoea	0			2 (3.3)	3	9.7	2 (2.2)	3	6.5
Vomiting	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Abdominal discomfort	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Barrett's oesophagus	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Colitis	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Constipation	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Dry mouth	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Faeces soft	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Gastrooesophageal reflux disease	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Intestinal ischaemia	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Irritable bowel syndrome	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Large intestine polyp	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Nausea	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Reflux gastritis	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4043 - entire trial population- safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Short-bowel syndrome	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Toothache	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Musculoskeletal and connective tissue disorders	5 (16.1)	7	45.9	14 (23.0)	18	58.2	19 (20.7)	25	54.1
Arthralgia	2 (6.5)	2	13.1	5 (8.2)	5	16.2	7 (7.6)	7	15.2
Back pain	1 (3.2)	2	13.1	3 (4.9)	3	9.7	4 (4.3)	5	10.8
Muscle spasms	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Musculoskeletal pain	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Myalgia	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Coccydynia	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Joint swelling	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Muscular weakness	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Osteoarthritis	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Pain in extremity	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Tendon pain	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Tenosynovitis	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Investigations	3 (9.7)	7	45.9	8 (13.1)	11	35.6	11 (12.0)	18	39.0
Weight increased	1 (3.2)	1	6.6	3 (4.9)	3	9.7	4 (4.3)	4	8.7
Blood creatine phosphokinase increased	0			3 (4.9)	3	9.7	3 (3.3)	3	6.5
Gamma-glutamyltransferase increased	2 (6.5)	2	13.1	0			2 (2.2)	2	4.3
Alanine aminotransferase increased	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Aspartate aminotransferase increased	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Blood calcium decreased	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Blood corticotrophin decreased	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Blood insulin increased	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Blood potassium decreased	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Blood thyroid stimulating hormone decreased	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Glomerular filtration rate decreased	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4043 - entire trial population- safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hormone level abnormal	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Injury, poisoning and procedural complications	2 (6.5)	2	13.1	7 (11.5)	8	25.9	9 (9.8)	10	21.7
Concussion	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Fall	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Heat illness	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Meniscus injury	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Muscle strain	0			1 (1.6)	2	6.5	1 (1.1)	2	4.3
Patella fracture	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Procedural complication	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Spinal column injury	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Wound	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Endocrine disorders	3 (9.7)	3	19.7	3 (4.9)	3	9.7	6 (6.5)	6	13.0
Hypothyroidism	2 (6.5)	2	13.1	1 (1.6)	1	3.2	3 (3.3)	3	6.5
Adrenal insufficiency	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Adrenocortical insufficiency acute	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Secondary hypothyroidism	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Psychiatric disorders	2 (6.5)	3	19.7	4 (6.6)	4	12.9	6 (6.5)	7	15.2
Sleep disorder	1 (3.2)	1	6.6	2 (3.3)	2	6.5	3 (3.3)	3	6.5
Depression	2 (6.5)	2	13.1	0			2 (2.2)	2	4.3
Anxiety	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Initial insomnia	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Skin and subcutaneous tissue disorders	2 (6.5)	2	13.1	4 (6.6)	5	16.2	6 (6.5)	7	15.2
Alopecia	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Rash	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Hair disorder	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Onychoclasis	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Pruritus	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4043 - entire trial population- safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Ear and labyrinth disorders	1 (3.2)	1	6.6	3 (4.9)	3	9.7	4 (4.3)	4	8.7
Vertigo	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Tinnitus	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Vertigo positional	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Metabolism and nutrition disorders	0			3 (4.9)	3	9.7	3 (3.3)	3	6.5
Fat redistribution	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Hypokalaemia	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Increased appetite	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Reproductive system and breast disorders	0			3 (4.9)	3	9.7	3 (3.3)	3	6.5
Breast disorder	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Dysmenorrhoea	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Menstruation irregular	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Respiratory, thoracic and mediastinal disorders	2 (6.5)	4	26.2	1 (1.6)	1	3.2	3 (3.3)	5	10.8
Epistaxis	1 (3.2)	3	19.7	0			1 (1.1)	3	6.5
Oropharyngeal pain	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Sleep apnoea syndrome	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Surgical and medical procedures	0			3 (4.9)	3	9.7	3 (3.3)	3	6.5
Dental care	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Dental operation	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Mammoplasty	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Eye disorders	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Dry eye	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Eye swelling	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Hepatobiliary disorders	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Cholelithiasis	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4043 - entire trial population- safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Renal and urinary disorders	1 (3.2)	1	6.6	1 (1.6)	2	6.5	2 (2.2)	3	6.5
Dysuria	0			1 (1.6)	2	6.5	1 (1.1)	2	4.3
Nephrolithiasis	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Cardiac disorders	1 (3.2)	2	13.1	0			1 (1.1)	2	4.3
Atrial flutter	1 (3.2)	2	13.1	0			1 (1.1)	2	4.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

18 Adverse Events by system organ class and preferred term – 4043 – Japanese subgroup – safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	6			11			17		
Total patient years	3.1			5.7			8.8		
All adverse events	1 (16.7)	4	128.0	11 (100.0)	36	634.6	12 (70.6)	40	454.7
Gastrointestinal disorders	0			7 (63.6)	10	176.3	7 (41.2)	10	113.7
Diarrhoea	0			2 (18.2)	3	52.9	2 (11.8)	3	34.1
Abdominal pain	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Colitis	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Constipation	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Dental caries	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Dry mouth	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Faeces soft	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Large intestine polyp	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Infections and infestations	1 (16.7)	1	32.0	6 (54.5)	7	123.4	7 (41.2)	8	90.9
Nasopharyngitis	1 (16.7)	1	32.0	4 (36.4)	4	70.5	5 (29.4)	5	56.8
Influenza	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Otitis media	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Sinusitis	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Musculoskeletal and connective tissue disorders	0			5 (45.5)	6	105.8	5 (29.4)	6	68.2
Arthralgia	0			2 (18.2)	2	35.3	2 (11.8)	2	22.7
Back pain	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Myalgia	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Pain in extremity	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Tenosynovitis	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Injury, poisoning and procedural complications	0			4 (36.4)	5	88.1	4 (23.5)	5	56.8
Fall	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - 4043 - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Heat illness	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Muscle strain	0			1 (9.1)	2	35.3	1 (5.9)	2	22.7
Patella fracture	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
General disorders and administration site conditions	0			2 (18.2)	2	35.3	2 (11.8)	2	22.7
Malaise	0			2 (18.2)	2	35.3	2 (11.8)	2	22.7
Endocrine disorders	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Adrenal insufficiency	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Eye disorders	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Dry eye	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Investigations	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Blood insulin increased	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Nervous system disorders	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Dizziness	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Reproductive system and breast disorders	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Menstruation irregular	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Respiratory, thoracic and mediastinal disorders	1 (16.7)	3	96.0	0			1 (5.9)	3	34.1
Epistaxis	1 (16.7)	3	96.0	0			1 (5.9)	3	34.1
Skin and subcutaneous tissue disorders	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Rash	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

19 Possibly or probably related adverse events by system organ class and preferred term - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	61			119			120			300		
Total patient years	39.8			77.5			79.9			197.2		
All possibly or probably related adverse events	12 (19.7)	19	47.7	37 (31.1)	76	98.0	29 (24.2)	94	117.7	78 (26.0)	189	95.8
General disorders and administration site conditions	4 (6.6)	7	17.6	17 (14.3)	23	29.7	6 (5.0)	9	11.3	27 (9.0)	39	19.8
Oedema peripheral	0			6 (5.0)	8	10.3	3 (2.5)	3	3.8	9 (3.0)	11	5.6
Injection site bruising	2 (3.3)	3	7.5	4 (3.4)	4	5.2	1 (0.8)	1	1.3	7 (2.3)	8	4.1
Fatigue	1 (1.6)	1	2.5	2 (1.7)	2	2.6	1 (0.8)	1	1.3	4 (1.3)	4	2.0
Injection site pain	1 (1.6)	1	2.5	1 (0.8)	1	1.3	1 (0.8)	2	2.5	3 (1.0)	4	2.0
Face oedema	1 (1.6)	1	2.5	1 (0.8)	1	1.3	0			2 (0.7)	2	1.0
Injection site reaction	0			1 (0.8)	1	1.3	1 (0.8)	2	2.5	2 (0.7)	3	1.5
Peripheral swelling	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Fat tissue decreased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Influenza like illness	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Injection site haematoma	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Pain	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Pre-existing condition improved	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Musculoskeletal and connective tissue disorders	1 (1.6)	1	2.5	12 (10.1)	19	24.5	9 (7.5)	10	12.5	22 (7.3)	30	15.2
Arthralgia	1 (1.6)	1	2.5	6 (5.0)	6	7.7	4 (3.3)	4	5.0	11 (3.7)	11	5.6
Back pain	0			1 (0.8)	1	1.3	2 (1.7)	2	2.5	3 (1.0)	3	1.5
Joint stiffness	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Joint swelling	0			2 (1.7)	3	3.9	0			2 (0.7)	3	1.5
Myalgia	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Intervertebral disc protrusion	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Joint noise	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Limb deformity	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Possibly or probably related adverse events by system organ class and preferred term - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Limb discomfort	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Muscular weakness	0			0			1 (0.8)	2	2.5	1 (0.3)	2	1.0
Musculoskeletal pain	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Musculoskeletal stiffness	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Pain in extremity	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Nervous system disorders	4 (6.6)	4	10.0	6 (5.0)	8	10.3	9 (7.5)	43	53.8	19 (6.3)	55	27.9
Headache	2 (3.3)	2	5.0	3 (2.5)	4	5.2	6 (5.0)	37	46.3	11 (3.7)	43	21.8
Dizziness	1 (1.6)	1	2.5	2 (1.7)	3	3.9	1 (0.8)	2	2.5	4 (1.3)	6	3.0
Paraesthesia	1 (1.6)	1	2.5	0			1 (0.8)	1	1.3	2 (0.7)	2	1.0
Hypersomnia	0			0			1 (0.8)	2	2.5	1 (0.3)	2	1.0
Hypoaesthesia	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Somnolence	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Investigations	3 (4.9)	3	7.5	4 (3.4)	8	10.3	4 (3.3)	9	11.3	11 (3.7)	20	10.1
Alanine aminotransferase increased	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Glycosylated haemoglobin increased	0			1 (0.8)	2	2.6	1 (0.8)	1	1.3	2 (0.7)	3	1.5
Thyroxine free decreased	1 (1.6)	1	2.5	0			1 (0.8)	2	2.5	2 (0.7)	3	1.5
Weight increased	0			1 (0.8)	1	1.3	1 (0.8)	1	1.3	2 (0.7)	2	1.0
Blood alkaline phosphatase increased	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Blood bilirubin increased	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Blood creatine phosphokinase increased	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Blood glucose increased	0			1 (0.8)	2	2.6	0			1 (0.3)	2	1.0
Blood insulin decreased	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Blood testosterone decreased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Gamma-glutamyltransferase increased	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Weight decreased	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
White blood cell count increased	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Skin and subcutaneous tissue disorders	3 (4.9)	4	10.0	2 (1.7)	2	2.6	6 (5.0)	7	8.8	11 (3.7)	13	6.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Possibly or probably related adverse events by system organ class and preferred term - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Lipohypertrophy	0			0			2 (1.7)	2	2.5	2 (0.7)	2	1.0
Acne	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Alopecia	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Dry skin	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Ecchymosis	1 (1.6)	1	2.5	0			0			1 (0.3)	1	0.5
Exfoliative rash	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Haemorrhage subcutaneous	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Lipodystrophy acquired	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Pruritus generalised	1 (1.6)	2	5.0	0			0			1 (0.3)	2	1.0
Pustular psoriasis	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Skin mass	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Gastrointestinal disorders	0			3 (2.5)	3	3.9	4 (3.3)	9	11.3	7 (2.3)	12	6.1
Abdominal pain upper	0			0			2 (1.7)	2	2.5	2 (0.7)	2	1.0
Abdominal discomfort	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Constipation	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Diarrhoea	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Dry mouth	0			0			1 (0.8)	2	2.5	1 (0.3)	2	1.0
Epigastric discomfort	0			0			1 (0.8)	3	3.8	1 (0.3)	3	1.5
Flatulence	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Nausea	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Injury, poisoning and procedural complications	0			1 (0.8)	1	1.3	2 (1.7)	2	2.5	3 (1.0)	3	1.5
Contusion	0			1 (0.8)	1	1.3	2 (1.7)	2	2.5	3 (1.0)	3	1.5
Metabolism and nutrition disorders	0			2 (1.7)	2	2.6	1 (0.8)	2	2.5	3 (1.0)	4	2.0
Diabetes mellitus	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Fluid retention	0			0			1 (0.8)	2	2.5	1 (0.3)	2	1.0
Obesity	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Vascular disorders	0			3 (2.5)	3	3.9	0			3 (1.0)	3	1.5
Hot flush	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Possibly or probably related adverse events by system organ class and preferred term - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hypertension	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Orthostatic hypotension	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Endocrine disorders	0			0			2 (1.7)	2	2.5	2 (0.7)	2	1.0
Adrenal insufficiency	0			0			2 (1.7)	2	2.5	2 (0.7)	2	1.0
Eye disorders	0			2 (1.7)	2	2.6	0			2 (0.7)	2	1.0
Glaucoma	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Vision blurred	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Blood and lymphatic system disorders	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Haemoconcentration	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Ear and labyrinth disorders	0			1 (0.8)	2	2.6	0			1 (0.3)	2	1.0
Ear pain	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Tinnitus	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Infections and infestations	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Fungal infection	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Reproductive system and breast disorders	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Nipple pain	0			0			1 (0.8)	1	1.3	1 (0.3)	1	0.5
Respiratory, thoracic and mediastinal disorders	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5
Snoring	0			1 (0.8)	1	1.3	0			1 (0.3)	1	0.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

20 Possibly or probably related adverse events by system organ class and preferred term - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	10			18			18			46		
Total patient years	6.7			12.1			12.1			31.0		
All possibly or probably related adverse events	2 (20.0)	2	29.7	9 (50.0)	11	90.7	4 (22.2)	9	74.2	15 (32.6)	22	71.0
General disorders and administration site conditions	0			4 (22.2)	4	33.0	2 (11.1)	2	16.5	6 (13.0)	6	19.4
Oedema peripheral	0			2 (11.1)	2	16.5	2 (11.1)	2	16.5	4 (8.7)	4	12.9
Face oedema	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Fat tissue decreased	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Musculoskeletal and connective tissue disorders	0			4 (22.2)	5	41.2	2 (11.1)	2	16.5	6 (13.0)	7	22.6
Arthralgia	0			2 (11.1)	2	16.5	1 (5.6)	1	8.2	3 (6.5)	3	9.7
Back pain	0			1 (5.6)	1	8.2	1 (5.6)	1	8.2	2 (4.3)	2	6.5
Limb discomfort	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Pain in extremity	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Investigations	2 (20.0)	2	29.7	0			0			2 (4.3)	2	6.5
Blood insulin decreased	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Thyroxine free decreased	1 (10.0)	1	14.9	0			0			1 (2.2)	1	3.2
Gastrointestinal disorders	0			0			1 (5.6)	2	16.5	1 (2.2)	2	6.5
Abdominal pain upper	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Diarrhoea	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Metabolism and nutrition disorders	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Diabetes mellitus	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Nervous system disorders	0			0			1 (5.6)	3	24.7	1 (2.2)	3	9.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Possibly or probably related adverse events by system organ class and preferred term - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Dizziness	0			0			1 (5.6)	2	16.5	1 (2.2)	2	6.5
Somnolence	0			0			1 (5.6)	1	8.2	1 (2.2)	1	3.2
Skin and subcutaneous tissue disorders	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2
Haemorrhage subcutaneous	0			1 (5.6)	1	8.2	0			1 (2.2)	1	3.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

21 Possibly or probably related adverse events by system organ class and preferred term - 4043 - entire trial population - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	31			61			92		
Total patient years	15.3			30.9			46.2		
All possibly or probably related adverse events	6 (19.4)	13	85.2	16 (26.2)	29	93.8	22 (23.9)	42	90.9
General disorders and administration site conditions	6 (19.4)	6	39.3	10 (16.4)	13	42.0	16 (17.4)	19	41.1
Fatigue	4 (12.9)	4	26.2	5 (8.2)	6	19.4	9 (9.8)	10	21.7
Asthenia	1 (3.2)	1	6.6	3 (4.9)	3	9.7	4 (4.3)	4	8.7
Malaise	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Pain	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Pre-existing condition improved	0			1 (1.6)	2	6.5	1 (1.1)	2	4.3
Nervous system disorders	2 (6.5)	4	26.2	4 (6.6)	5	16.2	6 (6.5)	9	19.5
Headache	2 (6.5)	2	13.1	2 (3.3)	2	6.5	4 (4.3)	4	8.7
Disturbance in attention	1 (3.2)	1	6.6	1 (1.6)	1	3.2	2 (2.2)	2	4.3
Dizziness	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Paraesthesia	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Somnolence	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Investigations	2 (6.5)	3	19.7	3 (4.9)	5	16.2	5 (5.4)	8	17.3
Weight increased	1 (3.2)	1	6.6	3 (4.9)	3	9.7	4 (4.3)	4	8.7
Blood creatine phosphokinase increased	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Gamma-glutamyltransferase increased	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Glomerular filtration rate decreased	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Hormone level abnormal	1 (3.2)	1	6.6	0			1 (1.1)	1	2.2
Metabolism and nutrition disorders	0			2 (3.3)	2	6.5	2 (2.2)	2	4.3
Fat redistribution	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Possibly or probably related adverse events by system organ class and preferred term - 4043 - entire trial population - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hypokalaemia	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Gastrointestinal disorders	0			1 (1.6)	2	6.5	1 (1.1)	2	4.3
Diarrhoea	0			1 (1.6)	2	6.5	1 (1.1)	2	4.3
Infections and infestations	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Gastroenteritis	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Musculoskeletal and connective tissue disorders	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2
Arthralgia	0			1 (1.6)	1	3.2	1 (1.1)	1	2.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

22 Possibly or probably related adverse events by system organ class and preferred term - 4043 - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	6			11			17		
Total patient years	3.1			5.7			8.8		
All possibly or probably related adverse events	0			2 (18.2)	5	88.1	2 (11.8)	5	56.8
Gastrointestinal disorders	0			1 (9.1)	2	35.3	1 (5.9)	2	22.7
Diarrhoea	0			1 (9.1)	2	35.3	1 (5.9)	2	22.7
General disorders and administration site conditions	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Malaise	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Musculoskeletal and connective tissue disorders	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Arthralgia	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Nervous system disorders	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4
Dizziness	0			1 (9.1)	1	17.6	1 (5.9)	1	11.4

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

23 Adverse events with fatal outcome - 4054 - Japanese subgroup - listing safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ Norditropin/ 204012	M/70/25.8	2	Infections and infestations/ Pneumonia/ PNEUMONIA	2017-01-01	360/ extension/ 14	N	Y/N	SEVERE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
Norditropin/ no treatment/ 216003	M/60/28.0	2	Infections and infestations/ Influenza/ INFLUENZA	2017-12-27 T15:00	493/ extension/ 7	N	Y/N	MODERATE/ UNLIKELY/ -	NOT APPLICABLE

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:13:57 - l_ae_4054.sas/l_ae_fatal_4054_jpn_sas.txt

24 Adverse events with fatal outcome - 4043 - Japanese subgroup - listing safety analysis set

There is no data to display

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:13:57 - l_ae.sas/l_ae_fatal_4043_jpn_sas.txt

25 Serious adverse events - 4054 - Japanese subgroup - listing safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
placebo/ somapacitan/ 204008	M/52/29.2	1	Investigations/ Electrocardiogram T wave abnormal/ ELECTROCARDIOGRAM T WAVE ABNORMAL	2015-11-13	176/ main/ 63	Y	Y/N	MILD/ UNLIKELY/ -	DRUG INTERRUPTED
		6	Respiratory, thoracic and mediastinal disorders/ Sleep apnoea syndrome/ SLEEP APNEA SYNDROME	2016-03-31	315/ extension/ -	N	Y/N	MILD/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
placebo/ somapacitan/ 213001	F/72/18.1	9	Infections and infestations/ Urinary tract infection/ URINARY FRACT INFECTION	2018-01-05	583/ extension/ 10	Y	Y/N	MODERATE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
placebo/ somapacitan/ 214003	M/56/27.3	2	Metabolism and nutrition disorders/ Hyponatraemia/ HYPONATREMIA	2017-02-05 T13:00	177/ main/ 6	Y	Y/N	MODERATE/ UNLIKELY/ -	DOSE NOT CHANGED
Norditropin/ Norditropin/ 204012	M/70/25.8	2	Infections and infestations/ Pneumonia/ PNEUMONIA	2017-01-01	360/ extension/ 14	N	Y/N	SEVERE/ UNLIKELY/ UNLIKELY	DOSE NOT CHANGED
Norditropin/ somapacitan/ 211004	M/68/23.3	2	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Plasma cell myeloma/ MULTIPLE MYELOMA	2016-04-27 T10:30	146/ main/ -	N	Y/N	SEVERE/ UNLIKELY/ UNLIKELY	DRUG WITHDRAWN

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

Serious adverse events - 4054 - Japanese subgroup - listing safety analysis set

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
Norditropin/ no treatment/ 216003	M/60/28.0	2	Infections and infestations/ Influenza/ INFLUENZA	2017-12-27 T15:00	493/ extension/ 7	N	Y/N	MODERATE/ UNLIKELY/ -	NOT APPLICABLE

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

26 Serious adverse events - 4043 - Japanese subgroup - listing safety analysis set

Treatment group/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	Syatem Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality	Action Taken
somapacitan/ 403003	M/63/31.0	1	Injury, poisoning and procedural complications/ Patella fracture/ PATELLA FRACTURE	2015-06-19	26/165	Y	Y/N	MODERATE/ UNLIKELY	DOSE NOT CHANGED

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
*AE causality is based on judgement of investigators.
MedDRA version 21.0.

27 Adverse events leading to withdrawal from trial product - 4054 - Japanese subgroup - listing randomised subjects

Treatment group(main/ extension)/ Subject ID	Sex (M/F)/ Age (Y)/ BMI (kg/m^2)	AE no	System Organ Class/ Preferred Term/ Reported Term	Onset Date Time	Study Day/ Study Period/ Duration (Days)	Recovered or Recovering (Y/N)	Serious/ MESI (Y/N)	Severity/ Causality main**/ Causality ext**	Action Taken
placebo/ somapacitan/ 204008	M/52/29.2	12	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Pituitary tumour/ ENLARGEMENT OF THE RESIDUAL PITUITARY TUMOR	2016-11-29	558/ extension/ -	N	N/N	MILD/ UNLIKELY/ UNLIKELY	DRUG WITHDRAWN
Norditropin/ somapacitan/ 211004	M/68/23.3	2	Neoplasms benign, malignant and unspecified (incl cysts and polyps)/ Plasma cell myeloma/ MULTIPLE MYELOMA	2016-04-27 T10:30	146/ main/ -	N	Y/N	SEVERE/ UNLIKELY/ UNLIKELY	DRUG WITHDRAWN
Norditropin/ no treatment/ 216003	M/60/28.0	1	Metabolism and nutrition disorders/ Diabetes mellitus/ DIABETES MELLITUS	2017-02-14 T09:17	177/ main/ 60	Y	N/N	MILD/ PROBABLE/ -	DRUG WITHDRAWN

BMI: Body mass index, F: Female, M: Male, N: No, Y: Yes, yrs: Years
**AE causality to trial product given in main and extension respectively is based on judgement of investigators.
MedDRA version 21.0.

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:14:00 - l_ae_4054.sas/l_ae_wd_4054_jpn_sas.txt

28 Adverse events leading to withdrawal from trial product - 4043 - Japanese subgroup - listing randomised subjects

There is no data to display

nn8640/nn8640-summary/aghd_iss_fda_nda
09MAY2019:09:13:59 - l_ae.sas/l_ae_wd_4043_jpn_sas.txt

29 Adverse Events - Male - 4043 - entire trial population - safety analysis set

	Norditropin N	(%)	E	R	somapacitan N	(%)	E	R	total N	(%)	E	R
Subjects Exposed	17				33				50			
Total patient years	8.6				16.9				25.5			
All adverse events	11	(64.7)	39	453.5	26	(78.8)	69	407.5	37	(74.0)	108	423.0
Serious adverse events	2	(11.8)	3	34.9	2	(6.1)	2	11.8	4	(8.0)	5	19.6
Medical events of special interest	0				0				0			
Severity												
Mild	9	(52.9)	28	325.6	20	(60.6)	48	283.5	29	(58.0)	76	297.7
Moderate	4	(23.5)	7	81.4	9	(27.3)	18	106.3	13	(26.0)	25	97.9
Severe	2	(11.8)	4	46.5	3	(9.1)	3	17.7	5	(10.0)	7	27.4
Causality												
Unlikely	11	(64.7)	33	383.7	22	(66.7)	50	295.3	33	(66.0)	83	325.1
Possible	2	(11.8)	4	46.5	6	(18.2)	11	65.0	8	(16.0)	15	58.8
Probable	2	(11.8)	2	23.3	5	(15.2)	8	47.3	7	(14.0)	10	39.2
Outcome												
Recovered/Resolved	10	(58.8)	26	302.3	23	(69.7)	50	295.3	33	(66.0)	76	297.7
Recovering/Resolving	2	(11.8)	4	46.5	5	(15.2)	6	35.4	7	(14.0)	10	39.2
Recovered/Resolved With Sequelae	1	(5.9)	1	11.6	0				1	(2.0)	1	3.9
Not Recovered/Not Resolved	7	(41.2)	8	93.0	10	(30.3)	13	76.8	17	(34.0)	21	82.3
Action												
Drug Withdrawn	0				1	(3.0)	2	11.8	1	(2.0)	2	7.8
Dose Not Changed	10	(58.8)	37	430.3	25	(75.8)	60	354.4	35	(70.0)	97	379.9
Not Applicable	2	(11.8)	2	23.3	6	(18.2)	7	41.3	8	(16.0)	9	35.3

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

Adverse Events - Male - 4043 - entire trial population - safety analysis set

	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Treatment discontinuations due to adverse events	0			1 (3.0)	2	11.8	1 (2.0)	2	7.8

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

30 Adverse Events - Male - 4043 - Japanese subgroup - safety analysis set

	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	2			4			6		
Total patient years	1.0			2.1			3.1		
All adverse events	0			4 (100.0)	14	672.8	4 (66.7)	14	448.6
Serious adverse events	0			1 (25.0)	1	48.1	1 (16.7)	1	32.0
Medical events of special interest	0			0			0		
Severity									
Mild	0			4 (100.0)	13	624.8	4 (66.7)	13	416.5
Moderate	0			1 (25.0)	1	48.1	1 (16.7)	1	32.0
Causality									
Unlikely	0			4 (100.0)	12	576.7	4 (66.7)	12	384.5
Possible	0			1 (25.0)	2	96.1	1 (16.7)	2	64.1
Outcome									
Recovered/Resolved	0			4 (100.0)	12	576.7	4 (66.7)	12	384.5
Recovering/Resolving	0			1 (25.0)	1	48.1	1 (16.7)	1	32.0
Not Recovered/Not Resolved	0			1 (25.0)	1	48.1	1 (16.7)	1	32.0
Action									
Dose Not Changed	0			4 (100.0)	13	624.8	4 (66.7)	13	416.5
Not Applicable	0			1 (25.0)	1	48.1	1 (16.7)	1	32.0
Treatment discontinuations due to adverse events	0			0			0		

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

31 Adverse Events - Female - 4043 - entire trial population - safety analysis set

	Norditropin N	(%)	E	R	somapacitan N	(%)	E	R	total N	(%)	E	R
Subjects Exposed	14				28				42			
Total patient years	6.7				14.0				20.7			
All adverse events	10	(71.4)	42	630.5	27	(96.4)	90	643.3	37	(88.1)	132	639.2
Serious adverse events	0				2	(7.1)	2	14.3	2	(4.8)	2	9.7
Medical events of special interest	0				0				0			
Severity												
Mild	9	(64.3)	30	450.4	24	(85.7)	71	507.5	33	(78.6)	101	489.1
Moderate	4	(28.6)	12	180.1	7	(25.0)	14	100.1	11	(26.2)	26	125.9
Severe	0				2	(7.1)	5	35.7	2	(4.8)	5	24.2
Causality												
Unlikely	10	(71.4)	35	525.4	24	(85.7)	80	571.8	34	(81.0)	115	556.9
Possible	1	(7.1)	1	15.0	3	(10.7)	4	28.6	4	(9.5)	5	24.2
Probable	2	(14.3)	6	90.1	3	(10.7)	6	42.9	5	(11.9)	12	58.1
Outcome												
Recovered/Resolved	10	(71.4)	31	465.4	23	(82.1)	59	421.7	33	(78.6)	90	435.8
Recovering/Resolving	2	(14.3)	2	30.0	4	(14.3)	4	28.6	6	(14.3)	6	29.1
Not Recovered/Not Resolved	3	(21.4)	9	135.1	12	(42.9)	26	185.8	15	(35.7)	35	169.5
Unknown	0				1	(3.6)	1	7.1	1	(2.4)	1	4.8
Action												
Drug Withdrawn	1	(7.1)	4	60.0	0				1	(2.4)	4	19.4
Dose Not Changed	10	(71.4)	37	555.5	27	(96.4)	86	614.7	37	(88.1)	123	595.6
Not Applicable	1	(7.1)	1	15.0	3	(10.7)	4	28.6	4	(9.5)	5	24.2

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

Adverse Events - Female - 4043 - entire trial population - safety analysis set

	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Treatment discontinuations due to adverse events	1 (7.1)	4	60.0	0			1 (2.4)	4	19.4

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

32 Adverse Events - Female - 4043 - Japanese subgroup - safety analysis set

	Norditropin N	(%)	E	R	somapacitan N	(%)	E	R	total N	(%)	E	R
Subjects Exposed	4				7				11			
Total patient years	2.1				3.6				5.7			
All adverse events	1	(25.0)	4	192.0	7	(100.0)	22	612.5	8	(72.7)	26	458.1
Serious adverse events	0				0				0			
Medical events of special interest	0				0				0			
Severity												
Mild	1	(25.0)	4	192.0	7	(100.0)	22	612.5	8	(72.7)	26	458.1
Causality												
Unlikely	1	(25.0)	4	192.0	7	(100.0)	19	528.9	8	(72.7)	23	405.2
Probable	0				1	(14.3)	3	83.5	1	(9.1)	3	52.9
Outcome												
Recovered/Resolved	1	(25.0)	4	192.0	7	(100.0)	16	445.4	8	(72.7)	20	352.4
Recovering/Resolving	0				1	(14.3)	1	27.8	1	(9.1)	1	17.6
Not Recovered/Not Resolved	0				3	(42.9)	5	139.2	3	(27.3)	5	88.1
Action												
Dose Not Changed	1	(25.0)	4	192.0	7	(100.0)	20	556.8	8	(72.7)	24	422.9
Not Applicable	0				1	(14.3)	2	55.7	1	(9.1)	2	35.2
Treatment discontinuations due to adverse events	0				0				0			

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

33 Adverse Events by system organ class and preferred term - Male - 4043 - entire trial population - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	17			33			50		
Total patient years	8.6			16.9			25.5		
All adverse events	11 (64.7)	39	453.5	26 (78.8)	69	407.5	37 (74.0)	108	423.0
Infections and infestations	6 (35.3)	8	93.0	9 (27.3)	11	65.0	15 (30.0)	19	74.4
Nasopharyngitis	3 (17.6)	3	34.9	4 (12.1)	4	23.6	7 (14.0)	7	27.4
Hordeolum	1 (5.9)	1	11.6	1 (3.0)	1	5.9	2 (4.0)	2	7.8
Conjunctivitis	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Device related sepsis	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Gastroenteritis	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Gastroenteritis viral	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Herpes zoster	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Influenza	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Lower respiratory tract infection	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Lung infection	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Parotitis	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Upper respiratory tract infection	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
General disorders and administration site conditions	4 (23.5)	4	46.5	9 (27.3)	12	70.9	13 (26.0)	16	62.7
Fatigue	3 (17.6)	3	34.9	5 (15.2)	6	35.4	8 (16.0)	9	35.3
Asthenia	0			2 (6.1)	2	11.8	2 (4.0)	2	7.8
Malaise	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Pain	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Pre-existing condition improved	0			1 (3.0)	2	11.8	1 (2.0)	2	7.8
Pyrexia	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Gastrointestinal disorders	1 (5.9)	2	23.3	9 (27.3)	11	65.0	10 (20.0)	13	50.9
Diarrhoea	0			2 (6.1)	3	17.7	2 (4.0)	3	11.8
Abdominal pain	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Abdominal pain upper	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Male - 4043 - entire trial population - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Constipation	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Dental caries	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Faeces soft	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Intestinal ischaemia	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Irritable bowel syndrome	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Large intestine polyp	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Short-bowel syndrome	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Toothache	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Nervous system disorders	5 (29.4)	5	58.1	4 (12.1)	7	41.3	9 (18.0)	12	47.0
Headache	3 (17.6)	3	34.9	2 (6.1)	4	23.6	5 (10.0)	7	27.4
Sciatica	0			2 (6.1)	2	11.8	2 (4.0)	2	7.8
Disturbance in attention	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Dizziness	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Hyposmia	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Investigations	2 (11.8)	5	58.1	6 (18.2)	9	53.2	8 (16.0)	14	54.8
Blood creatine phosphokinase increased	0			3 (9.1)	3	17.7	3 (6.0)	3	11.8
Gamma-glutamyltransferase increased	2 (11.8)	2	23.3	0			2 (4.0)	2	7.8
Weight increased	0			2 (6.1)	2	11.8	2 (4.0)	2	7.8
Alanine aminotransferase increased	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Aspartate aminotransferase increased	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Blood calcium decreased	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Blood corticotrophin decreased	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Blood potassium decreased	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Blood thyroid stimulating hormone decreased	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Glomerular filtration rate decreased	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Musculoskeletal and connective tissue disorders	2 (11.8)	4	46.5	6 (18.2)	7	41.3	8 (16.0)	11	43.1

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Male - 4043 - entire trial population - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Arthralgia	0			2 (6.1)	2	11.8	2 (4.0)	2	7.8
Back pain	1 (5.9)	2	23.3	0			1 (2.0)	2	7.8
Joint swelling	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Muscle spasms	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Muscular weakness	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Osteoarthritis	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Pain in extremity	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Tendon pain	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Tenosynovitis	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Injury, poisoning and procedural complications	2 (11.8)	2	23.3	3 (9.1)	4	23.6	5 (10.0)	6	23.5
Concussion	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Meniscus injury	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Muscle strain	0			1 (3.0)	2	11.8	1 (2.0)	2	7.8
Patella fracture	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Wound	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Endocrine disorders	3 (17.6)	3	34.9	1 (3.0)	1	5.9	4 (8.0)	4	15.7
Hypothyroidism	2 (11.8)	2	23.3	0			2 (4.0)	2	7.8
Adrenocortical insufficiency acute	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Secondary hypothyroidism	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Psychiatric disorders	1 (5.9)	2	23.3	1 (3.0)	1	5.9	2 (4.0)	3	11.8
Anxiety	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Depression	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Sleep disorder	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Respiratory, thoracic and mediastinal disorders	1 (5.9)	1	11.6	1 (3.0)	1	5.9	2 (4.0)	2	7.8
Oropharyngeal pain	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Sleep apnoea syndrome	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Surgical and medical procedures	0			2 (6.1)	2	11.8	2 (4.0)	2	7.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Male - 4043 - entire trial population - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Dental care	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Dental operation	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Cardiac disorders	1 (5.9)	2	23.3	0			1 (2.0)	2	7.8
Atrial flutter	1 (5.9)	2	23.3	0			1 (2.0)	2	7.8
Ear and labyrinth disorders	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Vertigo	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Hepatobiliary disorders	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Cholelithiasis	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Renal and urinary disorders	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Nephrolithiasis	1 (5.9)	1	11.6	0			1 (2.0)	1	3.9
Skin and subcutaneous tissue disorders	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9
Pruritus	0			1 (3.0)	1	5.9	1 (2.0)	1	3.9

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

34 Adverse Events by system organ class and preferred term - Male - 4043 - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	2			4			6		
Total patient years	1.0			2.1			3.1		
All adverse events	0			4 (100.0)	14	672.8	4 (66.7)	14	448.6
Gastrointestinal disorders	0			4 (100.0)	6	288.4	4 (66.7)	6	192.2
Diarrhoea	0			2 (50.0)	3	144.2	2 (33.3)	3	96.1
Constipation	0			1 (25.0)	1	48.1	1 (16.7)	1	32.0
Faeces soft	0			1 (25.0)	1	48.1	1 (16.7)	1	32.0
Large intestine polyp	0			1 (25.0)	1	48.1	1 (16.7)	1	32.0
Infections and infestations	0			2 (50.0)	2	96.1	2 (33.3)	2	64.1
Nasopharyngitis	0			2 (50.0)	2	96.1	2 (33.3)	2	64.1
Injury, poisoning and procedural complications	0			2 (50.0)	3	144.2	2 (33.3)	3	96.1
Muscle strain	0			1 (25.0)	2	96.1	1 (16.7)	2	64.1
Patella fracture	0			1 (25.0)	1	48.1	1 (16.7)	1	32.0
Musculoskeletal and connective tissue disorders	0			2 (50.0)	3	144.2	2 (33.3)	3	96.1
Arthralgia	0			1 (25.0)	1	48.1	1 (16.7)	1	32.0
Pain in extremity	0			1 (25.0)	1	48.1	1 (16.7)	1	32.0
Tenosynovitis	0			1 (25.0)	1	48.1	1 (16.7)	1	32.0

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

35 Adverse Events by system organ class and preferred term - Female - 4043 - entire trial population - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	14			28			42		
Total patient years	6.7			14.0			20.7		
All adverse events	10 (71.4)	42	630.5	27 (96.4)	90	643.3	37 (88.1)	132	639.2
Infections and infestations	6 (42.9)	10	150.1	14 (50.0)	19	135.8	20 (47.6)	29	140.4
Nasopharyngitis	5 (35.7)	8	120.1	8 (28.6)	9	64.3	13 (31.0)	17	82.3
Sinusitis	0			2 (7.1)	2	14.3	2 (4.8)	2	9.7
Urinary tract infection	0			2 (7.1)	3	21.4	2 (4.8)	3	14.5
Abscess	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
Bronchitis	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
Fungal infection	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Gastroenteritis	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Influenza	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Otitis media	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Vulvovaginal mycotic infection	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Nervous system disorders	5 (35.7)	12	180.1	9 (32.1)	12	85.8	14 (33.3)	24	116.2
Headache	3 (21.4)	7	105.1	5 (17.9)	7	50.0	8 (19.0)	14	67.8
Dizziness	2 (14.3)	2	30.0	1 (3.6)	1	7.1	3 (7.1)	3	14.5
Sciatica	0			2 (7.1)	2	14.3	2 (4.8)	2	9.7
Carpal tunnel syndrome	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Disturbance in attention	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
Hypoaesthesia	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
Paraesthesia	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Somnolence	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
General disorders and administration site conditions	5 (35.7)	5	75.1	6 (21.4)	8	57.2	11 (26.2)	13	62.9
Asthenia	1 (7.1)	1	15.0	2 (7.1)	3	21.4	3 (7.1)	4	19.4
Fatigue	2 (14.3)	2	30.0	1 (3.6)	1	7.1	3 (7.1)	3	14.5
Malaise	0			2 (7.1)	2	14.3	2 (4.8)	2	9.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Female - 4043 - entire trial population - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Inflammatory pain	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
Influenza like illness	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
Pain	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Pyrexia	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Musculoskeletal and connective tissue disorders	3 (21.4)	3	45.0	8 (28.6)	11	78.6	11 (26.2)	14	67.8
Arthralgia	2 (14.3)	2	30.0	3 (10.7)	3	21.4	5 (11.9)	5	24.2
Back pain	0			3 (10.7)	3	21.4	3 (7.1)	3	14.5
Musculoskeletal pain	0			2 (7.1)	2	14.3	2 (4.8)	2	9.7
Myalgia	1 (7.1)	1	15.0	1 (3.6)	1	7.1	2 (4.8)	2	9.7
Coccydynia	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Muscle spasms	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Gastrointestinal disorders	2 (14.3)	2	30.0	8 (28.6)	12	85.8	10 (23.8)	14	67.8
Abdominal pain	0			3 (10.7)	3	21.4	3 (7.1)	3	14.5
Vomiting	1 (7.1)	1	15.0	1 (3.6)	1	7.1	2 (4.8)	2	9.7
Abdominal discomfort	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Abdominal pain upper	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Barrett's oesophagus	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Colitis	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Dental caries	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Dry mouth	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Gastrooesophageal reflux disease	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Nausea	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Reflux gastritis	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
Skin and subcutaneous tissue disorders	2 (14.3)	2	30.0	3 (10.7)	4	28.6	5 (11.9)	6	29.1
Alopecia	0			2 (7.1)	2	14.3	2 (4.8)	2	9.7
Rash	1 (7.1)	1	15.0	1 (3.6)	1	7.1	2 (4.8)	2	9.7
Hair disorder	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
Onychoclasis	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Female - 4043 - entire trial population - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Injury, poisoning and procedural complications	0			4 (14.3)	4	28.6	4 (9.5)	4	19.4
Fall	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Heat illness	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Procedural complication	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Spinal column injury	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Psychiatric disorders	1 (7.1)	1	15.0	3 (10.7)	3	21.4	4 (9.5)	4	19.4
Sleep disorder	0			2 (7.1)	2	14.3	2 (4.8)	2	9.7
Depression	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
Initial insomnia	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Ear and labyrinth disorders	1 (7.1)	1	15.0	2 (7.1)	2	14.3	3 (7.1)	3	14.5
Tinnitus	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Vertigo	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
Vertigo positional	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Investigations	1 (7.1)	2	30.0	2 (7.1)	2	14.3	3 (7.1)	4	19.4
Weight increased	1 (7.1)	1	15.0	1 (3.6)	1	7.1	2 (4.8)	2	9.7
Blood insulin increased	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Hormone level abnormal	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
Metabolism and nutrition disorders	0			3 (10.7)	3	21.4	3 (7.1)	3	14.5
Fat redistribution	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Hypokalaemia	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Increased appetite	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Reproductive system and breast disorders	0			3 (10.7)	3	21.4	3 (7.1)	3	14.5
Breast disorder	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Dysmenorrhoea	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Menstruation irregular	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Endocrine disorders	0			2 (7.1)	2	14.3	2 (4.8)	2	9.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Female - 4043 - entire trial population - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Adrenal insufficiency	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Hypothyroidism	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Eye disorders	1 (7.1)	1	15.0	1 (3.6)	1	7.1	2 (4.8)	2	9.7
Dry eye	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Eye swelling	1 (7.1)	1	15.0	0			1 (2.4)	1	4.8
Hepatobiliary disorders	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Cholelithiasis	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Renal and urinary disorders	0			1 (3.6)	2	14.3	1 (2.4)	2	9.7
Dysuria	0			1 (3.6)	2	14.3	1 (2.4)	2	9.7
Respiratory, thoracic and mediastinal disorders	1 (7.1)	3	45.0	0			1 (2.4)	3	14.5
Epistaxis	1 (7.1)	3	45.0	0			1 (2.4)	3	14.5
Surgical and medical procedures	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8
Mammoplasty	0			1 (3.6)	1	7.1	1 (2.4)	1	4.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

36 Adverse Events by system organ class and preferred term - Female - 4043 - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	4			7			11		
Total patient years	2.1			3.6			5.7		
All adverse events	1 (25.0)	4	192.0	7 (100.0)	22	612.5	8 (72.7)	26	458.1
Infections and infestations	1 (25.0)	1	48.0	4 (57.1)	5	139.2	5 (45.5)	6	105.7
Nasopharyngitis	1 (25.0)	1	48.0	2 (28.6)	2	55.7	3 (27.3)	3	52.9
Influenza	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Otitis media	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Sinusitis	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Gastrointestinal disorders	0			3 (42.9)	4	111.4	3 (27.3)	4	70.5
Abdominal pain	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Colitis	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Dental caries	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Dry mouth	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Musculoskeletal and connective tissue disorders	0			3 (42.9)	3	83.5	3 (27.3)	3	52.9
Arthralgia	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Back pain	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Myalgia	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
General disorders and administration site conditions	0			2 (28.6)	2	55.7	2 (18.2)	2	35.2
Malaise	0			2 (28.6)	2	55.7	2 (18.2)	2	35.2
Injury, poisoning and procedural complications	0			2 (28.6)	2	55.7	2 (18.2)	2	35.2
Fall	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Heat illness	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Female - 4043 - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Endocrine disorders	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Adrenal insufficiency	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Eye disorders	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Dry eye	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Investigations	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Blood insulin increased	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Nervous system disorders	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Dizziness	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Reproductive system and breast disorders	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Menstruation irregular	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Respiratory, thoracic and mediastinal disorders	1 (25.0)	3	144.0	0			1 (9.1)	3	52.9
Epistaxis	1 (25.0)	3	144.0	0			1 (9.1)	3	52.9
Skin and subcutaneous tissue disorders	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6
Rash	0			1 (14.3)	1	27.8	1 (9.1)	1	17.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

37 Adverse Events - Childhood onset - 4054 main trial - entire trial population - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	20			33			38			91		
Total patient years	12.5			22.0			25.9			60.4		
All adverse events	11 (55.0)	31	247.7	25 (75.8)	117	530.7	27 (71.1)	114	440.5	63 (69.2)	262	433.5
Serious adverse events	0			2 (6.1)	2	9.1	2 (5.3)	2	7.7	4 (4.4)	4	6.6
Medical events of special interest	0			0			0			0		
Severity												
Mild	10 (50.0)	29	231.7	23 (69.7)	61	276.7	22 (57.9)	80	309.1	55 (60.4)	170	281.3
Moderate	2 (10.0)	2	16.0	9 (27.3)	56	254.0	12 (31.6)	32	123.6	23 (25.3)	90	148.9
Severe	0			0			2 (5.3)	2	7.7	2 (2.2)	2	3.3
Causality												
Unlikely	11 (55.0)	28	223.7	24 (72.7)	105	476.3	24 (63.2)	85	328.4	59 (64.8)	218	360.7
Possible	2 (10.0)	2	16.0	5 (15.2)	9	40.8	10 (26.3)	20	77.3	17 (18.7)	31	51.3
Probable	1 (5.0)	1	8.0	2 (6.1)	3	13.6	6 (15.8)	9	34.8	9 (9.9)	13	21.5
Outcome												
Recovered/Resolved	11 (55.0)	30	239.7	25 (75.8)	110	499.0	25 (65.8)	102	394.1	61 (67.0)	242	400.4
Recovering/Resolving	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Recovered/Resolved With Sequelae	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Not Recovered/Not Resolved	1 (5.0)	1	8.0	5 (15.2)	6	27.2	6 (15.8)	11	42.5	12 (13.2)	18	29.8
Action												
Drug Withdrawn	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Dose Reduced	0			1 (3.0)	1	4.5	1 (2.6)	2	7.7	2 (2.2)	3	5.0
Dose Not Changed	11 (55.0)	31	247.7	25 (75.8)	115	521.7	27 (71.1)	109	421.2	63 (69.2)	255	421.9

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

Adverse Events - Childhood onset - 4054 main trial - entire trial population - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Not Applicable	0			0			2 (5.3)	3	11.6	2 (2.2)	3	5.0
Treatment discontinuations due to adverse events	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

38 Adverse Events - Childhood onset - 4054 main trial - Japanese subgroup - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Subjects Exposed	0			1			3			4		
Total patient years	0.0			0.7			2.0			2.7		
All adverse events	0			1	(100.0)	1 148.5	2	(66.7)	10 494.9	3	(75.0)	11 408.3
Serious adverse events	0			0			0			0		
Medical events of special interest	0			0			0			0		
Severity												
Mild	0			1	(100.0)	1 148.5	2	(66.7)	10 494.9	3	(75.0)	11 408.3
Causality												
Unlikely	0			0			2	(66.7)	9 445.4	2	(50.0)	9 334.1
Possible	0			1	(100.0)	1 148.5	0			1	(25.0)	1 37.1
Probable	0			0			1	(33.3)	1 49.5	1	(25.0)	1 37.1
Outcome												
Recovered/Resolved	0			1	(100.0)	1 148.5	2	(66.7)	10 494.9	3	(75.0)	11 408.3
Action												
Dose Not Changed	0			1	(100.0)	1 148.5	2	(66.7)	10 494.9	3	(75.0)	11 408.3
Treatment discontinuations due to adverse events	0			0			0			0		

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

39 Adverse Events - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	41			86			82			209		
Total patient years	27.3			55.5			54.0			136.8		
All adverse events	35 (85.4)	151	553.0	71 (82.6)	317	571.2	60 (73.2)	274	507.4	166 (79.4)	742	542.4
Serious adverse events	5 (12.2)	7	25.6	9 (10.5)	11	19.8	5 (6.1)	10	18.5	19 (9.1)	28	20.5
Medical events of special interest	0			0			0			0		
Severity												
Mild	31 (75.6)	115	421.1	59 (68.6)	226	407.3	53 (64.6)	196	363.0	143 (68.4)	537	392.6
Moderate	15 (36.6)	30	109.9	33 (38.4)	81	146.0	22 (26.8)	69	127.8	70 (33.5)	180	131.6
Severe	4 (9.8)	6	22.0	9 (10.5)	10	18.0	5 (6.1)	9	16.7	18 (8.6)	25	18.3
Causality												
Unlikely	34 (82.9)	135	494.4	66 (76.7)	253	455.9	55 (67.1)	209	387.1	155 (74.2)	597	436.4
Possible	7 (17.1)	11	40.3	22 (25.6)	42	75.7	13 (15.9)	51	94.5	42 (20.1)	104	76.0
Probable	3 (7.3)	5	18.3	13 (15.1)	22	39.6	8 (9.8)	14	25.9	24 (11.5)	41	30.0
Outcome												
Recovered/Resolved	32 (78.0)	130	476.1	64 (74.4)	257	463.1	57 (69.5)	256	474.1	153 (73.2)	643	470.0
Recovering/Resolving	1 (2.4)	2	7.3	1 (1.2)	1	1.8	0			2 (1.0)	3	2.2
Recovered/Resolved With Sequelae	1 (2.4)	1	3.7	2 (2.3)	3	5.4	0			3 (1.4)	4	2.9
Not Recovered/Not Resolved	12 (29.3)	17	62.3	31 (36.0)	53	95.5	13 (15.9)	18	33.3	56 (26.8)	88	64.3
Fatal	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Unknown	0			1 (1.2)	3	5.4	0			1 (0.5)	3	2.2

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Adverse Events - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Action												
Drug Interrupted	3	(7.3)	5 18.3	5	(5.8)	8 14.4	0			8	(3.8)	13 9.5
Drug Withdrawn	1	(2.4)	1 3.7	3	(3.5)	3 5.4	0			4	(1.9)	4 2.9
Dose Reduced	0			4	(4.7)	5 9.0	1	(1.2)	1 1.9	5	(2.4)	6 4.4
Dose Not Changed	34	(82.9)	139 509.0	68	(79.1)	292 526.2	60	(73.2)	262 485.2	162	(77.5)	693 506.6
Not Applicable	3	(7.3)	6 22.0	6	(7.0)	9 16.2	4	(4.9)	11 20.4	13	(6.2)	26 19.0
Treatment discontinuations due to adverse events*	1	(2.4)	1 3.7	4	(4.7)	4 7.2	0			5	(2.4)	5 3.7

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

40 Adverse Events - Adulthood onset - 4054 main trial - Japanese subgroup - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	10			17			15			42		
Total patient years	6.7			11.4			10.1			28.3		
All adverse events	9 (90.0)	25	371.5	17 (100.0)	45	393.0	9 (60.0)	28	277.2	35 (83.3)	98	346.5
Serious adverse events	2 (20.0)	2	29.7	1 (5.9)	1	8.7	0			3 (7.1)	3	10.6
Medical events of special interest	0			0			0			0		
Severity												
Mild	8 (80.0)	23	341.8	15 (88.2)	40	349.4	9 (60.0)	26	257.4	32 (76.2)	89	314.7
Moderate	2 (20.0)	2	29.7	4 (23.5)	4	34.9	2 (13.3)	2	19.8	8 (19.0)	8	28.3
Severe	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Causality												
Unlikely	9 (90.0)	23	341.8	16 (94.1)	35	305.7	8 (53.3)	20	198.0	33 (78.6)	78	275.8
Possible	1 (10.0)	1	14.9	2 (11.8)	3	26.2	2 (13.3)	7	69.3	5 (11.9)	11	38.9
Probable	1 (10.0)	1	14.9	6 (35.3)	7	61.1	1 (6.7)	1	9.9	8 (19.0)	9	31.8
Outcome												
Recovered/Resolved	8 (80.0)	22	326.9	15 (88.2)	32	279.5	9 (60.0)	28	277.2	32 (76.2)	82	289.9
Recovering/Resolving	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Not Recovered/Not Resolved	3 (30.0)	3	44.6	7 (41.2)	12	104.8	0			10 (23.8)	15	53.0
Action												
Drug Interrupted	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Adverse Events - Adulthood onset - 4054 main trial - Japanese subgroup - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Drug Withdrawn	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Dose Reduced	0			2 (11.8)	3	26.2	1 (6.7)	1	9.9	3 (7.1)	4	14.1
Dose Not Changed	9 (90.0)	24	356.6	16 (94.1)	41	358.1	9 (60.0)	27	267.3	34 (81.0)	92	325.3
Treatment discontinuations due to adverse events*	0			2 (11.8)	2	17.5	0			2 (4.8)	2	7.1

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

41 Adverse Events by system organ class and preferred term - Childhood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	20			33			38			91		
Total patient years	12.5			22.0			25.9			60.4		
All adverse events	11 (55.0)	31	247.7	25 (75.8)	117	530.7	27 (71.1)	114	440.5	63 (69.2)	262	433.5
Infections and infestations	8 (40.0)	9	71.9	16 (48.5)	31	140.6	19 (50.0)	31	119.8	43 (47.3)	71	117.5
Nasopharyngitis	1 (5.0)	1	8.0	4 (12.1)	7	31.8	7 (18.4)	9	34.8	12 (13.2)	17	28.1
Upper respiratory tract infection	2 (10.0)	2	16.0	2 (6.1)	3	13.6	3 (7.9)	4	15.5	7 (7.7)	9	14.9
Gastroenteritis	1 (5.0)	1	8.0	2 (6.1)	3	13.6	2 (5.3)	2	7.7	5 (5.5)	6	9.9
Tonsillitis	1 (5.0)	1	8.0	2 (6.1)	2	9.1	2 (5.3)	2	7.7	5 (5.5)	5	8.3
Influenza	2 (10.0)	3	24.0	0			1 (2.6)	1	3.9	3 (3.3)	4	6.6
Respiratory tract infection	1 (5.0)	1	8.0	2 (6.1)	2	9.1	0			3 (3.3)	3	5.0
Respiratory tract infection viral	0			2 (6.1)	2	9.1	1 (2.6)	1	3.9	3 (3.3)	3	5.0
Bronchitis	0			1 (3.0)	1	4.5	1 (2.6)	1	3.9	2 (2.2)	2	3.3
Gastroenteritis viral	0			1 (3.0)	1	4.5	1 (2.6)	1	3.9	2 (2.2)	2	3.3
Rhinitis	0			2 (6.1)	2	9.1	0			2 (2.2)	2	3.3
Appendicitis	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Candida infection	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Cellulitis	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Cystitis	0			0			1 (2.6)	2	7.7	1 (1.1)	2	3.3
Fungal infection	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Gingivitis	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Herpes virus infection	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Herpes zoster	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Laryngitis	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Lower respiratory tract infection	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Paronychia	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Pharyngitis	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Pharyngitis streptococcal	0			0			1 (2.6)	2	7.7	1 (1.1)	2	3.3
Pulpitis dental	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Viral infection	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Childhood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Viral upper respiratory tract infection	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Musculoskeletal and connective tissue disorders	1 (5.0)	1	8.0	5 (15.2)	5	22.7	11 (28.9)	14	54.1	17 (18.7)	20	33.1
Arthralgia	0			2 (6.1)	2	9.1	2 (5.3)	2	7.7	4 (4.4)	4	6.6
Myalgia	1 (5.0)	1	8.0	1 (3.0)	1	4.5	0			2 (2.2)	2	3.3
Neck pain	0			1 (3.0)	1	4.5	1 (2.6)	1	3.9	2 (2.2)	2	3.3
Back pain	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Intervertebral disc protrusion	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Joint stiffness	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Limb deformity	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Muscle twitching	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Muscular weakness	0			0			1 (2.6)	2	7.7	1 (1.1)	2	3.3
Myositis	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Pain in extremity	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Pain in jaw	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Plantar fasciitis	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Tendonitis	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Skin and subcutaneous tissue disorders	4 (20.0)	6	47.9	3 (9.1)	5	22.7	8 (21.1)	8	30.9	15 (16.5)	19	31.4
Rash	1 (5.0)	1	8.0	1 (3.0)	2	9.1	1 (2.6)	1	3.9	3 (3.3)	4	6.6
Dry skin	1 (5.0)	1	8.0	0			1 (2.6)	1	3.9	2 (2.2)	2	3.3
Dermatitis	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Dermatitis allergic	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Dermatitis contact	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Ingrowing nail	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Lipodystrophy acquired	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Lipohypertrophy	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Prurigo	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Pruritus	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Pustular psoriasis	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Rash generalised	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Childhood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Rash maculo-papular	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Skin lesion	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Urticaria	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Nervous system disorders	3 (15.0)	5	40.0	5 (15.2)	44	199.6	5 (13.2)	6	23.2	13 (14.3)	55	91.0
Headache	3 (15.0)	5	40.0	3 (9.1)	38	172.4	2 (5.3)	2	7.7	8 (8.8)	45	74.5
Dizziness	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Dysgeusia	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Hypersomnia	0			0			1 (2.6)	2	7.7	1 (1.1)	2	3.3
Hypoaesthesia	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Migraine	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Paraesthesia	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Partial seizures	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Seizure	0			1 (3.0)	2	9.1	0			1 (1.1)	2	3.3
Gastrointestinal disorders	1 (5.0)	2	16.0	5 (15.2)	5	22.7	5 (13.2)	9	34.8	11 (12.1)	16	26.5
Abdominal pain upper	0			0			3 (7.9)	4	15.5	3 (3.3)	4	6.6
Diarrhoea	1 (5.0)	1	8.0	1 (3.0)	1	4.5	1 (2.6)	1	3.9	3 (3.3)	3	5.0
Dyspepsia	0			2 (6.1)	2	9.1	0			2 (2.2)	2	3.3
Toothache	1 (5.0)	1	8.0	1 (3.0)	1	4.5	0			2 (2.2)	2	3.3
Epigastric discomfort	0			0			1 (2.6)	3	11.6	1 (1.1)	3	5.0
Gastritis	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Stomatitis	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
General disorders and administration site conditions	2 (10.0)	3	24.0	3 (9.1)	8	36.3	6 (15.8)	11	42.5	11 (12.1)	22	36.4
Oedema peripheral	0			2 (6.1)	4	18.1	3 (7.9)	5	19.3	5 (5.5)	9	14.9
Fatigue	0			2 (6.1)	2	9.1	0			2 (2.2)	2	3.3
Influenza like illness	0			1 (3.0)	1	4.5	1 (2.6)	2	7.7	2 (2.2)	3	5.0
Face oedema	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Injection site haematoma	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Injection site pain	0			0			1 (2.6)	2	7.7	1 (1.1)	2	3.3
Malaise	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Non-cardiac chest pain	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Childhood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Peripheral swelling	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Pyrexia	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Investigations	1 (5.0)	1	8.0	4 (12.1)	5	22.7	6 (15.8)	12	46.4	11 (12.1)	18	29.8
Blood creatine phosphokinase increased	0			0			2 (5.3)	3	11.6	2 (2.2)	3	5.0
Weight increased	0			0			2 (5.3)	2	7.7	2 (2.2)	2	3.3
Alanine aminotransferase increased	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Blood alkaline phosphatase increased	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Blood potassium decreased	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Blood testosterone decreased	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Blood thyroid stimulating hormone decreased	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Body temperature increased	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Cortisol increased	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Electrocardiogram abnormal	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Gamma-glutamyltransferase increased	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Glomerular filtration rate increased	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Glycosylated haemoglobin increased	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Hepatic enzyme increased	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Thyroxine free decreased	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Injury, poisoning and procedural complications	0			4 (12.1)	4	18.1	3 (7.9)	3	11.6	7 (7.7)	7	11.6
Contusion	0			0			2 (5.3)	2	7.7	2 (2.2)	2	3.3
Arthropod bite	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Limb injury	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Muscle strain	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Prescription drug used without a prescription	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Thermal burn	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Childhood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Metabolism and nutrition disorders	1 (5.0)	1	8.0	2 (6.1)	2	9.1	3 (7.9)	4	15.5	6 (6.6)	7	11.6
Fluid retention	0			0			1 (2.6)	2	7.7	1 (1.1)	2	3.3
Hypercholesterolaemia	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Hypertriglyceridaemia	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Hypocalcaemia	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Hypoglycaemia	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Obesity	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Endocrine disorders	0			3 (9.1)	4	18.1	2 (5.3)	2	7.7	5 (5.5)	6	9.9
Secondary hypothyroidism	0			2 (6.1)	2	9.1	0			2 (2.2)	2	3.3
Adrenal insufficiency	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Glucocorticoid deficiency	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Hypothyroidism	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Secondary adrenocortical insufficiency	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Respiratory, thoracic and mediastinal disorders	1 (5.0)	1	8.0	1 (3.0)	1	4.5	3 (7.9)	3	11.6	5 (5.5)	5	8.3
Asthma	0			1 (3.0)	1	4.5	1 (2.6)	1	3.9	2 (2.2)	2	3.3
Cough	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Dyspnoea paroxysmal nocturnal	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Oropharyngeal pain	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Cardiac disorders	1 (5.0)	1	8.0	0			3 (7.9)	5	19.3	4 (4.4)	6	9.9
Aortic valve incompetence	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Cardiac discomfort	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Cardiovascular disorder	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Left ventricular dysfunction	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Mitral valve incompetence	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Sinus arrhythmia	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Blood and lymphatic system disorders	0			1 (3.0)	1	4.5	1 (2.6)	1	3.9	2 (2.2)	2	3.3
Anaemia	0			1 (3.0)	1	4.5	1 (2.6)	1	3.9	2 (2.2)	2	3.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Childhood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Eye disorders	0			0			2 (5.3)	2	7.7	2 (2.2)	2	3.3
Conjunctival haemorrhage	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Vision blurred	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Congenital, familial and genetic disorders	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Myotonia congenita	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Ear and labyrinth disorders	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Vertigo	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Psychiatric disorders	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Depression	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Renal and urinary disorders	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Chronic kidney disease	0			1 (3.0)	1	4.5	0			1 (1.1)	1	1.7
Reproductive system and breast disorders	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Dysmenorrhoea	1 (5.0)	1	8.0	0			0			1 (1.1)	1	1.7
Vascular disorders	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7
Hypertension	0			0			1 (2.6)	1	3.9	1 (1.1)	1	1.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

42 Adverse Events by system organ class and preferred term - Childhood onset - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	0			1			3			4		
Total patient years	0.0			0.7			2.0			2.7		
All adverse events	0			1 (100.0)	1	148.5	2 (66.7)	10	494.9	3 (75.0)	11	408.3
Infections and infestations	0			0			2 (66.7)	5	247.5	2 (50.0)	5	185.6
Gastroenteritis	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
Laryngitis	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
Nasopharyngitis	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
Tonsillitis	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
Upper respiratory tract infection	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
Gastrointestinal disorders	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
Gastritis	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
General disorders and administration site conditions	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
Oedema peripheral	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
Musculoskeletal and connective tissue disorders	0			1 (100.0)	1	148.5	0			1 (25.0)	1	37.1
Arthralgia	0			1 (100.0)	1	148.5	0			1 (25.0)	1	37.1
Nervous system disorders	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
Headache	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
Respiratory, thoracic and mediastinal disorders	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
Asthma	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1
Skin and subcutaneous tissue disorders	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Childhood onset - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Urticaria	0			0			1 (33.3)	1	49.5	1 (25.0)	1	37.1

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

43 Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	41			86			82			209		
Total patient years	27.3			55.5			54.0			136.8		
All adverse events	35 (85.4)	151	553.0	71 (82.6)	317	571.2	60 (73.2)	274	507.4	166 (79.4)	742	542.4
Infections and infestations	28 (68.3)	41	150.1	37 (43.0)	49	88.3	32 (39.0)	61	113.0	97 (46.4)	151	110.4
Nasopharyngitis	8 (19.5)	11	40.3	16 (18.6)	18	32.4	16 (19.5)	20	37.0	40 (19.1)	49	35.8
Upper respiratory tract infection	5 (12.2)	5	18.3	7 (8.1)	7	12.6	3 (3.7)	3	5.6	15 (7.2)	15	11.0
Sinusitis	3 (7.3)	6	22.0	2 (2.3)	2	3.6	2 (2.4)	2	3.7	7 (3.3)	10	7.3
Urinary tract infection	1 (2.4)	1	3.7	1 (1.2)	1	1.8	5 (6.1)	5	9.3	7 (3.3)	7	5.1
Bronchitis	3 (7.3)	3	11.0	2 (2.3)	2	3.6	0			5 (2.4)	5	3.7
Gastroenteritis	1 (2.4)	1	3.7	1 (1.2)	1	1.8	3 (3.7)	4	7.4	5 (2.4)	6	4.4
Ear infection	1 (2.4)	1	3.7	1 (1.2)	1	1.8	2 (2.4)	3	5.6	4 (1.9)	5	3.7
Herpes zoster	1 (2.4)	1	3.7	1 (1.2)	1	1.8	1 (1.2)	4	7.4	3 (1.4)	6	4.4
Influenza	0			1 (1.2)	1	1.8	2 (2.4)	2	3.7	3 (1.4)	3	2.2
Pharyngitis	1 (2.4)	1	3.7	2 (2.3)	2	3.6	0			3 (1.4)	3	2.2
Tooth infection	0			2 (2.3)	2	3.6	1 (1.2)	1	1.9	3 (1.4)	3	2.2
Viral upper respiratory tract infection	1 (2.4)	1	3.7	0			2 (2.4)	2	3.7	3 (1.4)	3	2.2
Clostridium difficile infection	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5
Cystitis	2 (4.9)	2	7.3	0			0			2 (1.0)	2	1.5
Gastroenteritis viral	2 (4.9)	2	7.3	0			0			2 (1.0)	2	1.5
Lower respiratory tract infection	0			1 (1.2)	2	3.6	1 (1.2)	1	1.9	2 (1.0)	3	2.2
Oral herpes	0			0			2 (2.4)	2	3.7	2 (1.0)	2	1.5
Pulpitis dental	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Tonsillitis	0			0			2 (2.4)	2	3.7	2 (1.0)	2	1.5
Appendicitis	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Diverticulitis	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Folliculitis	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Fungal infection	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Herpes simplex	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Hordeolum	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7

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MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Molluscum contagiosum	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Onychomycosis	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Otitis media	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Periodontitis	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Pilonidal cyst	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Pneumonia bacterial	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Post procedural infection	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Pyoderma	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Respiratory tract infection	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Sepsis	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Tinea infection	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Tooth abscess	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Upper respiratory tract infection bacterial	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Vaginal infection	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Vulvovaginal candidiasis	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Musculoskeletal and connective tissue disorders	9 (22.0)	13	47.6	26 (30.2)	40	72.1	18 (22.0)	26	48.2	53 (25.4)	79	57.7
Arthralgia	1 (2.4)	1	3.7	9 (10.5)	9	16.2	6 (7.3)	6	11.1	16 (7.7)	16	11.7
Back pain	2 (4.9)	2	7.3	4 (4.7)	4	7.2	10 (12.2)	10	18.5	16 (7.7)	16	11.7
Pain in extremity	1 (2.4)	1	3.7	5 (5.8)	5	9.0	1 (1.2)	1	1.9	7 (3.3)	7	5.1
Myalgia	2 (4.9)	2	7.3	2 (2.3)	2	3.6	1 (1.2)	1	1.9	5 (2.4)	5	3.7
Joint stiffness	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Joint swelling	0			2 (2.3)	3	5.4	0			2 (1.0)	3	2.2
Muscle spasms	1 (2.4)	2	7.3	0			1 (1.2)	1	1.9	2 (1.0)	3	2.2
Muscular weakness	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5
Musculoskeletal chest pain	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Musculoskeletal pain	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Rotator cuff syndrome	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Tendonitis	1 (2.4)	1	3.7	1 (1.2)	1	1.8	0			2 (1.0)	2	1.5
Bursitis	1 (2.4)	2	7.3	0			0			1 (0.5)	2	1.5
Costochondritis	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Exostosis	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Foot deformity	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Intervertebral disc degeneration	0			0			1 (1.2)	2	3.7	1 (0.5)	2	1.5
Joint effusion	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Joint noise	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Limb discomfort	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Musculoskeletal stiffness	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Nodal osteoarthritis	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Osteoarthritis	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Pain in jaw	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Periarthritis	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Spinal pain	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Tenosynovitis	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Gastrointestinal disorders	12 (29.3)	22	80.6	25 (29.1)	40	72.1	14 (17.1)	29	53.7	51 (24.4)	91	66.5
Diarrhoea	4 (9.8)	7	25.6	4 (4.7)	4	7.2	3 (3.7)	4	7.4	11 (5.3)	15	11.0
Nausea	1 (2.4)	1	3.7	6 (7.0)	8	14.4	2 (2.4)	2	3.7	9 (4.3)	11	8.0
Vomiting	1 (2.4)	2	7.3	4 (4.7)	5	9.0	4 (4.9)	4	7.4	9 (4.3)	11	8.0
Abdominal pain	1 (2.4)	1	3.7	2 (2.3)	3	5.4	3 (3.7)	4	7.4	6 (2.9)	8	5.8
Dyspepsia	1 (2.4)	2	7.3	2 (2.3)	2	3.6	2 (2.4)	2	3.7	5 (2.4)	6	4.4
Toothache	0			3 (3.5)	3	5.4	2 (2.4)	4	7.4	5 (2.4)	7	5.1
Abdominal pain upper	1 (2.4)	1	3.7	1 (1.2)	1	1.8	1 (1.2)	1	1.9	3 (1.4)	3	2.2
Dental caries	0			3 (3.5)	4	7.2	0			3 (1.4)	4	2.9
Abdominal discomfort	1 (2.4)	1	3.7	1 (1.2)	1	1.8	0			2 (1.0)	2	1.5
Abdominal distension	0			0			2 (2.4)	2	3.7	2 (1.0)	2	1.5
Abdominal tenderness	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Constipation	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Flatulence	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5
Food poisoning	1 (2.4)	1	3.7	1 (1.2)	1	1.8	0			2 (1.0)	2	1.5
Abdominal pain lower	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Ascites	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Dry mouth	0			0			1 (1.2)	2	3.7	1 (0.5)	2	1.5
Gastritis	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Gastrooesophageal reflux disease	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Hiatus hernia	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Inguinal hernia	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Large intestine polyp	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Lip swelling	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Oesophagitis ulcerative	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Pancreatitis acute	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Rectal polyp	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Stomatitis	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
General disorders and administration site conditions	7 (17.1)	10	36.6	24 (27.9)	38	68.5	13 (15.9)	17	31.5	44 (21.1)	65	47.5
Fatigue	2 (4.9)	2	7.3	5 (5.8)	5	9.0	3 (3.7)	3	5.6	10 (4.8)	10	7.3
Injection site bruising	2 (4.9)	3	11.0	6 (7.0)	6	10.8	1 (1.2)	1	1.9	9 (4.3)	10	7.3
Oedema peripheral	0			4 (4.7)	4	7.2	2 (2.4)	2	3.7	6 (2.9)	6	4.4
Pain	0			3 (3.5)	3	5.4	1 (1.2)	1	1.9	4 (1.9)	4	2.9
Asthenia	1 (2.4)	1	3.7	1 (1.2)	1	1.8	1 (1.2)	1	1.9	3 (1.4)	3	2.2
Peripheral swelling	1 (2.4)	1	3.7	2 (2.3)	2	3.6	0			3 (1.4)	3	2.2
Pyrexia	0			1 (1.2)	2	3.6	2 (2.4)	3	5.6	3 (1.4)	5	3.7
Chest pain	1 (2.4)	1	3.7	1 (1.2)	1	1.8	0			2 (1.0)	2	1.5
Face oedema	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5
Feeling hot	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Injection site pain	1 (2.4)	1	3.7	1 (1.2)	1	1.8	0			2 (1.0)	2	1.5
Injection site reaction	0			1 (1.2)	1	1.8	1 (1.2)	2	3.7	2 (1.0)	3	2.2
Malaise	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5
Nodule	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5
Axillary pain	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Chest discomfort	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Chills	0			1 (1.2)	2	3.6	0			1 (0.5)	2	1.5
Fat tissue decreased	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Gait disturbance	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Influenza like illness	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Non-cardiac chest pain	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Pre-existing condition improved	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Nervous system disorders	11 (26.8)	21	76.9	12 (14.0)	26	46.9	17 (20.7)	55	101.9	40 (19.1)	102	74.6

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MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Headache	7 (17.1)	10	36.6	8 (9.3)	12	21.6	8 (9.8)	43	79.6	23 (11.0)	65	47.5
Dizziness	1 (2.4)	1	3.7	4 (4.7)	7	12.6	3 (3.7)	4	7.4	8 (3.8)	12	8.8
Paraesthesia	2 (4.9)	2	7.3	0			3 (3.7)	4	7.4	5 (2.4)	6	4.4
Hypoaesthesia	1 (2.4)	1	3.7	3 (3.5)	4	7.2	0			4 (1.9)	5	3.7
Migraine	1 (2.4)	3	11.0	0			1 (1.2)	1	1.9	2 (1.0)	4	2.9
Tremor	1 (2.4)	1	3.7	1 (1.2)	2	3.6	0			2 (1.0)	3	2.2
Burning sensation	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Dysgeusia	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Hypersomnia	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Lethargy	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Memory impairment	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Sciatica	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Somnolence	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Skin and subcutaneous tissue disorders	8 (19.5)	10	36.6	10 (11.6)	13	23.4	12 (14.6)	16	29.6	30 (14.4)	39	28.5
Rash	1 (2.4)	1	3.7	2 (2.3)	2	3.6	2 (2.4)	2	3.7	5 (2.4)	5	3.7
Pruritus	0			3 (3.5)	3	5.4	1 (1.2)	1	1.9	4 (1.9)	4	2.9
Dermatitis contact	1 (2.4)	1	3.7	0			1 (1.2)	1	1.9	2 (1.0)	2	1.5
Dry skin	1 (2.4)	1	3.7	0			1 (1.2)	1	1.9	2 (1.0)	2	1.5
Eczema	2 (4.9)	2	7.3	0			0			2 (1.0)	2	1.5
Haemorrhage subcutaneous	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5
Acne	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Alopecia	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Dermatitis	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Dermatitis atopic	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Ecchymosis	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Exfoliative rash	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Hyperkeratosis	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Lipodystrophy acquired	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Lipohypertrophy	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Onychoclasis	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Papule	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Pruritus generalised	1 (2.4)	2	7.3	0			0			1 (0.5)	2	1.5

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MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Rash erythematous	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Rash macular	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Rash papular	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Skin burning sensation	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Skin erosion	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Skin mass	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Skin ulcer	0			1 (1.2)	2	3.6	0			1 (0.5)	2	1.5
Urticaria	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Investigations	6 (14.6)	9	33.0	13 (15.1)	24	43.2	8 (9.8)	16	29.6	27 (12.9)	49	35.8
Weight increased	0			1 (1.2)	1	1.8	2 (2.4)	2	3.7	3 (1.4)	3	2.2
Alanine aminotransferase increased	1 (2.4)	1	3.7	1 (1.2)	1	1.8	0			2 (1.0)	2	1.5
Blood creatine phosphokinase increased	0			0			2 (2.4)	3	5.6	2 (1.0)	3	2.2
Blood testosterone decreased	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Blood uric acid increased	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Creatinine renal clearance decreased	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5
Hepatic enzyme increased	2 (4.9)	2	7.3	0			0			2 (1.0)	2	1.5
Intraocular pressure increased	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5
Thyroxine free decreased	1 (2.4)	1	3.7	0			1 (1.2)	2	3.7	2 (1.0)	3	2.2
Aspartate aminotransferase increased	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Blood bilirubin increased	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Blood cholesterol increased	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Blood creatinine increased	0			0			1 (1.2)	2	3.7	1 (0.5)	2	1.5
Blood glucose increased	0			1 (1.2)	2	3.6	0			1 (0.5)	2	1.5
Blood insulin decreased	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Blood pressure increased	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Blood testosterone increased	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Creatinine renal clearance increased	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Electrocardiogram PR prolongation	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Electrocardiogram T wave abnormal	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7

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Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Glycosylated haemoglobin increased	0			1 (1.2)	2	3.6	0			1 (0.5)	2	1.5
Haematocrit increased	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Heart rate increased	0			1 (1.2)	3	5.4	0			1 (0.5)	3	2.2
Lymph node palpable	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Normetanephrine urine increased	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Platelet count increased	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Thyroid hormones decreased	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Thyroxine decreased	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Tri-iodothyronine decreased	0			1 (1.2)	2	3.6	0			1 (0.5)	2	1.5
Weight decreased	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
White blood cell count increased	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Respiratory, thoracic and mediastinal disorders	3 (7.3)	4	14.6	12 (14.0)	18	32.4	7 (8.5)	12	22.2	22 (10.5)	34	24.9
Cough	2 (4.9)	2	7.3	5 (5.8)	6	10.8	3 (3.7)	3	5.6	10 (4.8)	11	8.0
Oropharyngeal pain	2 (4.9)	2	7.3	1 (1.2)	1	1.8	4 (4.9)	4	7.4	7 (3.3)	7	5.1
Dyspnoea	0			3 (3.5)	3	5.4	0			3 (1.4)	3	2.2
Epistaxis	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Rhinitis allergic	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Nasal congestion	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Paranasal sinus hypersecretion	0			0			1 (1.2)	2	3.7	1 (0.5)	2	1.5
Pharyngeal erythema	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Respiratory tract congestion	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Sinus congestion	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Sleep apnoea syndrome	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Snoring	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Upper respiratory tract congestion	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Injury, poisoning and procedural complications	3 (7.3)	3	11.0	11 (12.8)	15	27.0	6 (7.3)	9	16.7	20 (9.6)	27	19.7
Contusion	1 (2.4)	1	3.7	3 (3.5)	4	7.2	0			4 (1.9)	5	3.7
Fall	0			2 (2.3)	2	3.6	2 (2.4)	3	5.6	4 (1.9)	5	3.7
Tooth fracture	1 (2.4)	1	3.7	2 (2.3)	2	3.6	0			3 (1.4)	3	2.2
Foot fracture	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5

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Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Laceration	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5
Arthropod bite	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Arthropod sting	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Drug dispensing error	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Muscle strain	0			0			1 (1.2)	2	3.7	1 (0.5)	2	1.5
Post procedural complication	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Procedural pain	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Radius fracture	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Tibia fracture	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Wrist fracture	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Metabolism and nutrition disorders	4 (9.8)	5	18.3	6 (7.0)	6	10.8	3 (3.7)	4	7.4	13 (6.2)	15	11.0
Gout	0			1 (1.2)	1	1.8	2 (2.4)	3	5.6	3 (1.4)	4	2.9
Diabetes mellitus	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Dyslipidaemia	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Hyperkalaemia	1 (2.4)	1	3.7	1 (1.2)	1	1.8	0			2 (1.0)	2	1.5
Dehydration	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Hyperlipidaemia	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Hyponatraemia	1 (2.4)	2	7.3	0			0			1 (0.5)	2	1.5
Vitamin D deficiency	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Renal and urinary disorders	1 (2.4)	1	3.7	6 (7.0)	7	12.6	3 (3.7)	4	7.4	10 (4.8)	12	8.8
Pollakiuria	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5
Bladder pain	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Calculus urinary	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Haematuria	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Micturition disorder	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Nephrolithiasis	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Nocturia	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Polyuria	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Renal cyst	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Urinary incontinence	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Urinary tract obstruction	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7

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Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Vascular disorders	1 (2.4)	1	3.7	5 (5.8)	6	10.8	4 (4.9)	4	7.4	10 (4.8)	11	8.0
Hypertension	1 (2.4)	1	3.7	4 (4.7)	4	7.2	3 (3.7)	3	5.6	8 (3.8)	8	5.8
Hot flush	0			1 (1.2)	1	1.8	1 (1.2)	1	1.9	2 (1.0)	2	1.5
Orthostatic hypotension	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Eye disorders	2 (4.9)	2	7.3	6 (7.0)	8	14.4	1 (1.2)	2	3.7	9 (4.3)	12	8.8
Cataract	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Vision blurred	1 (2.4)	1	3.7	1 (1.2)	1	1.8	0			2 (1.0)	2	1.5
Age-related macular degeneration	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Dry eye	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Eye pruritus	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Eyelid disorder	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Glaucoma	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Scleral disorder	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Visual acuity reduced	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Visual impairment	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Psychiatric disorders	2 (4.9)	2	7.3	3 (3.5)	3	5.4	4 (4.9)	5	9.3	9 (4.3)	10	7.3
Sleep disorder	1 (2.4)	1	3.7	0			3 (3.7)	3	5.6	4 (1.9)	4	2.9
Anxiety	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Attention deficit/hyperactivity disorder	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Emotional disorder	0			0			1 (1.2)	2	3.7	1 (0.5)	2	1.5
Insomnia	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Nervousness	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Blood and lymphatic system disorders	0			2 (2.3)	2	3.6	5 (6.1)	5	9.3	7 (3.3)	7	5.1
Lymphadenopathy	0			0			2 (2.4)	2	3.7	2 (1.0)	2	1.5
Anaemia	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Haemoconcentration	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Iron deficiency anaemia	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Polycythaemia	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Thrombocytopenia	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7

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Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Ear and labyrinth disorders	0			6 (7.0)	8	14.4	1 (1.2)	1	1.9	7 (3.3)	9	6.6
Ear pain	0			5 (5.8)	6	10.8	0			5 (2.4)	6	4.4
Ear discomfort	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Tinnitus	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Vertigo	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Endocrine disorders	2 (4.9)	2	7.3	1 (1.2)	1	1.8	4 (4.9)	4	7.4	7 (3.3)	7	5.1
Adrenal insufficiency	0			0			2 (2.4)	2	3.7	2 (1.0)	2	1.5
Adrenocortical insufficiency acute	1 (2.4)	1	3.7	0			1 (1.2)	1	1.9	2 (1.0)	2	1.5
Hypothyroidism	1 (2.4)	1	3.7	1 (1.2)	1	1.8	0			2 (1.0)	2	1.5
Thyroid mass	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Immune system disorders	2 (4.9)	2	7.3	2 (2.3)	2	3.6	2 (2.4)	2	3.7	6 (2.9)	6	4.4
Seasonal allergy	1 (2.4)	1	3.7	0			2 (2.4)	2	3.7	3 (1.4)	3	2.2
Allergy to plants	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Allergy to vaccine	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Food allergy	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Reproductive system and breast disorders	1 (2.4)	1	3.7	2 (2.3)	2	3.6	1 (1.2)	1	1.9	4 (1.9)	4	2.9
Cervical dysplasia	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Dysmenorrhoea	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Nipple pain	0			0			1 (1.2)	1	1.9	1 (0.5)	1	0.7
Vaginal discharge	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			3 (3.5)	3	5.4	0			3 (1.4)	3	2.2
Angiomyolipoma	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Melanocytic naevus	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Plasma cell myeloma	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Surgical and medical procedures	1 (2.4)	1	3.7	1 (1.2)	1	1.8	1 (1.2)	1	1.9	3 (1.4)	3	2.2
Tooth extraction	1 (2.4)	1	3.7	0			1 (1.2)	1	1.9	2 (1.0)	2	1.5
Skin operation	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Cardiac disorders	0			2 (2.3)	2	3.6	0			2 (1.0)	2	1.5
Bundle branch block right	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Palpitations	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Hepatobiliary disorders	0			2 (2.3)	3	5.4	0			2 (1.0)	3	2.2
Cholelithiasis	0			1 (1.2)	2	3.6	0			1 (0.5)	2	1.5
Hepatic cirrhosis	0			1 (1.2)	1	1.8	0			1 (0.5)	1	0.7
Product issues	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7
Device malfunction	1 (2.4)	1	3.7	0			0			1 (0.5)	1	0.7

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

44 Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	10			17			15			42		
Total patient years	6.7			11.4			10.1			28.3		
All adverse events	9 (90.0)	25	371.5	17 (100.0)	45	393.0	9 (60.0)	28	277.2	35 (83.3)	98	346.5
Infections and infestations	7 (70.0)	9	133.7	11 (64.7)	15	131.0	5 (33.3)	9	89.1	23 (54.8)	33	116.7
Nasopharyngitis	4 (40.0)	5	74.3	9 (52.9)	10	87.3	5 (33.3)	8	79.2	18 (42.9)	23	81.3
Cystitis	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Gastroenteritis	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Herpes zoster	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Molluscum contagiosum	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Periodontitis	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Pharyngitis	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Sinusitis	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Tinea infection	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Tonsillitis	0			0			1 (6.7)	1	9.9	1 (2.4)	1	3.5
Upper respiratory tract infection	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Musculoskeletal and connective tissue disorders	2 (20.0)	2	29.7	7 (41.2)	8	69.9	3 (20.0)	4	39.6	12 (28.6)	14	49.5
Arthralgia	0			1 (5.9)	1	8.7	2 (13.3)	2	19.8	3 (7.1)	3	10.6
Pain in extremity	0			3 (17.6)	3	26.2	0			3 (7.1)	3	10.6
Back pain	0			1 (5.9)	1	8.7	1 (6.7)	1	9.9	2 (4.8)	2	7.1
Limb discomfort	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Muscular weakness	0			0			1 (6.7)	1	9.9	1 (2.4)	1	3.5
Musculoskeletal chest pain	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Myalgia	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Nodal osteoarthritis	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Periarthritis	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
General disorders and administration site conditions	1 (10.0)	1	14.9	5 (29.4)	5	43.7	3 (20.0)	3	29.7	9 (21.4)	9	31.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Oedema peripheral	0			2 (11.8)	2	17.5	1 (6.7)	1	9.9	3 (7.1)	3	10.6
Face oedema	0			1 (5.9)	1	8.7	1 (6.7)	1	9.9	2 (4.8)	2	7.1
Malaise	0			1 (5.9)	1	8.7	1 (6.7)	1	9.9	2 (4.8)	2	7.1
Asthenia	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Fat tissue decreased	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Investigations	3 (30.0)	6	89.2	2 (11.8)	3	26.2	1 (6.7)	1	9.9	6 (14.3)	10	35.4
Alanine aminotransferase increased	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Aspartate aminotransferase increased	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Blood creatine phosphokinase increased	0			0			1 (6.7)	1	9.9	1 (2.4)	1	3.5
Blood insulin decreased	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Blood pressure increased	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Electrocardiogram T wave abnormal	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Hepatic enzyme increased	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Thyroxine free decreased	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Tri-iodothyronine decreased	0			1 (5.9)	2	17.5	0			1 (2.4)	2	7.1
Metabolism and nutrition disorders	4 (40.0)	5	74.3	2 (11.8)	2	17.5	0			6 (14.3)	7	24.8
Dehydration	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Diabetes mellitus	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Gout	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Hyperkalaemia	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Hyperlipidaemia	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Hyponatraemia	1 (10.0)	2	29.7	0			0			1 (2.4)	2	7.1
Gastrointestinal disorders	0			3 (17.6)	3	26.2	2 (13.3)	4	39.6	5 (11.9)	7	24.8
Dental caries	0			2 (11.8)	2	17.5	0			2 (4.8)	2	7.1
Vomiting	0			0			2 (13.3)	2	19.8	2 (4.8)	2	7.1
Abdominal pain upper	0			0			1 (6.7)	1	9.9	1 (2.4)	1	3.5
Diarrhoea	0			0			1 (6.7)	1	9.9	1 (2.4)	1	3.5
Dyspepsia	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Skin and subcutaneous tissue disorders	0			1 (5.9)	1	8.7	3 (20.0)	3	29.7	4 (9.5)	4	14.1
Haemorrhage subcutaneous	0			1 (5.9)	1	8.7	1 (6.7)	1	9.9	2 (4.8)	2	7.1
Dermatitis contact	0			0			1 (6.7)	1	9.9	1 (2.4)	1	3.5
Rash	0			0			1 (6.7)	1	9.9	1 (2.4)	1	3.5
Nervous system disorders	0			2 (11.8)	2	17.5	1 (6.7)	3	29.7	3 (7.1)	5	17.7
Headache	0			2 (11.8)	2	17.5	0			2 (4.8)	2	7.1
Dizziness	0			0			1 (6.7)	2	19.8	1 (2.4)	2	7.1
Somnolence	0			0			1 (6.7)	1	9.9	1 (2.4)	1	3.5
Injury, poisoning and procedural complications	1 (10.0)	1	14.9	0			1 (6.7)	1	9.9	2 (4.8)	2	7.1
Tooth fracture	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Wrist fracture	0			0			1 (6.7)	1	9.9	1 (2.4)	1	3.5
Endocrine disorders	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Hypothyroidism	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Plasma cell myeloma	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Psychiatric disorders	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Insomnia	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Renal and urinary disorders	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Pollakiuria	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Respiratory, thoracic and mediastinal disorders	0			1 (5.9)	2	17.5	0			1 (2.4)	2	7.1
Cough	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5
Rhinitis allergic	0			1 (5.9)	1	8.7	0			1 (2.4)	1	3.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - Adulthood onset - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Vascular disorders	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5
Hypertension	1 (10.0)	1	14.9	0			0			1 (2.4)	1	3.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

45 Adverse Events - age <65 years - 4054 main trial - entire trial population - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	51			101			107			259		
Total patient years	33.3			66.3			71.1			170.7		
All adverse events	37 (72.5)	139	417.4	82 (81.2)	358	539.6	76 (71.0)	343	482.7	195 (75.3)	840	492.1
Serious adverse events	4 (7.8)	6	18.0	8 (7.9)	10	15.1	7 (6.5)	12	16.9	19 (7.3)	28	16.4
Medical events of special interest	0			0			0			0		
Severity												
Mild	33 (64.7)	110	330.4	69 (68.3)	232	349.7	65 (60.7)	239	336.4	167 (64.5)	581	340.4
Moderate	14 (27.5)	25	75.1	34 (33.7)	119	179.4	31 (29.0)	93	130.9	79 (30.5)	237	138.8
Severe	2 (3.9)	4	12.0	6 (5.9)	7	10.6	7 (6.5)	11	15.5	15 (5.8)	22	12.9
Causality												
Unlikely	36 (70.6)	122	366.4	76 (75.2)	303	456.7	71 (66.4)	256	360.3	183 (70.7)	681	398.9
Possible	8 (15.7)	12	36.0	21 (20.8)	42	63.3	21 (19.6)	68	95.7	50 (19.3)	122	71.5
Probable	3 (5.9)	5	15.0	10 (9.9)	13	19.6	12 (11.2)	19	26.7	25 (9.7)	37	21.7
Outcome												
Recovered/Resolved	35 (68.6)	128	384.4	76 (75.2)	310	467.2	71 (66.4)	317	446.1	182 (70.3)	755	442.3
Recovering/Resolving	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2
Recovered/Resolved With Sequelae	1 (2.0)	1	3.0	2 (2.0)	3	4.5	1 (0.9)	1	1.4	4 (1.5)	5	2.9
Not Recovered/Not Resolved	10 (19.6)	10	30.0	27 (26.7)	40	60.3	18 (16.8)	25	35.2	55 (21.2)	75	43.9
Unknown	0			1 (1.0)	3	4.5	0			1 (0.4)	3	1.8
Action												
Drug Interrupted	2 (3.9)	2	6.0	4 (4.0)	6	9.0	0			6 (2.3)	8	4.7
Drug Withdrawn	0			4 (4.0)	4	6.0	0			4 (1.5)	4	2.3

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

Adverse Events - age <65 years - 4054 main trial - entire trial population - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Dose Reduced	0			5	(5.0)	6 9.0	2	(1.9)	3 4.2	7	(2.7)	9 5.3
Dose Not Changed	37	(72.5)	134 402.4	79	(78.2)	338 509.4	76	(71.0)	326 458.8	192	(74.1)	798 467.5
Not Applicable	2	(3.9)	3 9.0	4	(4.0)	4 6.0	6	(5.6)	14 19.7	12	(4.6)	21 12.3
Treatment discontinuations due to adverse events	0			4	(4.0)	4 6.0	0			4	(1.5)	4 2.3

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

46 Adverse Events - age <65 years - 4054 main trial - Japanese subgroup - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	6			15			14			35		
Total patient years	4.0			10.1			9.4			23.6		
All adverse events	6 (100.0)	15	371.7	15 (100.0)	40	395.9	8 (57.1)	33	350.0	29 (82.9)	88	373.4
Serious adverse events	2 (33.3)	2	49.6	0			0			2 (5.7)	2	8.5
Medical events of special interest	0			0			0			0		
Severity												
Mild	5 (83.3)	13	322.1	13 (86.7)	36	356.3	8 (57.1)	31	328.8	26 (74.3)	80	339.5
Moderate	2 (33.3)	2	49.6	4 (26.7)	4	39.6	2 (14.3)	2	21.2	8 (22.9)	8	33.9
Causality												
Unlikely	6 (100.0)	14	346.9	13 (86.7)	30	297.0	8 (57.1)	25	265.1	27 (77.1)	69	292.8
Possible	1 (16.7)	1	24.8	3 (20.0)	4	39.6	2 (14.3)	7	74.2	6 (17.1)	12	50.9
Probable	0			5 (33.3)	6	59.4	1 (7.1)	1	10.6	6 (17.1)	7	29.7
Outcome												
Recovered/Resolved	5 (83.3)	12	297.4	14 (93.3)	29	287.1	8 (57.1)	33	350.0	27 (77.1)	74	314.0
Recovering/Resolving	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Not Recovered/Not Resolved	3 (50.0)	3	74.3	6 (40.0)	10	99.0	0			9 (25.7)	13	55.2
Action												
Drug Interrupted	1 (16.7)	1	24.8	0			0			1 (2.9)	1	4.2
Drug Withdrawn	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Dose Reduced	0			2 (13.3)	3	29.7	1 (7.1)	1	10.6	3 (8.6)	4	17.0
Dose Not Changed	6 (100.0)	14	346.9	14 (93.3)	36	356.3	8 (57.1)	32	339.4	28 (80.0)	82	347.9

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

Adverse Events - age <65 years - 4054 main trial - Japanese subgroup - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N	(%)	E R	N	(%)	E R	N	(%)	E R	N	(%)	E R
Treatment discontinuations due to adverse events	0			1	(6.7)	1 9.9	0			1	(2.9)	1 4.2

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.

47 Adverse Events - age >=65 years - 4054 main trial - entire trial population - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	10			18			13			41		
Total patient years	6.5			11.2			8.8			26.5		
All adverse events	9 (90.0)	43	659.1	14 (77.8)	76	679.2	11 (84.6)	45	510.0	34 (82.9)	164	618.0
Serious adverse events	1 (10.0)	1	15.3	3 (16.7)	3	26.8	0			4 (9.8)	4	15.1
Medical events of special interest	0			0			0			0		
Severity												
Mild	8 (80.0)	34	521.1	13 (72.2)	55	491.5	10 (76.9)	37	419.3	31 (75.6)	126	474.8
Moderate	3 (30.0)	7	107.3	8 (44.4)	18	160.9	3 (23.1)	8	90.7	14 (34.1)	33	124.4
Severe	2 (20.0)	2	30.7	3 (16.7)	3	26.8	0			5 (12.2)	5	18.8
Causality												
Unlikely	9 (90.0)	41	628.4	14 (77.8)	55	491.5	8 (61.5)	38	430.6	31 (75.6)	134	504.9
Possible	1 (10.0)	1	15.3	6 (33.3)	9	80.4	2 (15.4)	3	34.0	9 (22.0)	13	49.0
Probable	1 (10.0)	1	15.3	5 (27.8)	12	107.2	2 (15.4)	4	45.3	8 (19.5)	17	64.1
Outcome												
Recovered/Resolved	8 (80.0)	32	490.5	13 (72.2)	57	509.4	11 (84.6)	41	464.6	32 (78.0)	130	489.9
Recovering/Resolving	1 (10.0)	2	30.7	0			0			1 (2.4)	2	7.5
Not Recovered/Not Resolved	3 (30.0)	8	122.6	9 (50.0)	19	169.8	1 (7.7)	4	45.3	13 (31.7)	31	116.8
Fatal	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Action												

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Adverse Events - age >=65 years - 4054 main trial - entire trial population - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Drug Interrupted	1 (10.0)	3	46.0	1 (5.6)	2	17.9	0			2 (4.9)	5	18.8
Drug Withdrawn	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Dose Not Changed	8 (80.0)	36	551.8	14 (77.8)	69	616.6	11 (84.6)	45	510.0	33 (80.5)	150	565.2
Not Applicable	1 (10.0)	3	46.0	2 (11.1)	5	44.7	0			3 (7.3)	8	30.1
Treatment discontinuations due to adverse events*	1 (10.0)	1	15.3	1 (5.6)	1	8.9	0			2 (4.9)	2	7.5

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

48 Adverse Events - age >=65 years - 4054 main trial - Japanese subgroup - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Subjects Exposed	4			3			4			11		
Total patient years	2.7			2.0			2.7			7.4		
All adverse events	3 (75.0)	10	371.2	3 (100.0)	6	297.0	3 (75.0)	5	185.6	9 (81.8)	21	283.5
Serious adverse events	0			1 (33.3)	1	49.5	0			1 (9.1)	1	13.5
Medical events of special interest	0			0			0			0		
Severity												
Mild	3 (75.0)	10	371.2	3 (100.0)	5	247.5	3 (75.0)	5	185.6	9 (81.8)	20	270.0
Severe	0			1 (33.3)	1	49.5	0			1 (9.1)	1	13.5
Causality												
Unlikely	3 (75.0)	9	334.1	3 (100.0)	5	247.5	2 (50.0)	4	148.5	8 (72.7)	18	243.0
Probable	1 (25.0)	1	37.1	1 (33.3)	1	49.5	1 (25.0)	1	37.1	3 (27.3)	3	40.5
Outcome												
Recovered/Resolved	3 (75.0)	10	371.2	2 (66.7)	4	198.0	3 (75.0)	5	185.6	8 (72.7)	19	256.5
Not Recovered/Not Resolved	0			1 (33.3)	2	99.0	0			1 (9.1)	2	27.0
Action												
Dose Not Changed	3 (75.0)	10	371.2	3 (100.0)	6	297.0	3 (75.0)	5	185.6	9 (81.8)	21	283.5

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

Adverse Events - age >=65 years - 4054 main trial - Japanese subgroup - safety analysis set

	placebo			Norditropin			somapacitan			total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R	N (%)	E	R
Treatment discontinuations due to adverse events*	0			1 (33.3)	1	49.5	0			1 (9.1)	1	13.5

N: Number of subjects, %: Percentage of exposed subjects having the event, E: Number of adverse events reported, R: Event rate per 100 patient years
AE causality is based on judgement of investigators.
MedDRA version 21.0.
*For subject 211004 the AE leading to treatment discontinuation started in the main trial (while on Norditropin®) but was diagnosed in the extension trial. The patient continued in the extension and was treated with somapacitan in the extension part of the trial until discontinuation.

49 Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	51			101			107			259		
Total patient years	33.3			66.3			71.1			170.7		
All adverse events	37 (72.5)	139	417.4	82 (81.2)	358	539.6	76 (71.0)	343	482.7	195 (75.3)	840	492.1
Infections and infestations	28 (54.9)	36	108.1	45 (44.6)	68	102.5	45 (42.1)	84	118.2	118 (45.6)	188	110.1
Nasopharyngitis	7 (13.7)	10	30.0	18 (17.8)	23	34.7	20 (18.7)	26	36.6	45 (17.4)	59	34.6
Upper respiratory tract infection	4 (7.8)	4	12.0	7 (6.9)	8	12.1	6 (5.6)	7	9.9	17 (6.6)	19	11.1
Gastroenteritis	2 (3.9)	2	6.0	3 (3.0)	4	6.0	5 (4.7)	6	8.4	10 (3.9)	12	7.0
Tonsillitis	1 (2.0)	1	3.0	2 (2.0)	2	3.0	4 (3.7)	4	5.6	7 (2.7)	7	4.1
Bronchitis	2 (3.9)	2	6.0	3 (3.0)	3	4.5	1 (0.9)	1	1.4	6 (2.3)	6	3.5
Sinusitis	2 (3.9)	3	9.0	2 (2.0)	2	3.0	2 (1.9)	2	2.8	6 (2.3)	7	4.1
Influenza	2 (3.9)	3	9.0	1 (1.0)	1	1.5	2 (1.9)	2	2.8	5 (1.9)	6	3.5
Urinary tract infection	1 (2.0)	1	3.0	0			4 (3.7)	4	5.6	5 (1.9)	5	2.9
Ear infection	1 (2.0)	1	3.0	1 (1.0)	1	1.5	2 (1.9)	3	4.2	4 (1.5)	5	2.9
Respiratory tract infection	2 (3.9)	2	6.0	2 (2.0)	2	3.0	0			4 (1.5)	4	2.3
Cystitis	2 (3.9)	2	6.0	0			1 (0.9)	2	2.8	3 (1.2)	4	2.3
Gastroenteritis viral	1 (2.0)	1	3.0	1 (1.0)	1	1.5	1 (0.9)	1	1.4	3 (1.2)	3	1.8
Herpes zoster	1 (2.0)	1	3.0	0			2 (1.9)	5	7.0	3 (1.2)	6	3.5
Pharyngitis	0			3 (3.0)	3	4.5	0			3 (1.2)	3	1.8
Pulpitis dental	0			3 (3.0)	3	4.5	0			3 (1.2)	3	1.8
Respiratory tract infection viral	0			2 (2.0)	2	3.0	1 (0.9)	1	1.4	3 (1.2)	3	1.8
Viral upper respiratory tract infection	0			1 (1.0)	1	1.5	2 (1.9)	2	2.8	3 (1.2)	3	1.8
Appendicitis	0			1 (1.0)	1	1.5	1 (0.9)	1	1.4	2 (0.8)	2	1.2
Lower respiratory tract infection	0			0			2 (1.9)	2	2.8	2 (0.8)	2	1.2
Oral herpes	0			0			2 (1.9)	2	2.8	2 (0.8)	2	1.2
Rhinitis	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2
Tooth infection	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2
Candida infection	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Cellulitis	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Folliculitis	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Fungal infection	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Gingivitis	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Herpes simplex	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Herpes virus infection	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Laryngitis	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Molluscum contagiosum	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Onychomycosis	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Otitis media	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Paronychia	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Pharyngitis streptococcal	0			0			1 (0.9)	2	2.8	1 (0.4)	2	1.2
Pilonidal cyst	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Pyoderma	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Sepsis	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Tinea infection	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Tooth abscess	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Upper respiratory tract infection bacterial	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Vaginal infection	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Viral infection	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Vulvovaginal candidiasis	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Musculoskeletal and connective tissue disorders	8 (15.7)	10	30.0	24 (23.8)	36	54.3	27 (25.2)	38	53.5	59 (22.8)	84	49.2
Arthralgia	1 (2.0)	1	3.0	8 (7.9)	8	12.1	7 (6.5)	7	9.9	16 (6.2)	16	9.4
Back pain	1 (2.0)	1	3.0	4 (4.0)	4	6.0	10 (9.3)	10	14.1	15 (5.8)	15	8.8
Pain in extremity	1 (2.0)	1	3.0	5 (5.0)	5	7.5	2 (1.9)	2	2.8	8 (3.1)	8	4.7
Myalgia	2 (3.9)	2	6.0	3 (3.0)	3	4.5	1 (0.9)	1	1.4	6 (2.3)	6	3.5
Muscular weakness	0			1 (1.0)	1	1.5	2 (1.9)	3	4.2	3 (1.2)	4	2.3
Tendonitis	1 (2.0)	1	3.0	1 (1.0)	1	1.5	1 (0.9)	1	1.4	3 (1.2)	3	1.8
Joint swelling	0			2 (2.0)	3	4.5	0			2 (0.8)	3	1.8
Musculoskeletal pain	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2
Neck pain	0			1 (1.0)	1	1.5	1 (0.9)	1	1.4	2 (0.8)	2	1.2
Pain in jaw	0			1 (1.0)	1	1.5	1 (0.9)	1	1.4	2 (0.8)	2	1.2
Rotator cuff syndrome	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Bursitis	1 (2.0)	2	6.0	0			0			1 (0.4)	2	1.2
Costochondritis	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Exostosis	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Intervertebral disc degeneration	0			0			1 (0.9)	2	2.8	1 (0.4)	2	1.2
Intervertebral disc protrusion	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Joint effusion	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Joint noise	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Joint stiffness	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Limb deformity	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Limb discomfort	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Muscle spasms	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Muscle twitching	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Musculoskeletal stiffness	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Myositis	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Nodal osteoarthritis	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Osteoarthritis	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Periarthritis	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Plantar fasciitis	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Tenosynovitis	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Gastrointestinal disorders	11 (21.6)	19	57.1	24 (23.8)	37	55.8	17 (15.9)	32	45.0	52 (20.1)	88	51.6
Diarrhoea	5 (9.8)	8	24.0	3 (3.0)	3	4.5	3 (2.8)	3	4.2	11 (4.2)	14	8.2
Nausea	1 (2.0)	1	3.0	5 (5.0)	7	10.6	2 (1.9)	2	2.8	8 (3.1)	10	5.9
Vomiting	1 (2.0)	2	6.0	3 (3.0)	4	6.0	4 (3.7)	4	5.6	8 (3.1)	10	5.9
Dyspepsia	1 (2.0)	2	6.0	4 (4.0)	4	6.0	2 (1.9)	2	2.8	7 (2.7)	8	4.7
Toothache	1 (2.0)	1	3.0	4 (4.0)	4	6.0	2 (1.9)	4	5.6	7 (2.7)	9	5.3
Abdominal pain upper	1 (2.0)	1	3.0	1 (1.0)	1	1.5	4 (3.7)	5	7.0	6 (2.3)	7	4.1
Abdominal pain	1 (2.0)	1	3.0	2 (2.0)	3	4.5	2 (1.9)	2	2.8	5 (1.9)	6	3.5
Abdominal distension	0			0			2 (1.9)	2	2.8	2 (0.8)	2	1.2
Abdominal tenderness	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2
Dental caries	0			2 (2.0)	3	4.5	0			2 (0.8)	3	1.8
Flatulence	0			1 (1.0)	1	1.5	1 (0.9)	1	1.4	2 (0.8)	2	1.2
Food poisoning	1 (2.0)	1	3.0	1 (1.0)	1	1.5	0			2 (0.8)	2	1.2
Stomatitis	0			1 (1.0)	1	1.5	1 (0.9)	1	1.4	2 (0.8)	2	1.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Abdominal pain lower	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Constipation	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Epigastric discomfort	0			0			1 (0.9)	3	4.2	1 (0.4)	3	1.8
Gastritis	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Gastrooesophageal reflux disease	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Inguinal hernia	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Large intestine polyp	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Pancreatitis acute	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Rectal polyp	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Nervous system disorders	12 (23.5)	21	63.1	15 (14.9)	67	101.0	19 (17.8)	58	81.6	46 (17.8)	146	85.5
Headache	10 (19.6)	15	45.0	11 (10.9)	50	75.4	8 (7.5)	43	60.5	29 (11.2)	108	63.3
Dizziness	0			2 (2.0)	4	6.0	4 (3.7)	5	7.0	6 (2.3)	9	5.3
Hypoaesthesia	0			3 (3.0)	4	6.0	1 (0.9)	1	1.4	4 (1.5)	5	2.9
Paraesthesia	1 (2.0)	1	3.0	1 (1.0)	1	1.5	2 (1.9)	3	4.2	4 (1.5)	5	2.9
Migraine	1 (2.0)	3	9.0	1 (1.0)	1	1.5	1 (0.9)	1	1.4	3 (1.2)	5	2.9
Hypersomnia	0			0			2 (1.9)	3	4.2	2 (0.8)	3	1.8
Burning sensation	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Dysgeusia	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Lethargy	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Memory impairment	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Partial seizures	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Sciatica	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Seizure	0			1 (1.0)	2	3.0	0			1 (0.4)	2	1.2
Somnolence	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Tremor	0			1 (1.0)	2	3.0	0			1 (0.4)	2	1.2
General disorders and administration site conditions	7 (13.7)	11	33.0	20 (19.8)	37	55.8	16 (15.0)	23	32.4	43 (16.6)	71	41.6
Fatigue	1 (2.0)	1	3.0	6 (5.9)	6	9.0	3 (2.8)	3	4.2	10 (3.9)	10	5.9
Oedema peripheral	0			5 (5.0)	7	10.6	5 (4.7)	7	9.9	10 (3.9)	14	8.2
Injection site bruising	2 (3.9)	3	9.0	2 (2.0)	2	3.0	0			4 (1.5)	5	2.9
Pyrexia	0			1 (1.0)	2	3.0	3 (2.8)	4	5.6	4 (1.5)	6	3.5
Influenza like illness	0			2 (2.0)	2	3.0	1 (0.9)	2	2.8	3 (1.2)	4	2.3

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Injection site pain	1 (2.0)	1	3.0	1 (1.0)	1	1.5	1 (0.9)	2	2.8	3 (1.2)	4	2.3
Malaise	1 (2.0)	1	3.0	1 (1.0)	1	1.5	1 (0.9)	1	1.4	3 (1.2)	3	1.8
Pain	0			2 (2.0)	2	3.0	1 (0.9)	1	1.4	3 (1.2)	3	1.8
Peripheral swelling	1 (2.0)	1	3.0	2 (2.0)	2	3.0	0			3 (1.2)	3	1.8
Asthenia	1 (2.0)	1	3.0	1 (1.0)	1	1.5	0			2 (0.8)	2	1.2
Chest pain	1 (2.0)	1	3.0	1 (1.0)	1	1.5	0			2 (0.8)	2	1.2
Face oedema	1 (2.0)	1	3.0	1 (1.0)	1	1.5	0			2 (0.8)	2	1.2
Feeling hot	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2
Non-cardiac chest pain	0			0			2 (1.9)	2	2.8	2 (0.8)	2	1.2
Axillary pain	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Chest discomfort	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Chills	0			1 (1.0)	2	3.0	0			1 (0.4)	2	1.2
Fat tissue decreased	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Injection site haematoma	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Injection site reaction	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Nodule	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Pre-existing condition improved	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Skin and subcutaneous tissue disorders	12 (23.5)	16	48.1	8 (7.9)	11	16.6	18 (16.8)	22	31.0	38 (14.7)	49	28.7
Rash	2 (3.9)	2	6.0	2 (2.0)	3	4.5	3 (2.8)	3	4.2	7 (2.7)	8	4.7
Dry skin	2 (3.9)	2	6.0	0			2 (1.9)	2	2.8	4 (1.5)	4	2.3
Pruritus	0			3 (3.0)	3	4.5	1 (0.9)	1	1.4	4 (1.5)	4	2.3
Dermatitis	2 (3.9)	2	6.0	0			0			2 (0.8)	2	1.2
Dermatitis contact	1 (2.0)	1	3.0	1 (1.0)	1	1.5	0			2 (0.8)	2	1.2
Eczema	2 (3.9)	2	6.0	0			0			2 (0.8)	2	1.2
Lipodystrophy acquired	0			0			2 (1.9)	2	2.8	2 (0.8)	2	1.2
Lipohypertrophy	0			0			2 (1.9)	2	2.8	2 (0.8)	2	1.2
Acne	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Alopecia	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Dermatitis allergic	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Dermatitis atopic	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Ecchymosis	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Haemorrhage subcutaneous	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6

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MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Hyperkeratosis	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Ingrowing nail	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Papule	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Prurigo	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Pruritus generalised	1 (2.0)	2	6.0	0			0			1 (0.4)	2	1.2
Pustular psoriasis	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Rash erythematous	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Rash generalised	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Rash macular	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Rash maculo-papular	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Rash papular	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Skin burning sensation	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Skin erosion	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Skin lesion	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Skin mass	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Urticaria	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Investigations	5 (9.8)	6	18.0	13 (12.9)	24	36.2	13 (12.1)	24	33.8	31 (12.0)	54	31.6
Blood creatine phosphokinase increased	0			0			4 (3.7)	6	8.4	4 (1.5)	6	3.5
Weight increased	0			0			4 (3.7)	4	5.6	4 (1.5)	4	2.3
Blood testosterone decreased	0			3 (3.0)	3	4.5	0			3 (1.2)	3	1.8
Alanine aminotransferase increased	0			1 (1.0)	1	1.5	1 (0.9)	1	1.4	2 (0.8)	2	1.2
Glycosylated haemoglobin increased	0			1 (1.0)	2	3.0	1 (0.9)	1	1.4	2 (0.8)	3	1.8
Hepatic enzyme increased	1 (2.0)	1	3.0	0			1 (0.9)	1	1.4	2 (0.8)	2	1.2
Intraocular pressure increased	0			1 (1.0)	1	1.5	1 (0.9)	1	1.4	2 (0.8)	2	1.2
Thyroxine free decreased	0			1 (1.0)	1	1.5	1 (0.9)	2	2.8	2 (0.8)	3	1.8
Blood alkaline phosphatase increased	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Blood bilirubin increased	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Blood cholesterol increased	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Blood glucose increased	0			1 (1.0)	2	3.0	0			1 (0.4)	2	1.2
Blood insulin decreased	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Blood potassium decreased	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6

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MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Blood pressure increased	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Blood testosterone increased	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Blood thyroid stimulating hormone decreased	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Blood uric acid increased	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Body temperature increased	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Cortisol increased	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Electrocardiogram T wave abnormal	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Electrocardiogram abnormal	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Gamma-glutamyltransferase increased	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Glomerular filtration rate increased	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Haematocrit increased	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Heart rate increased	0			1 (1.0)	3	4.5	0			1 (0.4)	3	1.8
Lymph node palpable	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Normetanephrine urine increased	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Platelet count increased	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Thyroid hormones decreased	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Thyroxine decreased	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Tri-iodothyronine decreased	0			1 (1.0)	2	3.0	0			1 (0.4)	2	1.2
White blood cell count increased	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Respiratory, thoracic and mediastinal disorders	3 (5.9)	4	12.0	10 (9.9)	16	24.1	9 (8.4)	14	19.7	22 (8.5)	34	19.9
Cough	2 (3.9)	2	6.0	4 (4.0)	5	7.5	2 (1.9)	2	2.8	8 (3.1)	9	5.3
Oropharyngeal pain	2 (3.9)	2	6.0	1 (1.0)	1	1.5	5 (4.7)	5	7.0	8 (3.1)	8	4.7
Asthma	0			1 (1.0)	1	1.5	1 (0.9)	1	1.4	2 (0.8)	2	1.2
Dyspnoea	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2
Epistaxis	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2
Rhinitis allergic	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2
Dyspnoea paroxysmal nocturnal	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Nasal congestion	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Paranasal sinus hypersecretion	0			0			1 (0.9)	2	2.8	1 (0.4)	2	1.2
Pharyngeal erythema	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6

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MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Respiratory tract congestion	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Sinus congestion	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Snoring	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Upper respiratory tract congestion	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Injury, poisoning and procedural complications	3 (5.9)	3	9.0	11 (10.9)	15	22.6	7 (6.5)	8	11.3	21 (8.1)	26	15.2
Contusion	1 (2.0)	1	3.0	2 (2.0)	3	4.5	2 (1.9)	2	2.8	5 (1.9)	6	3.5
Tooth fracture	1 (2.0)	1	3.0	2 (2.0)	2	3.0	0			3 (1.2)	3	1.8
Fall	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2
Foot fracture	0			1 (1.0)	1	1.5	1 (0.9)	1	1.4	2 (0.8)	2	1.2
Laceration	0			1 (1.0)	1	1.5	1 (0.9)	1	1.4	2 (0.8)	2	1.2
Muscle strain	0			1 (1.0)	1	1.5	1 (0.9)	2	2.8	2 (0.8)	3	1.8
Arthropod bite	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Limb injury	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Prescription drug used without a prescription	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Procedural pain	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Radius fracture	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Thermal burn	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Tibia fracture	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Wrist fracture	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Metabolism and nutrition disorders	2 (3.9)	3	9.0	6 (5.9)	6	9.0	4 (3.7)	5	7.0	12 (4.6)	14	8.2
Dyslipidaemia	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2
Diabetes mellitus	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Fluid retention	0			0			1 (0.9)	2	2.8	1 (0.4)	2	1.2
Gout	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Hypercholesterolaemia	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Hypertriglyceridaemia	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Hypocalcaemia	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Hypoglycaemia	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Hyponatraemia	1 (2.0)	2	6.0	0			0			1 (0.4)	2	1.2
Obesity	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6

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MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Vitamin D deficiency	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Endocrine disorders	1 (2.0)	1	3.0	4 (4.0)	5	7.5	6 (5.6)	6	8.4	11 (4.2)	12	7.0
Adrenal insufficiency	0			0			3 (2.8)	3	4.2	3 (1.2)	3	1.8
Hypothyroidism	1 (2.0)	1	3.0	1 (1.0)	1	1.5	1 (0.9)	1	1.4	3 (1.2)	3	1.8
Secondary hypothyroidism	0			2 (2.0)	2	3.0	0			2 (0.8)	2	1.2
Adrenocortical insufficiency acute	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Glucocorticoid deficiency	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Secondary adrenocortical insufficiency	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Thyroid mass	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Blood and lymphatic system disorders	0			3 (3.0)	3	4.5	6 (5.6)	6	8.4	9 (3.5)	9	5.3
Anaemia	0			1 (1.0)	1	1.5	2 (1.9)	2	2.8	3 (1.2)	3	1.8
Lymphadenopathy	0			0			2 (1.9)	2	2.8	2 (0.8)	2	1.2
Haemoconcentration	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Iron deficiency anaemia	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Polycythaemia	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Thrombocytopenia	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Vascular disorders	1 (2.0)	1	3.0	3 (3.0)	3	4.5	5 (4.7)	5	7.0	9 (3.5)	9	5.3
Hypertension	1 (2.0)	1	3.0	2 (2.0)	2	3.0	4 (3.7)	4	5.6	7 (2.7)	7	4.1
Hot flush	0			1 (1.0)	1	1.5	1 (0.9)	1	1.4	2 (0.8)	2	1.2
Psychiatric disorders	1 (2.0)	1	3.0	3 (3.0)	3	4.5	4 (3.7)	5	7.0	8 (3.1)	9	5.3
Sleep disorder	1 (2.0)	1	3.0	0			2 (1.9)	2	2.8	3 (1.2)	3	1.8
Attention deficit/hyperactivity disorder	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Depression	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Emotional disorder	0			0			1 (0.9)	2	2.8	1 (0.4)	2	1.2
Insomnia	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Nervousness	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Ear and labyrinth disorders	0			7 (6.9)	9	13.6	0			7 (2.7)	9	5.3

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MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Ear pain	0			5 (5.0)	6	9.0	0			5 (1.9)	6	3.5
Ear discomfort	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Tinnitus	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Vertigo	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Eye disorders	1 (2.0)	1	3.0	4 (4.0)	4	6.0	2 (1.9)	2	2.8	7 (2.7)	7	4.1
Vision blurred	1 (2.0)	1	3.0	1 (1.0)	1	1.5	1 (0.9)	1	1.4	3 (1.2)	3	1.8
Conjunctival haemorrhage	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Eyelid disorder	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Glaucoma	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Visual impairment	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Renal and urinary disorders	0			5 (5.0)	5	7.5	1 (0.9)	1	1.4	6 (2.3)	6	3.5
Calculus urinary	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Chronic kidney disease	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Micturition disorder	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Nephrolithiasis	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Pollakiuria	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Urinary incontinence	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Cardiac disorders	1 (2.0)	1	3.0	1 (1.0)	1	1.5	3 (2.8)	5	7.0	5 (1.9)	7	4.1
Aortic valve incompetence	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Bundle branch block right	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Cardiac discomfort	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Cardiovascular disorder	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Left ventricular dysfunction	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Mitral valve incompetence	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Sinus arrhythmia	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Immune system disorders	1 (2.0)	1	3.0	2 (2.0)	2	3.0	2 (1.9)	2	2.8	5 (1.9)	5	2.9
Seasonal allergy	0			0			2 (1.9)	2	2.8	2 (0.8)	2	1.2
Allergy to plants	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Allergy to vaccine	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Food allergy	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6

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Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Reproductive system and breast disorders	2 (3.9)	2	6.0	2 (2.0)	2	3.0	1 (0.9)	1	1.4	5 (1.9)	5	2.9
Dysmenorrhoea	2 (3.9)	2	6.0	0			0			2 (0.8)	2	1.2
Cervical dysplasia	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Nipple pain	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Vaginal discharge	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Surgical and medical procedures	1 (2.0)	1	3.0	1 (1.0)	1	1.5	1 (0.9)	1	1.4	3 (1.2)	3	1.8
Tooth extraction	1 (2.0)	1	3.0	0			1 (0.9)	1	1.4	2 (0.8)	2	1.2
Skin operation	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Congenital, familial and genetic disorders	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Myotonia congenita	0			0			1 (0.9)	1	1.4	1 (0.4)	1	0.6
Hepatobiliary disorders	0			1 (1.0)	2	3.0	0			1 (0.4)	2	1.2
Cholelithiasis	0			1 (1.0)	2	3.0	0			1 (0.4)	2	1.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Melanocytic naevus	0			1 (1.0)	1	1.5	0			1 (0.4)	1	0.6
Product issues	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6
Device malfunction	1 (2.0)	1	3.0	0			0			1 (0.4)	1	0.6

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

50 Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	6			15			14			35		
Total patient years	4.0			10.1			9.4			23.6		
All adverse events	6 (100.0)	15	371.7	15 (100.0)	40	395.9	8 (57.1)	33	350.0	29 (82.9)	88	373.4
Infections and infestations	5 (83.3)	6	148.7	9 (60.0)	13	128.7	5 (35.7)	12	127.3	19 (54.3)	31	131.5
Nasopharyngitis	2 (33.3)	3	74.3	8 (53.3)	9	89.1	4 (28.6)	7	74.2	14 (40.0)	19	80.6
Gastroenteritis	0			1 (6.7)	1	9.9	1 (7.1)	1	10.6	2 (5.7)	2	8.5
Tonsillitis	0			0			2 (14.3)	2	21.2	2 (5.7)	2	8.5
Upper respiratory tract infection	0			1 (6.7)	1	9.9	1 (7.1)	1	10.6	2 (5.7)	2	8.5
Cystitis	1 (16.7)	1	24.8	0			0			1 (2.9)	1	4.2
Herpes zoster	1 (16.7)	1	24.8	0			0			1 (2.9)	1	4.2
Laryngitis	0			0			1 (7.1)	1	10.6	1 (2.9)	1	4.2
Molluscum contagiosum	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Sinusitis	1 (16.7)	1	24.8	0			0			1 (2.9)	1	4.2
Tinea infection	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Musculoskeletal and connective tissue disorders	1 (16.7)	1	24.8	7 (46.7)	8	79.2	2 (14.3)	3	31.8	10 (28.6)	12	50.9
Arthralgia	0			2 (13.3)	2	19.8	1 (7.1)	1	10.6	3 (8.6)	3	12.7
Pain in extremity	0			3 (20.0)	3	29.7	0			3 (8.6)	3	12.7
Back pain	0			1 (6.7)	1	9.9	1 (7.1)	1	10.6	2 (5.7)	2	8.5
Limb discomfort	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Muscular weakness	0			0			1 (7.1)	1	10.6	1 (2.9)	1	4.2
Nodal osteoarthritis	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Periarthritis	1 (16.7)	1	24.8	0			0			1 (2.9)	1	4.2
General disorders and administration site conditions	1 (16.7)	1	24.8	5 (33.3)	5	49.5	3 (21.4)	3	31.8	9 (25.7)	9	38.2
Oedema peripheral	0			2 (13.3)	2	19.8	2 (14.3)	2	21.2	4 (11.4)	4	17.0
Malaise	0			1 (6.7)	1	9.9	1 (7.1)	1	10.6	2 (5.7)	2	8.5
Asthenia	1 (16.7)	1	24.8	0			0			1 (2.9)	1	4.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Face oedema	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Fat tissue decreased	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Gastrointestinal disorders	0			2 (13.3)	2	19.8	3 (21.4)	5	53.0	5 (14.3)	7	29.7
Vomiting	0			0			2 (14.3)	2	21.2	2 (5.7)	2	8.5
Abdominal pain upper	0			0			1 (7.1)	1	10.6	1 (2.9)	1	4.2
Dental caries	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Diarrhoea	0			0			1 (7.1)	1	10.6	1 (2.9)	1	4.2
Dyspepsia	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Gastritis	0			0			1 (7.1)	1	10.6	1 (2.9)	1	4.2
Investigations	2 (33.3)	3	74.3	2 (13.3)	3	29.7	1 (7.1)	1	10.6	5 (14.3)	7	29.7
Blood creatine phosphokinase increased	0			0			1 (7.1)	1	10.6	1 (2.9)	1	4.2
Blood insulin decreased	1 (16.7)	1	24.8	0			0			1 (2.9)	1	4.2
Blood pressure increased	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Electrocardiogram T wave abnormal	1 (16.7)	1	24.8	0			0			1 (2.9)	1	4.2
Hepatic enzyme increased	1 (16.7)	1	24.8	0			0			1 (2.9)	1	4.2
Tri-iodothyronine decreased	0			1 (6.7)	2	19.8	0			1 (2.9)	2	8.5
Nervous system disorders	0			2 (13.3)	2	19.8	2 (14.3)	4	42.4	4 (11.4)	6	25.5
Headache	0			2 (13.3)	2	19.8	1 (7.1)	1	10.6	3 (8.6)	3	12.7
Dizziness	0			0			1 (7.1)	2	21.2	1 (2.9)	2	8.5
Somnolence	0			0			1 (7.1)	1	10.6	1 (2.9)	1	4.2
Metabolism and nutrition disorders	1 (16.7)	2	49.6	2 (13.3)	2	19.8	0			3 (8.6)	4	17.0
Diabetes mellitus	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Gout	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Hyponatraemia	1 (16.7)	2	49.6	0			0			1 (2.9)	2	8.5
Skin and subcutaneous tissue disorders	0			0			3 (21.4)	3	31.8	3 (8.6)	3	12.7
Haemorrhage subcutaneous	0			0			1 (7.1)	1	10.6	1 (2.9)	1	4.2
Rash	0			0			1 (7.1)	1	10.6	1 (2.9)	1	4.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age <65 years - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Urticaria	0			0			1 (7.1)	1	10.6	1 (2.9)	1	4.2
Injury, poisoning and procedural complications	1 (16.7)	1	24.8	0			1 (7.1)	1	10.6	2 (5.7)	2	8.5
Tooth fracture	1 (16.7)	1	24.8	0			0			1 (2.9)	1	4.2
Wrist fracture	0			0			1 (7.1)	1	10.6	1 (2.9)	1	4.2
Respiratory, thoracic and mediastinal disorders	0			1 (6.7)	2	19.8	1 (7.1)	1	10.6	2 (5.7)	3	12.7
Asthma	0			0			1 (7.1)	1	10.6	1 (2.9)	1	4.2
Cough	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Rhinitis allergic	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Endocrine disorders	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Hypothyroidism	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Psychiatric disorders	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Insomnia	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Renal and urinary disorders	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Pollakiuria	0			1 (6.7)	1	9.9	0			1 (2.9)	1	4.2
Vascular disorders	1 (16.7)	1	24.8	0			0			1 (2.9)	1	4.2
Hypertension	1 (16.7)	1	24.8	0			0			1 (2.9)	1	4.2

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

51 Adverse Events by system organ class and preferred term - age >=65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	10			18			13			41		
Total patient years	6.5			11.2			8.8			26.5		
All adverse events	9 (90.0)	43	659.1	14 (77.8)	76	679.2	11 (84.6)	45	510.0	34 (82.9)	164	618.0
Infections and infestations	8 (80.0)	14	214.6	8 (44.4)	12	107.2	6 (46.2)	8	90.7	22 (53.7)	34	128.1
Nasopharyngitis	2 (20.0)	2	30.7	2 (11.1)	2	17.9	3 (23.1)	3	34.0	7 (17.1)	7	26.4
Upper respiratory tract infection	3 (30.0)	3	46.0	2 (11.1)	2	17.9	0			5 (12.2)	5	18.8
Clostridium difficile infection	0			1 (5.6)	1	8.9	1 (7.7)	1	11.3	2 (4.9)	2	7.5
Urinary tract infection	0			1 (5.6)	1	8.9	1 (7.7)	1	11.3	2 (4.9)	2	7.5
Bronchitis	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Diverticulitis	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Fungal infection	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Gastroenteritis viral	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Herpes zoster	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Hordeolum	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Influenza	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Lower respiratory tract infection	0			1 (5.6)	2	17.9	0			1 (2.4)	2	7.5
Periodontitis	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Pharyngitis	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Pneumonia bacterial	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Post procedural infection	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Sinusitis	1 (10.0)	3	46.0	0			0			1 (2.4)	3	11.3
Tooth infection	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Viral upper respiratory tract infection	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
General disorders and administration site conditions	2 (20.0)	2	30.7	7 (38.9)	9	80.4	3 (23.1)	5	56.7	12 (29.3)	16	60.3
Injection site bruising	0			4 (22.2)	4	35.7	1 (7.7)	1	11.3	5 (12.2)	5	18.8
Fatigue	1 (10.0)	1	15.3	1 (5.6)	1	8.9	0			2 (4.9)	2	7.5
Asthenia	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age >=65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Face oedema	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Gait disturbance	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Injection site reaction	0			0			1 (7.7)	2	22.7	1 (2.4)	2	7.5
Nodule	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Oedema peripheral	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Pain	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Peripheral swelling	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Musculoskeletal and connective tissue disorders	2 (20.0)	4	61.3	7 (38.9)	9	80.4	2 (15.4)	2	22.7	11 (26.8)	15	56.5
Arthralgia	0			3 (16.7)	3	26.8	1 (7.7)	1	11.3	4 (9.8)	4	15.1
Back pain	1 (10.0)	1	15.3	0			1 (7.7)	1	11.3	2 (4.9)	2	7.5
Joint stiffness	0			2 (11.1)	2	17.9	0			2 (4.9)	2	7.5
Musculoskeletal chest pain	0			2 (11.1)	2	17.9	0			2 (4.9)	2	7.5
Foot deformity	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Muscle spasms	1 (10.0)	2	30.7	0			0			1 (2.4)	2	7.5
Myalgia	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Spinal pain	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Gastrointestinal disorders	2 (20.0)	5	76.6	6 (33.3)	8	71.5	2 (15.4)	6	68.0	10 (24.4)	19	71.6
Diarrhoea	0			2 (11.1)	2	17.9	1 (7.7)	2	22.7	3 (7.3)	4	15.1
Abdominal discomfort	1 (10.0)	1	15.3	1 (5.6)	1	8.9	0			2 (4.9)	2	7.5
Abdominal pain	0			0			1 (7.7)	2	22.7	1 (2.4)	2	7.5
Ascites	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Constipation	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Dental caries	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Dry mouth	0			0			1 (7.7)	2	22.7	1 (2.4)	2	7.5
Gastritis	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Hiatus hernia	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Lip swelling	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Nausea	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Oesophagitis ulcerative	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Vomiting	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age >=65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Investigations	2 (20.0)	4	61.3	4 (22.2)	5	44.7	1 (7.7)	4	45.3	7 (17.1)	13	49.0
Creatinine renal clearance decreased	0			1 (5.6)	1	8.9	1 (7.7)	1	11.3	2 (4.9)	2	7.5
Alanine aminotransferase increased	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Aspartate aminotransferase increased	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Blood creatinine increased	0			0			1 (7.7)	2	22.7	1 (2.4)	2	7.5
Blood uric acid increased	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Creatinine renal clearance increased	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Electrocardiogram PR prolongation	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Hepatic enzyme increased	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Thyroxine free decreased	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Weight decreased	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Weight increased	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Metabolism and nutrition disorders	3 (30.0)	3	46.0	2 (11.1)	2	17.9	2 (15.4)	3	34.0	7 (17.1)	8	30.1
Gout	0			0			2 (15.4)	3	34.0	2 (4.9)	3	11.3
Hyperkalaemia	1 (10.0)	1	15.3	1 (5.6)	1	8.9	0			2 (4.9)	2	7.5
Dehydration	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Diabetes mellitus	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Hyperlipidaemia	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Nervous system disorders	2 (20.0)	5	76.6	2 (11.1)	3	26.8	3 (23.1)	3	34.0	7 (17.1)	11	41.5
Dizziness	1 (10.0)	1	15.3	2 (11.1)	3	26.8	0			3 (7.3)	4	15.1
Headache	0			0			2 (15.4)	2	22.7	2 (4.9)	2	7.5
Paraesthesia	1 (10.0)	1	15.3	0			1 (7.7)	1	11.3	2 (4.9)	2	7.5
Dysgeusia	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Hypoaesthesia	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Tremor	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Skin and subcutaneous tissue disorders	0			5 (27.8)	7	62.6	2 (15.4)	2	22.7	7 (17.1)	9	33.9
Dermatitis contact	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age >=65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Exfoliative rash	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Haemorrhage subcutaneous	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Onychoclasis	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Pruritus	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Rash	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Skin ulcer	0			1 (5.6)	2	17.9	0			1 (2.4)	2	7.5
Urticaria	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Injury, poisoning and procedural complications	0			4 (22.2)	4	35.7	2 (15.4)	4	45.3	6 (14.6)	8	30.1
Fall	0			0			2 (15.4)	3	34.0	2 (4.9)	3	11.3
Arthropod bite	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Arthropod sting	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Contusion	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Drug dispensing error	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Post procedural complication	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Renal and urinary disorders	1 (10.0)	1	15.3	2 (11.1)	3	26.8	2 (15.4)	3	34.0	5 (12.2)	7	26.4
Bladder pain	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Haematuria	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Nocturia	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Pollakiuria	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Polyuria	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Renal cyst	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Urinary tract obstruction	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Respiratory, thoracic and mediastinal disorders	1 (10.0)	1	15.3	3 (16.7)	3	26.8	1 (7.7)	1	11.3	5 (12.2)	5	18.8
Cough	1 (10.0)	1	15.3	1 (5.6)	1	8.9	1 (7.7)	1	11.3	3 (7.3)	3	11.3
Dyspnoea	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Sleep apnoea syndrome	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Eye disorders	1 (10.0)	1	15.3	2 (11.1)	4	35.7	1 (7.7)	2	22.7	4 (9.8)	7	26.4
Cataract	0			2 (11.1)	2	17.9	0			2 (4.9)	2	7.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age >=65 years - 4054 main trial - entire trial population - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Age-related macular degeneration	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Dry eye	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Eye pruritus	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Scleral disorder	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Visual acuity reduced	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			2 (11.1)	2	17.9	0			2 (4.9)	2	7.5
Angiomyolipoma	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Plasma cell myeloma	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Psychiatric disorders	1 (10.0)	1	15.3	0			1 (7.7)	1	11.3	2 (4.9)	2	7.5
Anxiety	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Sleep disorder	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Vascular disorders	0			2 (11.1)	3	26.8	0			2 (4.9)	3	11.3
Hypertension	0			2 (11.1)	2	17.9	0			2 (4.9)	2	7.5
Orthostatic hypotension	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Cardiac disorders	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Palpitations	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Ear and labyrinth disorders	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Vertigo	0			0			1 (7.7)	1	11.3	1 (2.4)	1	3.8
Endocrine disorders	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Adrenocortical insufficiency acute	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Hepatobiliary disorders	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Hepatic cirrhosis	0			1 (5.6)	1	8.9	0			1 (2.4)	1	3.8
Immune system disorders	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8
Seasonal allergy	1 (10.0)	1	15.3	0			0			1 (2.4)	1	3.8

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

52 Adverse Events by system organ class and preferred term - age >=65 years - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Subjects Exposed	4			3			4			11		
Total patient years	2.7			2.0			2.7			7.4		
All adverse events	3 (75.0)	10	371.2	3 (100.0)	6	297.0	3 (75.0)	5	185.6	9 (81.8)	21	283.5
Infections and infestations	2 (50.0)	3	111.4	2 (66.7)	2	99.0	2 (50.0)	2	74.2	6 (54.5)	7	94.5
Nasopharyngitis	2 (50.0)	2	74.2	1 (33.3)	1	49.5	2 (50.0)	2	74.2	5 (45.5)	5	67.5
Periodontitis	0			1 (33.3)	1	49.5	0			1 (9.1)	1	13.5
Pharyngitis	1 (25.0)	1	37.1	0			0			1 (9.1)	1	13.5
Metabolism and nutrition disorders	3 (75.0)	3	111.4	0			0			3 (27.3)	3	40.5
Dehydration	1 (25.0)	1	37.1	0			0			1 (9.1)	1	13.5
Hyperkalaemia	1 (25.0)	1	37.1	0			0			1 (9.1)	1	13.5
Hyperlipidaemia	1 (25.0)	1	37.1	0			0			1 (9.1)	1	13.5
Musculoskeletal and connective tissue disorders	1 (25.0)	1	37.1	1 (33.3)	1	49.5	1 (25.0)	1	37.1	3 (27.3)	3	40.5
Arthralgia	0			0			1 (25.0)	1	37.1	1 (9.1)	1	13.5
Musculoskeletal chest pain	0			1 (33.3)	1	49.5	0			1 (9.1)	1	13.5
Myalgia	1 (25.0)	1	37.1	0			0			1 (9.1)	1	13.5
Skin and subcutaneous tissue disorders	0			1 (33.3)	1	49.5	1 (25.0)	1	37.1	2 (18.2)	2	27.0
Dermatitis contact	0			0			1 (25.0)	1	37.1	1 (9.1)	1	13.5
Haemorrhage subcutaneous	0			1 (33.3)	1	49.5	0			1 (9.1)	1	13.5
Gastrointestinal disorders	0			1 (33.3)	1	49.5	0			1 (9.1)	1	13.5
Dental caries	0			1 (33.3)	1	49.5	0			1 (9.1)	1	13.5
General disorders and administration site conditions	0			0			1 (25.0)	1	37.1	1 (9.1)	1	13.5
Face oedema	0			0			1 (25.0)	1	37.1	1 (9.1)	1	13.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

Adverse Events by system organ class and preferred term - age >=65 years - 4054 main trial - Japanese subgroup - safety analysis set

MedDRA system organ class Preferred term	placebo N (%)	E	R	Norditropin N (%)	E	R	somapacitan N (%)	E	R	total N (%)	E	R
Investigations	1 (25.0)	3	111.4	0			0			1 (9.1)	3	40.5
Alanine aminotransferase increased	1 (25.0)	1	37.1	0			0			1 (9.1)	1	13.5
Aspartate aminotransferase increased	1 (25.0)	1	37.1	0			0			1 (9.1)	1	13.5
Thyroxine free decreased	1 (25.0)	1	37.1	0			0			1 (9.1)	1	13.5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0			1 (33.3)	1	49.5	0			1 (9.1)	1	13.5
Plasma cell myeloma	0			1 (33.3)	1	49.5	0			1 (9.1)	1	13.5

%: Percentage of exposed subjects having the event, E: Number of adverse events reported, N: Number of subjects having the given event, or an event in the given system organ class at least once, R: Event rate per 100 patient years
MedDRA version 21.0.

ソマプシタン（遺伝子組換え）

2.7.4.7 付録

3. 小児患者を対象とした試験の解析帳票
（重篤な有害事象の叙述及び一覧を含む）

ノボ ノルディスク ファーマ株式会社

Table of contents

Page

1: Listings of adverse events with fatal outcome....2
2: Listings of serious adverse events 3
3: Listings of adverse events leading to premature discontinuation of trial product 6

Listings of deaths, SAEs and AE leading to premature drug discontinuation in the ongoing trial NN8640-4172 in children with GHD

1: Listings of adverse events with fatal outcome

There are no data for this output.

MedDRA version 21.0.
Data lock point 07MAY2019.
Table reflects the blinded data available in the central database at data lock point of the ongoing trial 4172 and data are not cleaned.

nn8640/nn8640-4172-ext2/cutoff_20190507_er
21MAY2019:13:11:00 - l_ae_fatal.sas/l_ae_fatal_sas.txt

2: Listings of serious adverse events

Subject ID/ Sex (M/F)/ Age (yrs)	AE no.	System Organ Class/ Preferred Term/ Reported Term	Onset Date/ Outcome	Study day/ Duration (days) Period	Serious/ MESI (Y/N)	Technical complaint (Y/N)	Severity/ Causality**	Action taken to trial product	Life-threatening (Y/N)
551005/ F/[redacted]	1	General disorders and administration site conditions/ Generalised Oedema/ Generalised Oedema	30APR2017/ Recovered/ Resolved	3/ 9/ Main	Y/N	N	Moderate/ Probable	Drug Interrupted	N
	2	Gastrointestinal disorders/ Vomiting/ Vomiting	01MAY2017/ Recovered/ Resolved	4/ 3/ Main	Y/N	N	Moderate/ Probable	Drug Interrupted	N
	5	Infections and infestations/ Tonsillitis/ Tonsillitis	28APR2018/ Recovered/ Resolved	366/ 10/ Extension	Y/N	N	Moderate/ Unlikely	Dose Not Changed	N
603001/ M/[redacted]	3	Endocrine disorders/ Hypopituitarism/ Multiple Pituitary Deficiency (Chronic Condition)	17JUL2016/ Not Recovered/ Not Resolved	96/ ./ Main	Y/N	N	Mild/ Unlikely	Dose Not Changed	N

AE: Adverse event, F: Female, M: Male, MESI: Medical event of special interest, N: No, Y: Yes, yrs: Years
**AE causality is based on judgement of investigators.
MedDRA version 21.0.
Data lock point 07MAY2019.
Table reflects the blinded data available in the central database at data lock point of the ongoing trial 4172 and data are not cleaned.

Listings of serious adverse events

Subject ID/ Sex (M/F)/ Age (yrs)	AE no.	System Organ Class/ Preferred Term/ Reported Term	Onset Date/ Outcome	Study day/ Duration (days) Period	Serious/ MESI (Y/N)	Technical complaint (Y/N)	Severity/ Causality**	Action taken to trial product	Life-threatening (Y/N)
603001/ M/[redacted]	6	Infections and infestations/ Gastroenteritis/ Acute Gastroentritis	16FEB2017/ Recovered/ Resolved	310/ 2/ Extension	Y/N	N	Moderate/ Unlikely	Dose Not Changed	N
	12	Infections and infestations/ Gastroenteritis/ Acute Gastroentritis	23FEB2018/ Recovered/ Resolved	682/ 2/ Safety extension	Y/N	N	Moderate/ Unlikely	Dose Not Changed	N
702001/ M/[redacted]	5	Surgical and medical procedures/ Adenoidectomy/ Adenoidektomiya	04MAY2017/ Recovered/ Resolved	381/ 1/ Safety extension	Y/N	N	Severe/ Unlikely	Dose Not Changed	N
750001/ F/[redacted]	5	Immune system disorders/ Anaphylactic Reaction/ Anaphylaxis	02SEP2018/ Recovered/ Resolved	683/ 2/ Safety extension	Y/N	N	Moderate/ Unlikely	Dose Not Changed	N

AE: Adverse event, F: Female, M: Male, MESI: Medical event of special interest, N: No, Y: Yes, yrs: Years
**AE causality is based on judgement of investigators.
MedDRA version 21.0.
Data lock point 07MAY2019.
Table reflects the blinded data available in the central database at data lock point of the ongoing trial 4172 and data are not cleaned.

Listings of serious adverse events

Subject ID/ Sex (M/F)/ Age (yrs)	AE no.	System Organ Class/ Preferred Term/ Reported Term	Onset Date/ Outcome	Study day/ Duration (days) Period	Serious/ MESI (Y/N)	Technical complaint (Y/N)	Severity/ Causality**	Action taken to trial product	Life-threatening (Y/N)
750002/ M/[redacted]	4	Infections and infestations/ Respiratory Syncytial Virus Bronchitis/ Bronchitis,respiratory Syncytial Virus Infection	15SEP2017/ Recovered/ Resolved	290/ 12/ Extension	Y/N	N	Moderate/ Unlikely	Dose Not Changed	N
	5	Renal and urinary disorders/ Nephrotic Syndrome/ Nephrotic Syndrome	30NOV2017/ Not Recovered/ Not Resolved	366/ ./ Safety extension	Y/N	N	Moderate/ Unlikely	Drug Withdrawn	N

AE: Adverse event, F: Female, M: Male, MESI: Medical event of special interest, N: No, Y: Yes, yrs: Years
**AE causality is based on judgement of investigators.
MedDRA version 21.0.
Data lock point 07MAY2019.
Table reflects the blinded data available in the central database at data lock point of the ongoing trial 4172 and data are not cleaned.

3: Listings of adverse events leading to premature discontinuation of trial product

Subject ID	Sex (M/F)/ Age (yrs)	AE no.	System Organ Class/ Preferred Term/ Reported Term	Onset Date/ Outcome	Study day/ Duration (days) Period	Serious/ MESI (Y/N)	Technical complaint (Y/N)	Severity/ Causality**	Action taken to trial product
651004	M/[redacted]	2	Immune system disorders/ Drug Hypersensitivity/ Allergy To Norditropin	06APR2017/ Not Recovered/ Not Resolved	45/ ./ Main	N/N	N	Mild/ Probable	Drug Withdrawn
750002	M/[redacted]	5	Renal and urinary disorders/ Nephrotic Syndrome/ Nephrotic Syndrome	30NOV2017/ Not Recovered/ Not Resolved	366/ ./ Safety extension	Y/N	N	Moderate/ Unlikely	Drug Withdrawn

AE: Adverse event, F: Female, M: Male, MESI: Medical event of special interest, N: No, Y: Yes, yrs: Years
**AE causality is based on judgement of investigators.
MedDRA version 21.0.
Data lock point 07MAY2019.
Table reflects the blinded data available in the central database at data lock point of the ongoing trial 4172 and data are not cleaned.

Overview of fatal cases from ongoing trials

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Trial ID/Subject ID	SOC/ Preferred Term/ Reported Term	AE No.	Onset Date/ Resolved Date/ Event Outcome/ Event Serious	AE Duration	Onset Latency	Investigator's Causality	Severity
	No_Cases_Found							

Overview of fatal cases from ongoing trials, Narratives

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Fields	Details
	Trial Id	No_Cases_Found
	Subject Id	-
	AE No.	.
	Case Narrative	

Overview of serious adverse events from ongoing trials

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Trial ID/Subject ID	SOC/ Preferred Term/ Reported Term	AE No.	Onset Date/ Resolved Date/ Event Outcome/ Event Serious	AE Duration	Onset Latency	Investigator's Causality	Severity
532603	NN8640-4172| 603001	Infections and infestations | Gastroenteritis| Acute Gastroentritis	6	16FEB2017| 17FEB2017| Recovered| Yes	1 days	309 Days	UNLIKELY	MODERATE

Overview of serious adverse events from ongoing trials

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Trial ID/Subject ID	SOC/ Preferred Term/ Reported Term	AE No.	Onset Date/ Resolved Date/ Event Outcome/ Event Serious	AE Duration	Onset Latency	Investigator's Causality	Severity
539071	NN8640-4172| 603001	Endocrine disorders | Hypopituitarism| Multiple pituitary deficiency (chronic condition)	3	17JUL2016| .| Not recovered| Yes		95 Days	UNLIKELY	MILD

Overview of serious adverse events from ongoing trials

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Trial ID/Subject ID	SOC/ Preferred Term/ Reported Term	AE No.	Onset Date/ Resolved Date/ Event Outcome/ Event Serious	AE Duration	Onset Latency	Investigator's Causality	Severity
543799	NN8640-4172| 551005	General disorders and administration site conditions | Generalised oedema | Generalised Oedema	1	30APR2017| 08MAY2017| Recovered| Yes	8 days	2 Days	PROBABLE	MODERATE
	NN8640-4172| 551005	Gastrointestinal disorders | Vomiting| Vomiting	2	01MAY2017| 03MAY2017| Recovered| Yes	2 days	3 Days	PROBABLE	MODERATE

Overview of serious adverse events from ongoing trials

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Trial ID/Subject ID	SOC/ Preferred Term/ Reported Term	AE No.	Onset Date/ Resolved Date/ Event Outcome/ Event Serious	AE Duration	Onset Latency	Investigator's Causality	Severity
545308	NN8640-4172| 702001	Surgical and medical procedures | Adenoidectomy | Adenoidektomiya	5	04MAY2017| 04MAY2017| Recovered| Yes	0 days	380 Days	UNLIKELY	SEVERE

Overview of serious adverse events from ongoing trials

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Trial ID/Subject ID	SOC/ Preferred Term/ Reported Term	AE No.	Onset Date/ Resolved Date/ Event Outcome/ Event Serious	AE Duration	Onset Latency	Investigator's Causality	Severity
564514	NN8640-4172| 750002	Infections and infestations | Respiratory syncytial virus bronchitis | bronchitis,respiratory syncytial virus infection	4	15SEP2017| 26SEP2017| Recovered| Yes	11 days	289 Days	UNLIKELY	MODERATE

Overview of serious adverse events from ongoing trials

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Trial ID/Subject ID	SOC/ Preferred Term/ Reported Term	AE No.	Onset Date/ Resolved Date/ Event Outcome/ Event Serious	AE Duration	Onset Latency	Investigator's Causality	Severity
575590	NN8640-4172| 750002	Renal and urinary disorders | Nephrotic syndrome| nephrotic syndrome	5	30NOV2017| .| Not recovered| Yes		365 Days	UNLIKELY	MODERATE

Overview of serious adverse events from ongoing trials

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Trial ID/Subject ID	SOC/ Preferred Term/ Reported Term	AE No.	Onset Date/ Resolved Date/ Event Outcome/ Event Serious	AE Duration	Onset Latency	Investigator's Causality	Severity
587806	NN8640-4172| 603001	Infections and infestations | Gastroenteritis| Acute Gastroentritis	12	23FEB2018| 24FEB2018| Recovered| Yes	1 days	681 Days	UNLIKELY	MODERATE

Overview of serious adverse events from ongoing trials

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Trial ID/Subject ID	SOC/ Preferred Term/ Reported Term	AE No.	Onset Date/ Resolved Date/ Event Outcome/ Event Serious	AE Duration	Onset Latency	Investigator's Causality	Severity
598447	NN8640-4172| 551005	Infections and infestations | Tonsillitis| Tonsillitis	5	28APR2018| 07MAY2018| Recovered| Yes	9 days	365 Days	UNLIKELY	MODERATE

Overview of serious adverse events from ongoing trials

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Trial ID/Subject ID	SOC/ Preferred Term/ Reported Term	AE No.	Onset Date/ Resolved Date/ Event Outcome/ Event Serious	AE Duration	Onset Latency	Investigator's Causality	Severity
619784	NN8640-4172| 750001	Immune system disorders | Anaphylactic reaction | anaphylaxis	5	02SEP2018| 03SEP2018| Recovered| Yes	1 days	682 Days	UNLIKELY	MODERATE

Overview of serious adverse events from ongoing trials, Narratives

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Fields	Details
532603	Trial Id	NN8640-4172
	Subject Id	603001
	System organ class/Preferred Term/Reported Term	Infections and infestations | Gastroenteritis | Acute Gastroentritis
	AE No.	6
	Onset Date/Resolved Date/Event Outcome/Event Serious	16FEB2017| 17FEB2017| Recovered| Yes
	AE Duration	1 days
	Onset Latency	309 Days
	Investigator's Causality	UNLIKELY
	Severity	MODERATE

ARGUS Case Number	Fields	Details
	Case Narrative	Trial ID: NN8640-4172 Trial title: A randomised, multinational, active-controlled, open-labelled, dose finding, double-blinded, parallel group trial, investigating efficacy and safety of once-weekly NNC0195-0092 treatment compared to daily growth hormone treatment (Norditropin FlexPro) in growth hormone treatment naive pre-pubertal children with growth hormone deficiency. The trial is designed as a 4 arm parallel group trial with 3 blinded doses levels of once-weekly NNC0195-0092 treatment and 1 active open labelled control arm of once daily Norditropin FlexPro Phase: 2 Trial Drugs: NNC0195-0092 5 mg/1.5 ml PDS290-10, NNC0195-0092 10 mg/1.5 ml PDS290-10, NNC0195-0092 15 mg/1.5 ml PDS290-15, Norditropin FlexPro 6.7 mg/ml. Patient's height: 9[redacted] cm. Patient's weight: 1[redacted] kg. Patient's BMI: 15.51. This Clinical Trial case from ISRAEL was reported by an Investigator as "Acute Gastroentritis" and concerned a[redacted]Years old Male patient who was treated with Blinded NNC0195-0092 vs Norditropin (Blinded NNC0195-0092 vs Norditropin) from 13-APR-2016 and ongoing due to "Growth hormone deficiency". Medical history included growth hormone deficiency, iron deficiency anemia, pituitary and pituitary stalk hypoplasia and ectopic neuro hypophisis. Treatment medications included - ceftriaxone(ceftriaxone), dextrose and sodium chloride(glucose, sodium chloride), sodium chloride(sodium chloride). On 16-FEB-2017 the patient was hospitalised with symptoms of vomiting, diarrhoea and sleepiness. Acute gastroenteritis was diagnosed. During hospitalisation, the patient received treatment with ant biotics Ceftriaxone (ceftriaxone) and fluids; intravenously Dextrose 5 % + Sodium Chloride 0.9 % (glucose, sodium chloride) and with intravenous Sodium Chloride 0.9 % (sodium chloride). In hospital, the patient also received his concomitant medications by IV (intravenously). The patient was diagnosed with multiple pituitary deficiency on 17-JUL-2016 during trial conduct (captured in Argus 539071). On 17-FEB-2017 the patient was discharged and considered recovered from the event "Acute Gastroentritis". Action taken to Blinded NNC0195-0092 vs Norditropin was reported as No Change. Investigator's causality (Blinded NNC0195-0092 vs Norditropin) - Acute Gastroentritis : Unl kely Sponsor's causality (Blinded NNC0195-0092 vs Norditropin) - Acute Gastroentritis : Unl kely Since last submission of the case, following information was updated (NOT YET SUBMITTED): - detailed course of event - Trial product information updated Narrative updated accordingly

Overview of serious adverse events from ongoing trials, Narratives

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Fields	Details
539071	Trial Id	NN8640-4172
	Subject Id	603001
	System organ class/Preferred Term/Reported Term	Endocrine disorders | Hypopituitarism| Multiple pituitary deficiency (chronic condition)
	AE No.	3
	Onset Date/Resolved Date/Event Outcome/Event Serious	17JUL2016| .| Not recovered| Yes
	Onset Latency	95 Days
	Investigator's Causality	UNLIKELY
	Severity	MILD
	Case Narrative	Trial ID: NN8640-4172 Trial title: A randomised, multinational, active-controlled, open-labelled, dose finding, double-blinded, parallel group trial, investigating efficacy and safety of once-weekly NNC0195-0092 treatment compared to daily growth hormone treatment (Norditropin FlexPro) in growth hormone treatment naive pre-pubertal children with growth hormone deficiency. The trial is designed as a 4 arm parallel group trial with 3 blinded doses levels of once-weekly NNC0195-0092 treatment and 1 active open labelled control arm of once daily Norditropin FlexPro Phase: 2 Trial Drugs: NNC0195-0092 5 mg/1.5 ml PDS290-10, NNC0195-0092 10 mg/1.5 ml PDS290-10, NNC0195-0092 15 mg/1.5 ml PDS290-15, Norditropin FlexPro 6.7 mg/ml. Patient's height: 9[redacted] cm. Patient's weight: 1[redacted] kg. Patient's BMI: 15.51200010. This Clinical Trial case from ISRAEL was reported by an Investigator as "Multiple pituitary deficiency (chronic condition)" and concerned a [redacted]Years old Male patient who was treated with Blinded NNC0195-0092 vs Norditropin (NN8640-4172) from 13-APR-2016 and ongoing due to "Growth hormone deficiency". Medical history included growth hormone deficiency, iron deficiency anemia, pituitary and pituitary stalk hypoplasia and ectopic neuro hypophisis, pituitary and pituitary stalk hypoplasia and ectopic neuro hypophisis. Treatment medications included - hydrocortisone(hydrocortisone), eltroxin(levothyroxine sodium). On 17-JUL-2016 the patient experienced Multiple pituitary deficiency due to Cortisol blood test. The patient started with isolated GH def. (Growth Hormone deficiency) and later developed additional pituitary deficits includes TSH (Thyroid-stimulating hormone) and ACTH (Adrenocorticotropic hormone). ACTH (Blood corticotrophin) test results: T4 (Thyroxine): 0.7 ng/dL, TSH (Blood thyroid stimulating hormone) 2.8 mU/L, Cortisol (Blood cortisol) up to 17.4 ug/dL The patient was treated with Hydrocortisone and Eltroxin. The condition was seen as chronic and the investigator will follow up on regular basis. Action taken to Blinded NNC0195-0092 vs Norditropin was reported as No Change. The outcome for the event "Multiple pituitary deficiency (chronic condition)" was Not recovered. Investigator's causality (Blinded NNC0195-0092 vs Norditropin) - Multiple pituitary deficiency (chronic condition) : Unl kely Sponsor's causality (Blinded NNC0195-0092 vs Norditropin) - Multiple pituitary deficiency (chronic condition) : Unlikely

Overview of serious adverse events from ongoing trials, Narratives

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Fields	Details
543799	Trial Id	NN8640-4172
	Subject Id	551005
	System organ class/Preferred Term/Reported Term	General disorders and administration site conditions | Generalised oedema | Generalised Oedema
	AE No.	1
	Onset Date/Resolved Date/Event Outcome/Event Serious	30APR2017| 08MAY2017| Recovered| Yes
	AE Duration	8 days
	Onset Latency	2 Days
	Investigator's Causality	PROBABLE
	Severity	MODERATE
	Trial Id	NN8640-4172
	Subject Id	551005
	System organ class/Preferred Term/Reported Term	Gastrointestinal disorders | Vomiting| Vomiting
	AE No.	2
	Onset Date/Resolved Date/Event Outcome/Event Serious	01MAY2017| 03MAY2017| Recovered| Yes
	AE Duration	2 days
	Onset Latency	3 Days
	Investigator's Causality	PROBABLE
	Severity	MODERATE

ARGUS Case Number	Fields	Details
	Case Narrative	Trial ID: NN8640-4172 Trial title: A randomised, multinational, active-controlled, open-labelled, dose finding, double-blinded, parallel group trial, investigating efficacy and safety of once-weekly NNC0195-0092 treatment compared to daily growth hormone treatment (Norditropin FlexPro) in growth hormone treatment naive pre-pubertal children with growth hormone deficiency. The trial is designed as a 4 arm parallel group trial with 3 blinded doses levels of once-weekly NNC0195-0092 treatment and 1 active open labelled control arm of once daily Norditropin FlexPro Phase: 2 Trial Drugs: NNC0195-0092 5 mg/1.5 ml PDS290-10, NNC0195-0092 10 mg/1.5 ml PDS290-10, NNC0195-0092 15 mg/1.5 ml PDS290-15, Norditropin FlexPro 6.7 mg/ml. Patient's height: 6[redacted] cm. Patient's weight:[redacted]kg. Patient's BMI: 14.64799980. This Clinical Trial case from INDIA was reported by an Investigator as "Vomiting" and "Generalised Oedema" and concerned a 3[redacted]Months old Female patient who was treated with Blinded NNC0195-0092 vs Norditropin (NN8640-4172) from 28-APR-2017 to 28-APR-2017 and from 17-JUN-2017 and ongoing, due to "Growth hormone deficiency". Medical history included growth hormone deficiency. Treatment medications included – emeset (ondansetron hydrochloride), ceftriaxone (ceftriaxone), normal saline (sodium chloride), ORS (glucose, potassium chloride, sodium chloride, sodium citrate), prowel (metoclopramide hydrochloride), lanzol (lansoprazole), bifilac (bacillus coagulans), potassium chloride (potassium chloride), pedicloryl (triclofos sodium). On 30-APR-2017 the patient presented with generalised oedema. On 01-MAY-2017 the patient experienced vomiting. On 02-MAY-2017 the patient was admitted to hospital due to gradually progressive oedema and vomiting. The patient was dehydrated, due to the vomiting and irritable and was tachycardic with generalised oedema. On examination, the patient had oedema all over the body and was tired and irritable. On the same date C-reactive protein (ultrasensitive) was 0.88 mg/L (reference range: 0.0-1.0) and white blood cell count (WBC) was 15.86 K/uL (reference range: 5-15). The patient was admitted to the paediatric intensive care unit for observation and stabilization. The patient was treated with IV (intravenous) fluids, injection with Emeset, ORS powder, junior Lanzol DT, Bifilac, Pro-Wel, Pedicloryl, Normal Saline, Inj. Potassium Chloride and Ceftriaxone due to the poor oral intake and vomiting. The patient developed high grade continuous fever after admission, which was not expected to be related to trial product (non-serious event). A paediatric cardiology consultation was sought as the patient had tachycardia and generalised oedema. A bedside ECHO (echocardiogram) showed no structural lesion and good ventricular function. Since the patient had persistent high grade fever with irritability, a paediatric neurology consultation was also sought. MRI (nuclear magnetic resonance imaging) done was normal and oph thalmic evaluation (dilated fundus examination) showed no papilledema. Blood counts showed leucocytosis with negative inflammatory markers. The tachycardia was seen as related to the fever and leucocytosis was seen as associated to generalised oedema. Blood and urine culture were stable. During hospitalisation blood count was measured as: 02-MAY-2017: 15.86 ku/ml 03-MAY-2017: 16.71 ku/ml 04-MAY-2017: 9.08 ku/ml 05-MAY-2017: 9.58 ku/ml 07-MAY-2017: 12.86 ku/ml with referece values 5-15 ku/ml The patient was started on IV Ceftriaxone for 5 days from 03-MAY-2017 to 08-MAY-2017 after sending for blood and urine cultures. The fever subsided after 48 hours and she improved symptomatically and started tolerating oral food. The patient remained afebrile and oedema reduced and blood counts showed improving trend. On 08-MAY-2017 the patient was discharged from hospital. At this time she was afebrile, the oedema was better and she was hemodynamically stable. Action taken to NNC0195-0092 vs Norditropin was reported as Drug discontinued temporarily for both events. The next dose of trial drug should have been taken 1 week after 28-APR-2017, but was not given. On 03-MAY-2017 the outcome for the event "Vomiting" was recovered. On 08-MAY-2017 the outcome for the event "Generalised Oedema" was recovered. On 17-JUN-2017, after recovery, the trial drug was re-introduced at decreased dose. The events did not reappear. Investigator's causality (NNC0195-0092) - Vomiting: Probable Generalised Oedema: Probable Sponsor's causality (NNC0195-0092) - Vomiting: Unl kely Generalised Oedema: Unlikely Since last submission of the case, following information was updated: - Trial drug re-introduced - Decreased dose - Narrative updated Company comment: The patient experienced leukocytosis, vomiting and fever and was treated with ant biotics. Trial product was re-introduced without reoccurrence of the events. As papilledema was excluded, ruling out intracranial hypertension, sponsor finds an inflammatory response or other underlying disease the most likely

ARGUS Case Number	Fields	Details
		cause of the events 'vomiting' and 'generalised edema'. Hence sponsor evaluates the events more likely related to the patients underlying disease (infection or immunosuppression) and unl kely related to trial product treatment.

Overview of serious adverse events from ongoing trials, Narratives

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Fields	Details
545308	Trial Id	NN8640-4172
	Subject Id	702001
	System organ class/Preferred Term/Reported Term	Surgical and medical procedures | Adenoidectomy | Adenoidektomiya
	AE No.	5
	Onset Date/Resolved Date/Event Outcome/Event Serious	04MAY2017| 04MAY2017| Recovered| Yes
	AE Duration	0 days
	Onset Latency	380 Days
	Investigator's Causality	UNLIKELY
	Severity	SEVERE

Overview of serious adverse events from ongoing trials, Narratives

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Fields	Details
	Case Narrative	Trial ID: NN8640-4172 Trial title: A randomised, multinational, active-controlled, open-labelled, dose finding, double-blinded, parallel group trial, investigating efficacy and safety of once-weekly NNC0195-0092 treatment compared to daily growth hormone treatment (Norditropin FlexPro) in growth hormone treatment naive pre-pubertal children with growth hormone deficiency. The trial is designed as a 4 arm parallel group trial with 3 blinded doses levels of once-weekly NNC0195-0092 treatment and 1 active open labeled control arm of once daily Norditropin FlexPro Phase: 2 Trial Drugs: NNC0195-0092 5 mg/1.5 ml PDS290-10, NNC0195-0092 10 mg/1.5 ml PDS290-10, NNC0195-0092 15 mg/1.5 ml PDS290-15, Norditropin FlexPro 6.7 mg/ml Patient's height: 10[redacted] cm. Patient's weight: 1[redacted] kg. Patient's BMI: 15.72. This Clinical Trial case from UKRAINE was reported by an Investigator as "Adenoidektomiya" and concerned a [redacted]year-old Male patient who was treated with Norditropin (NN8640-4172) from 19-APR-2016 and ongoing due to "growth hormone deficiency". Medical history included growth hormone deficiency, ¿asy cognitive disorder, cyst epiphysis, significant behavioral disorders, attention deficit, moderate external hydrocephalus and adenoids II since 18-SEP-2015. Treatment medications included - buprofen(buprofen), tranexamic acid(tranexamic acid), atropine sulfate aguettant(atropine sulfate), diphenhydramine(diphenhydramine), propofol(propofol), suxamethonium(suxamethonium chloride), fentanyl (fentanyl citrate), ondansetron(ondansetron), aquamax(cetostearyl alcohol, paraffin, liquid, phenoxyethanol, polysorbate 60, white soft paraffin), benzydamine(benzydamine). Since 18-SEP-2015, prior to entering the trial, the patient has had adenoids II. The condition did not worsen since SEP-2015. ¿onservative treatment did not help. Surgery was scheduled after the first year in study (not pre-planned), but since the study was extended to three years, the patient's mother decided not to wait that long. The patient had had nasal congestion, shortness of nasal breathing, frequent colds and snoring at night snuffle. On 03-MAY-2017, the patient was admitted to hospital, and on 04-MAY-2017 a routine adenoidectomy was performed under general anaesthesia with intubation. On 04-MAY-2017, the patient was considered recovered from both the adenoidectomy and from the adenoids. On 05-MAY-2017, the patient was discharged from hospital and started treatment with Benzydamine until 10-MAY-2017. On 06-MAY-2017, the patient started treatment with Aquamax until 11-MAY-2017 due to the adenoidectomy. During the hospitalisation the patient was treated with Ibuprofen, Tranexamic acid, Atropine sulfate aguettant, Diphenhydramine, Suxamethonium, Fentanyl and ondansetron. Action taken to Norditropin was reported as No Change. On 04-MAY-2017 the outcome for the event "Adenoidektomiya" was recovered. Investigator's causality (Norditropin) - Adenoidektomiya: Unlikely Sponsor's causality (Norditropin) - Adenoidektomiya: Unlikely Since last submission of the case the following information was updated: - Reported event updated wording - Indication for concomitant medication updated - Medical history updated - Trial product corrected in narrative to reflect that the patient was randomised to open label Norditropin Narrative updated accordingly

Overview of serious adverse events from ongoing trials, Narratives

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Fields	Details
564514	Trial Id	NN8640-4172
	Subject Id	750002
	System organ class/Preferred Term/Reported Term	Infections and infestations | Respiratory syncytial virus bronchitis | bronchitis,respiratory syncytial virus infection
	AE No.	4
	Onset Date/Resolved Date/Event Outcome/Event Serious	15SEP2017| 26SEP2017| Recovered| Yes
	AE Duration	11 days
	Onset Latency	289 Days
	Investigator's Causality	UNLIKELY
	Severity	MODERATE

ARGUS Case Number	Fields	Details
	Case Narrative	Trial ID: NN8640-4172 Trial title: A randomised, multinational, active-controlled, open-labelled, dose finding, double-blinded, parallel group trial, investigating efficacy and safety of once-weekly NNC0195-0092 treatment compared to daily growth hormone treatment (Norditropin FlexPro) in growth hormone treatment naive pre-pubertal children with growth hormone deficiency. The trial is designed as a 4 arm parallel group trial with 3 blinded doses levels of once-weekly NNC0195-0092 treatment and 1 active open labelled control arm of once daily Norditropin FlexPro Phase: 2 Trial Drugs: NNC0195-0092 5 mg/1.5 ml PDS290-10, NNC0195-0092 10 mg/1.5 ml PDS290-10, NNC0195-0092 15 mg/1.5 ml PDS290-15, Norditropin FlexPro 6.7 mg/ml. Patient's height: 9[redacted] cm. Patient's weight: 1[redacted] kg. Patient's BMI: 15.51200010. This Clinical Trial case from JAPAN was reported by an Investigator as "bronchitis, respiratory syncytial virus infection" and concerned a[redacted]Years old Male patient who was treated with Norditropin from 30-NOV-2016 and ongoing due to "Growth hormone deficiency". Medical history included growth hormone deficiency, epilepsy, asthma, food allergy, mental retardation. Concomitant medications included - sa butamol sulfate (salbutamol sulfate). Treatment medications included – Acetaminophen (paracetamol), dexamethasone (dexamethasone), methylprednisolone sodium succinate (methylprednisolone sodium succinate), Veen D (calcium chloride dihydrate, glucose, potassium chloride, sodium acetate, sodium chloride). On 15-SEP-2017 the patient experienced fever and wheezing. This was the reported onset date of the event "bronchitis, respiratory syncytial virus infection". On 19-SEP-2017 a respiratory syncytial (RS) virus test was performed, which was positive and the patient was admitted to hospital for respiratory care. On the same date a chest x-ray showed: Hilar shadow increase; Peribronchial shadow increase; Lower respiratory infection. After being treated by steriod and oxygen, the patient's respiratory distress recovered. Steroid and oxygen were discontinued after 8 days of treatment. There was no recurrence of respiratory symptom after discontinuation of therapy. On 26-SEP-2017 the patient was discharged from hospital. Action taken to Norditropin was reported as No Change. On 26-SEP-2017 the outcome for the event "bronchitis, respiratory syncytial virus infection" was recovered. Investigator's causality (Norditropin) - Bronchitis, respiratory syncytial virus infection: Unl kely Sponsor's causality (Norditropin) - Bronchitis, respiratory syncytial virus infection: Unlikely

Overview of serious adverse events from ongoing trials, Narratives

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Fields	Details
575590	Trial Id	NN8640-4172
	Subject Id	750002
	System organ class/Preferred Term/Reported Term	Renal and urinary disorders | Nephrotic syndrome | nephrotic syndrome
	AE No.	5
	Onset Date/Resolved Date/Event Outcome/Event Serious	30NOV2017| .| Not recovered| Yes
	Onset Latency	365 Days
	Investigator's Causality	UNLIKELY
	Severity	MODERATE

ARGUS Case Number	Fields	Details
	Case Narrative	Trial ID: NN8640-4172 Trial title: A randomised, multinational, active-controlled, open-labelled, dose finding, double-blinded, parallel group trial, investigating efficacy and safety of once-weekly NNC0195-0092 treatment compared to daily growth hormone treatment (Norditropin FlexPro) in growth hormone treatment naive pre-pubertal children with growth hormone deficiency. The trial is designed as a 4 arm parallel group trial with 3 blinded doses levels of once-weekly NNC0195-0092 treatment and 1 active open labelled control arm of once daily Norditropin FlexPro Phase: 2 Trial Drugs: NNC0195-0092 5 mg/1.5 ml PDS290-10, NNC0195-0092 10 mg/1.5 ml PDS290-10, NNC0195-0092 15 mg/1.5 ml PDS290-15, Norditropin FlexPro 6.7 mg/ml. Patient's height: 9[redacted] cm. Patient's weight: 1[redacted] kg. Patient's BMI: 15.51200010. This Clinical Trial case from JAPAN was reported by an Investigator as "nephrotic syndrome" and concerned a [redacted] Years old Male patient who was treated with Blinded NNC0195-0092 vs Norditropin (NN8640-4172) from 30-NOV-2016 to 28-NOV-2017 due to "Growth hormone deficiency". Medical history included growth hormone deficiency, epilepsy, asthma, food allergy, mental retardation. Treatment medications included - prednisolone(prednisolone), albuminar(albumin human), furosemide(furosemide), amlodipine(amlodipine). On 30-NOV-2017 the patient experienced nephrotic syndrome and was admitted to hospital. He presented with oedema and revealed to have hypoa buminemia and hypercholesterolemia by laboratory test on 29-NOV-2017. On 30-NOV-2017 Lab tests performed: Albumin: 0.8 g/dl (ref 3.6 – 4.7) T-cholestrol: 631.0 mg/dl (ref 125-230) On 30-NOV-2017, he was diagnosed to have nephrotic syndroma. On 01-DEC-2017 he started treatment with steroid, Prednisolone, Albuminar and Furosemide, all given intravenous. On 07-DEC-2017 he started treatment with Amlodipine. On 08-DEC-2017 he started treatment with oral Prednisolone On 16-FEB-2018 protein in urine test was 4.0 (units and ref. range not provided) The patient was diagnosed with steroid-resistant nephrotic syndrome with the progress of the treatment. AE diagnosis not updated to final diagnosis as nephrotic syndrome included Steroid-resistant nephrotic syndrome. The treatment under hospitalization is ongoing in department of nephrology and rheumatology. Although the dialysis treatment was finished, severe proteinuria is remaining. The AE was not recovered, but the investigator judged that the follow-up of the AE as the clinical trial was not needed because the medical treatment under hospitalization will be continued for a long term. On 31-MAR-2018 the patient was discharged from hospital. Action taken to Blinded NNC0195-0092 vs Norditropin was reported as Product discontinued. The outcome for the event "nephrotic syndrome" was Not recovered, and was evaluated as chronic. Investigator's causality (Blinded NNC0195-0092 vs Norditropin) - nephrotic syndrome : Unl kely Sponsor's causality (Blinded NNC0195-0092 vs Norditropin) - nephrotic syndrome : Unlikely

ARGUS Case Number	Fields	Details
587806	Trial Id	NN8640-4172
	Subject Id	603001
	System organ class/Preferred Term/Reported Term	Infections and infestations | Gastroenteritis | Acute Gastroentritis
	AE No.	12
	Onset Date/Resolved Date/Event Outcome/Event Serious	23FEB2018| 24FEB2018| Recovered| Yes
	AE Duration	1 days
	Onset Latency	681 Days
	Investigator's Causality	UNLIKELY
	Severity	MODERATE
	Case Narrative	Trial ID: NN8640-4172 Trial title: A randomised, multinational, active-controlled, open-labelled, dose finding, double-blinded, parallel group trial, investigating efficacy and safety of once-weekly NNC0195-0092 treatment compared to daily growth hormone treatment (Norditropin FlexPro) in growth hormone treatment naive pre-pubertal children with growth hormone deficiency. The trial is designed as a 4 arm parallel group trial with 3 blinded doses levels of once-weekly NNC0195-0092 treatment and 1 active open labelled control arm of once daily Norditropin FlexPro Phase: 2 Trial Drugs: NNC0195-0092 5 mg/1.5 ml PDS290-10, NNC0195-0092 10 mg/1.5 ml PDS290-10, NNC0195-0092 15 mg/1.5 ml PDS290-15, Norditropin FlexPro 6.7 mg/ml. Patient's height: 9[redacted] cm. Patient's weight: 1[redacted] kg. Patient's BMI: 15.51200010. This Clinical Trial case from ISRAEL was reported by an Investigator as "Acute Gastroentritis" and concerned a [redacted]Years old Male patient who was treated with Blinded NNC0195-0092 vs Norditropin (NN8640-4172) from 13-APR-2016 and ongoing due to "Growth hormone deficiency", Medical history included growth hormone deficiency, iron deficiency anemia, pituitary and pituitary sta k hypoplasia and ectopic neuro hypophisis. Concomitant medications included – hydrocortisone (hydrocortisone). Treatment medications included - glucose + sodium chloride (glucose, sodium chloride). On 23-FEB-2018 in the morning, the patient experienced excessive vomiting and diarrhoea without fever. Due to the excessive vomiting and inability to receive his usual oral hydrocortisone treatment, he was hospitalized to receive hydrocortisone as IV (intravenous) and received half standard (glucose 5%, 0.45% NACL) IV fluids, as well during the hospitalisation. He was diagnosed with acute gastroenteritis. On 24-FEB-2018 he was discharged from hospital. According to the Doctor, this was not related to the GH treatment. Action taken to Blinded NNC0195-0092 vs Norditropin was reported as No Change. On 24-FEB-2018 the outcome for the event "Acute Gastroentritis" was Recovered. Investigator's causality (Blinded NNC0195-0092 vs Norditropin) - Acute Gastroentritis: Unl kely Sponsor's causality (Blinded NNC0195-0092 vs Norditropin) - Acute Gastroentritis: Unl kely

ARGUS Case Number	Fields	Details
598447	Trial Id	NN8640-4172
	Subject Id	551005
	System organ class/Preferred Term/Reported Term	Infections and infestations | Tonsillitis| Tonsillitis
	AE No.	5
	Onset Date/Resolved Date/Event Outcome/Event Serious	28APR2018| 07MAY2018| Recovered| Yes
	AE Duration	9 days
	Onset Latency	365 Days
	Investigator's Causality	UNLIKELY
	Severity	MODERATE
	Case Narrative	Trial ID: NN8640-4172 Trial title: A randomised, multinational, active-controlled, open-labelled, dose finding, double-blinded, parallel group trial, investigating efficacy and safety of once-weekly NNC0195-0092 treatment compared to daily growth hormone treatment (Norditropin FlexPro) in growth hormone treatment naive pre-pubertal children with growth hormone deficiency. The trial is designed as a 4 arm parallel group trial with 3 blinded doses levels of once-weekly NNC0195-0092 treatment and 1 active open labelled control arm of once daily Norditropin FlexPro Phase: 2 Trial Drugs: NNC0195-0092 5 mg/1.5 ml PDS290-10, NNC0195-0092 10 mg/1.5 ml PDS290-10, NNC0195-0092 15 mg/1.5 ml PDS290-15, Norditropin FlexPro 6.7 mg/ml. Patient's height: 6[redacted] cm. Patient's weight: [redacted] kg. Patient's BMI: 14.64799980. This Clinical Trial case from INDIA was reported by an Investigator as "Tonsillitis" and concerned a [redacted] Years old Female patient who was treated with Blinded NNC0195-0092 vs Norditropin (NN8640-4172) from 28-APR-2017 and ongoing due to "Growth hormone deficiency", Medical history included growth hormone deficiency. Treatment medications included - dolo (paracetamol), amoxicillin (amoxicillin trihydrate). On 28-APR-2018 the patient experienced fever and complaints and signs of Tonsillitis. On 29-APR-2018 she was admitted to hospital. During the hospitalisation she was treated with tablets of Polo and Amoxicillin capsules. On 01-MAY-2018 the patient was discharged from hospital. She was advised to continue the treatment with capsule Amoxicillin for 3 days. On 07-MAY-2018 the patient was at site for visit 7. She was evaluated as completely recovered from Tonsillitis. Action taken to Blinded NNC0195-0092 vs Norditropin was reported as No Change. On 07-MAY-2018 the outcome for the event "Tonsillitis" was Recovered. Investigator's causality (Blinded NNC0195-0092 vs Norditropin) - Tonsillitis : Unlikely Sponsor's causality (Blinded NNC0195-0092 vs Norditropin) - Tonsillitis : Unlikely Since last submission of the case, following information was updated: (Not yet submitted) - Date for recovery - Treatment updated - Updated information on outcome at site visit. - Information on discharge summary and the patients condition at discharge removed from source data. Narrative updated accordingly.

ARGUS Case Number	Fields	Details
619784	Trial Id	NN8640-4172
	Subject Id	750001
	System organ class/Preferred Term/Reported Term	Immune system disorders | Anaphylactic reaction | anaphylaxis
	AE No.	5
	Onset Date/Resolved Date/Event Outcome/Event Serious	02SEP2018| 03SEP2018| Recovered| Yes
	AE Duration	1 days
	Onset Latency	682 Days
	Investigator's Causality	UNLIKELY
	Severity	MODERATE
	Case Narrative	Trial ID: NN8640-4172 Trial title: A randomised, multinational, active-controlled, open-labelled, dose finding, double-blinded, parallel group trial, investigating efficacy and safety of once-weekly NNC0195-0092 treatment compared to daily growth hormone treatment (Norditropin FlexPro) in growth hormone treatment naive pre-pubertal children with growth hormone deficiency. The trial is designed as a 4 arm parallel group trial with 3 blinded doses levels of once-weekly NNC0195-0092 treatment and 1 active open labelled control arm of once daily Norditropin FlexPro Phase: 2 Trial Drugs: NNC0195-0092 5 mg/1.5 ml PDS290-10, NNC0195-0092 10 mg/1.5 ml PDS290-10, NNC0195-0092 15 mg/1.5 ml PDS290-15, Norditropin FlexPro 6.7 mg/ml. Patient's height: 8[redacted] cm. Patient's weight: 1[redacted] kg. Patient's BMI: 13.5210. This Clinical Trial case from JAPAN was reported by an Investigator as "anaphylaxis" and concerned a [redacted] Years old Female patient who was treated with Blinded NNC0195-0092 vs Norditropin (NN8640-4172) from 20-OCT-2016 and ongoing due to "Growth hormone deficiency". Medical history included growth hormone deficiency, food allergy. Treatment medications included - epipen(epinephrine), methylprednisol sodium succinate(methylprednisolone sodium succinate), hydroxyzine hydrochloride(hydroxyzine hydrochloride). On 02-SEP-2018 the patient experienced eruption and was wheezing after eating chocolate. The patient was known with food allergy. The patient was transferred to the emergency room at a medical centre. She was diagnosed and admitted to hospital at children's medical centre. The patient was treated with Epipen intramuscular injection and with Methylprednisol sodium succinate and Hydroxyzine hydrochloride as intravenous treatment, on the same day. On 03-SEP-2018 she was improved and was discharged from hospital. Action taken to Blinded NNC0195-0092 vs Norditropin was reported as No Change. On 03-SEP-2018 the outcome for the event "anaphylaxis" was Recovered. Investigator's causality (Blinded NNC0195-0092 vs Norditropin) - anaphylaxis : Unlikely Sponsor's causality (Blinded NNC0195-0092 vs Norditropin) - anaphylaxis : Unlikely

Overview of event of special interest from ongoing trials

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Trial ID/Subject ID	SOC/ Preferred Term/ Reported Term	AE No.	Onset Date/ Resolved Date/ Event Outcome/ Event Serious	AE Duration	Onset Latency	Investigator's Causality	Severity
	No_Cases_Found							

Overview of event of special interest from ongoing trials, Narratives

Trials: NN8640-4172
Submission data lock date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Fields	Details
	Trial Id	No_Cases_Found
	Subject Id	-
	AE No.	.
	Case Narrative	

Overview of pregnancy cases from ongoing and completed trials

Trials: NN8640-4172
DLP Date: 08MAY2019

Final Version: 3.0

ARGUS Case Number	Fields	Details
	Country/Report Type	
	Age/Gender	
	Trial ID	No_Cases_Found
	Subject ID	
	System organ class/Preferred Term/Reported Term	
	Onset Latency	
	AE No.	.
	Onset Date/Resolved Date/Event Outcome/Event Serious	
	Treatment Start/Stop Dates	
	Investigator's Causality	
	Severity	
	Case Narrative	

ソマプシタン（遺伝子組換え）

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 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。