Clinical trial results:
A multicentre, multinational, randomised, parallel-group, placebo-controlled (double blind) and active-controlled (open) trial to compare the efficacy and safety of once-weekly dosing of NNC0195-0092 with once-weekly dosing of placebo and daily Norditropin® FlexPro® in adults with growth hormone deficiency for 35 weeks, followed by a 53-week open-label extension period

Summary

EudraCT number	2013-002892-16
Trial protocol	SE GB DE LT LV
Global end of trial date	07 May 2018

Results information

Result version number	v1 (current)
This version publication date	22 May 2019
First version publication date	22 May 2019

Trial information

Trial identification

Sponsor protocol code	NN8640-4054

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02229851
WHO universal trial number (UTN)	U1111-1145-0211

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 May 2017
Global end of trial reached?	Yes
Global end of trial date	07 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of once-weekly dosing of somapacitan (NNC0195-0092) compared to placebo after 34 weeks of treatment in AGHD patients

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (Oct 2013) and ICH Good Clinical Practice, including archiving of essential documents (May 1996) and EN ISO 14155 Part 1 and 2 and FDA 21 CFR 312.120.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	31 October 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	India: 28
Country: Number of subjects enrolled	Japan: 46
Country: Number of subjects enrolled	Lithuania: 8
Country: Number of subjects enrolled	Latvia: 3
Country: Number of subjects enrolled	Malaysia: 7
Country: Number of subjects enrolled	Poland: 11
Country: Number of subjects enrolled	Romania: 28
Country: Number of subjects enrolled	Russian Federation: 18
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Turkey: 8
Country: Number of subjects enrolled	Ukraine: 8
Country: Number of subjects enrolled	Australia: 30
Country: Number of subjects enrolled	United States: 79
Country: Number of subjects enrolled	South Africa: 9
Worldwide total number of subjects	300
EEA total number of subjects	67

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	259
From 65 to 84 years	41
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 92 sites in 16 countries namely Australia, Germany, India, Japan, Latvia, Lithuania, Malaysia, Poland, Romania, Russian federation, South Africa, Sweden, Turkey, Ukraine, United Kingdom and United States.

Pre-assignment

Screening details:

In the main phase of the study, 8 weeks of titration was followed by 26 weeks of fixed dose administration followed by a 1 week washout period. In the open-label extension phase, 8 weeks of titration was followed by 44 weeks of fixed dose administration followed by a 1-week washout period.

Period 1

Period 1 title	Main phase (Double-blind phase)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

For the main part of the trial, somapacitan PDS290 10 mg/1.5 ml and somapacitan PDS290 placebo pens were visually identical and labelled blinded, whereas Norditropin® FlexPro® was open-labelled.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received placebo (somapacitan) for 34 weeks (8 weeks dose titration followed by 26 weeks fixed dose treatment) in the main phase of the trial.

Arm type	Placebo
Investigational medicinal product name	Somapacitan PDS290 Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects injected themselves once-weekly subcutaneously (s.c.; under the skin) in the morning (before 10 AM). On site visit days this was extended until 12:00 PM (noon). Injections were taken in the thigh and/or abdomen alternating within these body areas for every injection. Subjects were trained to use the pen injector under the supervision of site staff. Dose adjustments were allowed during the first 8 weeks titration period (at week 2, 4, 6 and 8). Dose adjustments were based on insulin like growth factor - I (IGF-I) standard deviation score (SDS). The minimum and maximum weekly dose was set to 0.1 mg and 8 mg, respectively.

Arm title	Norditropin

Arm description:

Subjects recieved Norditropin® FlexPro® 10 mg/1.5 mL for 34 weeks (8 weeks dose titration followed by 26 weeks fixed dose treatment) in the main phase of the trial.

Arm type	Active comparator
Investigational medicinal product name	Somatropin
Investigational medicinal product code	
Other name	Norditropin® FlexPro® 10 mg/1.5 mL
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects injected themselves daily subcutaneously (s.c.; under the skin) in the evening, which was usual practice except when administered under observation. On site visit days the product was administered in the morning (up to 12 PM) and at least 12 hours after injection, the evening before. Injections were taken in the thigh and/or abdomen alternating within these body areas for every injection. Subjects were trained to use the pen injector under the supervision of site staff. Dose adjustments were allowed during the first 8 weeks titration period (at week 2, 4, 6 and 8). Dose adjustments were based on insulin like growth factor - I (IGF-I) standard deviation score (SDS). The minimum and maximum weekly dose was set to 0.05 mg and 1.1 mg, respectively. In Japanese subjects, the maximum daily dose was set to 1.0 mg.

Arm title	Somapacitan

Arm description:

Subjects received Somapacitan PDS290 10mg/1.5mL for 34 weeks (8 weeks dose titration followed by 26 weeks fixed dose treatment) in the main phase of the trial.

Arm type	Experimental
Investigational medicinal product name	Somapacitan PDS290 10mg/1.5mL
Investigational medicinal product code	
Other name	NNC0195-0092
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects injected themselves once-weekly subcutaneously (s.c.; under the skin) in the morning (before 10 AM). On site visit days this was extended until 12:00 PM (noon). Injections were taken in the thigh and/or abdomen alternating within these body areas for every injection. Subjects were trained to use the pen injector under the supervision of site staff. Dose adjustments were allowed during the first 8 weeks titration period (at week 2, 4, 6 and 8). Dose adjustments were based on insulin like growth factor - I (IGF-I) standard deviation score (SDS). The minimum and maximum weekly dose was set to 0.1 mg and 8 mg, respectively.

Number of subjects in period 1	Placebo	Norditropin	Somapacitan
Started	61	119	120
Completed	55	105	114
Not completed	6	14	6
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	4	12	4
Unclassified	1	1	-
Lost to follow-up	-	1	-
Protocol deviation	-	-	2

Period 2

Period 2 title	Extension phase (Open-label phase)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Somapacitan

Arm description:

Subjects who received placebo in the main period, were switched to receive somapacitan for 52 weeks (8 weeks dose titration followed by 44 weeks fixed dose treatment) in the extension period of the trial.

Arm type	Experimental
Investigational medicinal product name	Somapacitan PDS290 10mg/1.5mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were trained for use of the pen injector under the supervision of site staff. Patients receiving Somapacitan injected themselves once a week, subcutaneously, in the morning before 10 AM. On site visit days, the time window was extended to 12:00 noon.

Arm title	Somapacitan/Somapacitan

Arm description:

Subjects who received somapacitan in the main period, continued to receive somapacitan for 52 weeks (8 weeks dose titration followed by 44 weeks fixed dose treatment) in the extension period of the trial.

Arm type	Experimental
Investigational medicinal product name	Somapacitan PDS290 10mg/1.5mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were trained for use of the pen injector under the supervision of site staff. Patients receiving Somapacitan injected themselves once a week, subcutaneously, in the morning before 10 AM. On site visit days, the time window was extended to 12:00 noon.

Arm title	Norditropin/Norditropin

Arm description:

Subjects who received norditropin in the main period, continued to receive norditropin for 52 weeks (8 weeks dose titration followed by 44 weeks fixed dose treatment) in the extension period of the trial.

Arm type	Active comparator
Investigational medicinal product name	Somatropin
Investigational medicinal product code	
Other name	Norditropin® FlexPro® 10 mg/1.5 mL
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were trained for use of the pen injector under the supervision of site staff. Patients receiving Norditropin injected themselves daily, subcutaneously, in the evening, while during observed trial drug administration, they injected themselves in the morning (before 12:00 PM and at least 12 hours after the previous injection).

Arm title	Norditropin/Somapacitan

Arm description:

Subjects who received norditropin in the main period, were switched to receive somapacitan for 52 weeks (8 weeks dose titration followed by 44 weeks fixed dose treatment) in the extension period of the trial.

Arm type	Experimental

Investigational medicinal product name	Somapacitan PDS290 10mg/1.5mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were trained for use of the pen injector under the supervision of site staff. Patients receiving Somapacitan injected themselves once a week, subcutaneously, in the morning before 10 AM. On site visit days, the time window was extended to 12:00 noon.

Number of subjects in period 2[1]	Placebo/Somapacitan	Somapacitan/Somapacitan	Norditropin/Norditropin
Started	55	114	52
Completed	53	109	47
Not completed	2	5	5
Adverse event, serious fatal	1	-	1
Consent withdrawn by subject	1	4	3
Lost to follow-up	-	1	1

Number of subjects in period 2[1]	Norditropin/Somapacitan
Started	51
Completed	48
Not completed	3
Adverse event, serious fatal	1
Consent withdrawn by subject	1
Lost to follow-up	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Two subjects on Norditropin, who completed the main phase didn’t initiate treatment in the extension phase.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo (somapacitan) for 34 weeks (8 weeks dose titration followed by 26 weeks fixed dose treatment) in the main phase of the trial.	
Reporting group title	Norditropin
Reporting group description:	
Subjects recieved Norditropin® FlexPro® 10 mg/1.5 mL for 34 weeks (8 weeks dose titration followed by 26 weeks fixed dose treatment) in the main phase of the trial.	
Reporting group title	Somapacitan
Reporting group description:	
Subjects received Somapacitan PDS290 10mg/1.5mL for 34 weeks (8 weeks dose titration followed by 26 weeks fixed dose treatment) in the main phase of the trial.	

Reporting group values	Placebo	Norditropin	Somapacitan
Number of subjects	61	119	120
Age Categorical Units: Subjects			
Adults (18-64 years)	51	101	107
From 65-84 years	10	18	13
Age Continuous Units: years			
arithmetic mean	45.0	45.7	44.6
standard deviation	± 15.7	± 15.3	± 14.3
Gender Categorical Units: Subjects			
Female	32	61	62
Male	29	58	58

Reporting group values	Total		
Number of subjects	300		
Age Categorical Units: Subjects			
Adults (18-64 years)	259		
From 65-84 years	41		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical Units: Subjects			
Female	155		
Male	145		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received placebo (somapacitan) for 34 weeks (8 weeks dose titration followed by 26 weeks fixed dose treatment) in the main phase of the trial.	
Reporting group title	Norditropin
Reporting group description:	
Subjects recieved Norditropin® FlexPro® 10 mg/1.5 mL for 34 weeks (8 weeks dose titration followed by 26 weeks fixed dose treatment) in the main phase of the trial.	
Reporting group title	Somapacitan
Reporting group description:	
Subjects received Somapacitan PDS290 10mg/1.5mL for 34 weeks (8 weeks dose titration followed by 26 weeks fixed dose treatment) in the main phase of the trial.	
Reporting group title	Placebo/Somapacitan
Reporting group description:	
Subjects who received placebo in the main period, were switched to receive somapacitan for 52 weeks (8 weeks dose titration followed by 44 weeks fixed dose treatment) in the extension period of the trial.	
Reporting group title	Somapacitan/Somapacitan
Reporting group description:	
Subjects who received somapacitan in the main period, continued to receive somapacitan for 52 weeks (8 weeks dose titration followed by 44 weeks fixed dose treatment) in the extension period of the trial.	
Reporting group title	Norditropin/Norditropin
Reporting group description:	
Subjects who received norditropin in the main period, continued to receive norditropin for 52 weeks (8 weeks dose titration followed by 44 weeks fixed dose treatment) in the extension period of the trial.	
Reporting group title	Norditropin/Somapacitan
Reporting group description:	
Subjects who received norditropin in the main period, were switched to receive somapacitan for 52 weeks (8 weeks dose titration followed by 44 weeks fixed dose treatment) in the extension period of the trial.	
Subject analysis set title	Placebo/Somapacitan
Subject analysis set type	Safety analysis
Subject analysis set description:	
This analysis set represents all the subjects that received placebo in the main study and switched to receive somapacitan in the extesion period	
Subject analysis set title	Somapacitan/Somapacitan
Subject analysis set type	Safety analysis
Subject analysis set description:	
This analysis set represents all the subjects that received somapacitan in the main phase and continued to receive somapacitan in the extension study	
Subject analysis set title	Norditropin/Norditropin
Subject analysis set type	Safety analysis
Subject analysis set description:	
This analysis set represents all the subjects that received Norditropin in the main phase and were re-randomised to receive Norditropin in the extension phase	
Subject analysis set title	Norditropin/Somapacitan
Subject analysis set type	Safety analysis
Subject analysis set description:	
This analysis set represents all the subjects that received Norditropin in the main phase of the study and were re-randomised to receive somapacitan in the extension study	
Subject analysis set title	Norditropin/-
Subject analysis set type	Safety analysis

Subject analysis set description:

This subject analysis set represents all the subjects that received Norditropin in the main phase of the study but discontinued the study after the main phase and did not continue into the extension phase

Primary: Change in truncal fat percentage

End point title	Change in truncal fat percentage

End point description:

Change in truncal fat percentage was measured from baseline (week -3) until the end of the main treatment period (week 34). Results are based on the full analysis set (FAS), which included subjects who received at least one dose of randomised treatment. Number of subjects analysed (n) = Number of subjects with available data for respective arm.

End point type	Primary

End point timeframe:

From baseline to end of main treatment period (Week 34)

End point values	Placebo	Norditropin	Somapacitan	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	119	120	
Units: Percentage of truncal fat				
arithmetic mean (standard deviation)				
Baseline (n=60, 119 and 119)	36.90 (± 8.98)	38.10 (± 9.65)	39.11 (± 8.81)	
Change from baseline (week 34) (n=56, 111 and 116)	0.49 (± 3.31)	-2.39 (± 4.48)	-1.17 (± 2.89)	

Statistical analyses

Statistical analysis title	Treatment difference (Somapacitan - Placebo)

Statistical analysis description:

Changes in truncal fat percentage from baseline to the 34 week's measurements was analysed using an analysis of covariance model with treatment, growth hormone deficiency (GHD) onset type, sex, region, diabetes mellitus (DM) and sex by region by DM interaction as factors and baseline as a covariate. The analysis was conducted using a multiple imputation technique where trajectory after a withdrawn subjects last observation was imputed based on data from the placebo arm.

Comparison groups	Placebo v Somapacitan
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.009
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-1.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.68
upper limit	-0.38

Secondary: Change in truncal fat mass (kg)

End point title	Change in truncal fat mass (kg)

End point description:

The change in truncal fat mass (TFM) was measured from baseline (week -3) until end of main treatment period (week 34). Results are based on the FAS, which included all subjects who received at least one dose of randomised treatment. Number of subjects analysed (n) = Number of subjects with available data for respective arm. Results are presented in grams.

End point type	Secondary

End point timeframe:

From baseline to end of main treatment period (Week 34)

End point values	Placebo	Norditropin	Somapacitan	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	119	120	
Units: Grams				
arithmetic mean (standard deviation)				
Baseline (week -3) (n = 60, 119, 119)	12669.57 (± 6010.05)	14121.73 (± 6318.79)	14777.05 (± 6269.71)	
Change from baseline(week 34) (n =56,111,116)	417.86 (± 1536.36)	-619.67 (± 1887.50)	-180.98 (± 1762.31)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in truncal lean body mass (kg)

End point title	Change in truncal lean body mass (kg)

End point description:

Change in truncal lean body mass was evaluated from baseline (week -3) until end of main treatment period (week 34). Results are based on the FAS, which included all subjects who received at least one dose of randomised treatment. Number of subjects analysed (n) = Number of subjects with available data for respective arm. Results are presented in grams.

End point type	Secondary

End point timeframe:

From baseline to end of main treatment period (Week 34)

End point values	Placebo	Norditropin	Somapacitan	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	119	120	
Units: Grams				
arithmetic mean (standard deviation)				
Baseline (week -3) (n = 60, 119, 119)	20698.51 (± 5569.03)	22464.16 (± 7338.22)	22297.20 (± 22297.20)	
Change from baseline (week 34) (n = 56, 111, 116)	402.69 (± 1247.67)	832.77 (± 1409.74)	800.27 (± 1377.75)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of adverse events, including injection site reactions (week 35)

End point title	Incidence of adverse events, including injection site reactions (week 35)

End point description:

All presented adverse events (AEs) are treatment emergent, which was defined as an AE with onset date after first trial product administration and no later than 7 days of last trial product administration. The results were based on the safety analysis set (SAS) which included all randomised subjects who received at least one dose of randomised treatment.

End point type	Secondary

End point timeframe:

In the main trial period (up to week 35) (including follow-up visits/washout periods)

End point values	Placebo	Norditropin	Somapacitan	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	119	120	
Units: Number of adverse events				
Main study	184	426	385	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of adverse events, including injection site reactions (week 88)

End point title	Incidence of adverse events, including injection site reactions (week 88)

End point description:

All presented adverse events (AEs) are treatment emergent, which was defined as an AE with onset date after first trial product administration and no later than 7 days of last trial product administration. The results were based on the SAS which included all randomised subjects who received at least one dose of randomised treatment.

End point type	Secondary

End point timeframe:

In both the main trial period (up to week 35) and extension trial period (up to week 88) (including follow-up visits/washout periods)

End point values	Placebo/Somapacitan	Somapacitan/Somapacitan	Norditropin/Norditropin	Norditropin/Somapacitan
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	49	101	46	46
Units: Number of adverse events	395	699	384	385

End point values	Norditropin/-			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: Number of adverse events	49			

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of anti-NNC0195-0092 antibodies (week 35)

End point title	Occurrence of anti-NNC0195-0092 antibodies (week 35)

End point description:

Presented results are the occurrence of anti-NNC0195-0092 antibodies at week 35. The results were based on the SAS which included all randomised subjects who received at least one dose of randomised treatment.

End point type	Secondary

End point timeframe:

In the main trial period (up to week 35) (including follow-up visits/washout periods)

End point values	Placebo	Norditropin	Somapacitan	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	101	117	
Units: Subjects	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of anti-NNC0195-0092 antibodies (week 88)

End point title	Occurrence of anti-NNC0195-0092 antibodies (week 88)

End point description:

Presented results are the occurrence of anti-NNC0195-0092 antibodies at week 88. The results were based on the SAS which included all randomised subjects who received at least one dose of randomised treatment.

End point type	Secondary

End point timeframe:

In both the main trial period (up to week 35) and extension trial period (up to week 88) (including follow-up visits/washout periods)

End point values	Placebo/Somapacitan	Somapacitan/Somapacitan	Norditropin/Norditropin	Norditropin/Somapacitan
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	54	109	48	48
Units: Subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

In both the main trial period (up to week 35) and extension trial period (up to week 88) (including follow-up visits/washout periods)

Adverse event reporting additional description:

All presented AEs are treatment emergent. The results are based on the safety analysis set (SAS).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21

Reporting groups

Reporting group title	Placebo/Somapacitan

Reporting group description:

Subjects who received placebo in the main period, were switched to receive somapacitan for 52 weeks (8 weeks dose titration followed by 44 weeks fixed dose treatment) in the extension period of the trial.

Reporting group title	Somapacitan/Somapacitan

Reporting group description:

Subjects who received somapacitan in the main period, continued to receive somapacitan for 52 weeks (8 weeks dose titration followed by 44 weeks fixed dose treatment) in the extension period of the trial.

Reporting group title	Norditropin/Norditropin

Reporting group description:

Subjects who received norditropin in the main period, continued to receive norditropin for 52 weeks (8 weeks dose titration followed by 44 weeks fixed dose treatment) in the extension period of the trial.

Reporting group title	Norditropin/Somapacitan

Reporting group description:

Subjects who received norditropin in the main period, were switched to receive somapacitan for 52 weeks (8 weeks dose titration followed by 44 weeks fixed dose treatment) in the extension period of the trial.

Reporting group title	Norditropin/No treatment

Reporting group description:

Subjects in this group received norditropin in the main phase of the study but were not re-randomised in the extension phase of the study and hence did not receive any product.

Serious adverse events	Placebo/Somapacitan	Somapacitan/Somapacitan	Norditropin/Norditropin
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 61 (13.11%)	13 / 120 (10.83%)	5 / 52 (9.62%)
number of deaths (all causes)	2	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Arterial stent insertion			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystectomy			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia repair			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			

subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sleep apnoea syndrome			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood testosterone increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram T wave abnormal			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cholangiogram			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Drug dispensing error			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth fracture			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiogenic shock			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Ventricular extrasystoles			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Haemoconcentration			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			

subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 61 (3.28%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dental cyst			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			

Secondary adrenocortical insufficiency			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes insipidus			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypopituitarism			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenocortical insufficiency acute			
subjects affected / exposed	2 / 61 (3.28%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 61 (0.00%)	2 / 120 (1.67%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	1 / 61 (1.64%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Herpes simplex			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia viral			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			

subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Norditropin/Somapacitan	Norditropin/No treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 51 (13.73%)	4 / 16 (25.00%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Arterial stent insertion			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystectomy			

subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia repair			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fatigue			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sleep apnoea syndrome			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood testosterone increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiogram			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Drug dispensing error			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			

subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth fracture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiogenic shock			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Haemoconcentration			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental cyst			

subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Secondary adrenocortical insufficiency			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes insipidus			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypopituitarism			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenocortical insufficiency acute			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			

subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo/Somapacitan	Somapacitan/Somapacitan	Norditropin/Norditropin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 61 (73.77%)	83 / 120 (69.17%)	39 / 52 (75.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 61 (3.28%)	6 / 120 (5.00%)	3 / 52 (5.77%)
occurrences (all)	2	6	3

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 61 (4.92%)	7 / 120 (5.83%)	4 / 52 (7.69%)
occurrences (all)	3	9	4
Injection site bruising			
subjects affected / exposed	2 / 61 (3.28%)	1 / 120 (0.83%)	3 / 52 (5.77%)
occurrences (all)	3	1	3
Oedema peripheral			
subjects affected / exposed	3 / 61 (4.92%)	8 / 120 (6.67%)	4 / 52 (7.69%)
occurrences (all)	4	19	7
Chills			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 61 (1.64%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences (all)	2	1	0
Pyrexia			
subjects affected / exposed	1 / 61 (1.64%)	4 / 120 (3.33%)	0 / 52 (0.00%)
occurrences (all)	1	6	0
Immune system disorders			
Allergy to plants			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 61 (6.56%)	6 / 120 (5.00%)	2 / 52 (3.85%)
occurrences (all)	4	8	2
Dyspnoea			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	4 / 61 (6.56%)	6 / 120 (5.00%)	0 / 52 (0.00%)
occurrences (all)	4	6	0
Respiratory tract congestion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0

Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 61 (3.28%)	7 / 120 (5.83%)	0 / 52 (0.00%)
occurrences (all)	2	9	0
Blood testosterone decreased			
subjects affected / exposed	1 / 61 (1.64%)	0 / 120 (0.00%)	2 / 52 (3.85%)
occurrences (all)	1	0	2
Thyroxine free decreased			
subjects affected / exposed	3 / 61 (4.92%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences (all)	3	2	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	1 / 61 (1.64%)	2 / 120 (1.67%)	3 / 52 (5.77%)
occurrences (all)	1	3	5
Foot fracture			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	1 / 52 (1.92%)
occurrences (all)	0	1	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	1 / 52 (1.92%)
occurrences (all)	0	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 61 (22.95%)	17 / 120 (14.17%)	11 / 52 (21.15%)
occurrences (all)	43	56	65
Dizziness			
subjects affected / exposed	3 / 61 (4.92%)	9 / 120 (7.50%)	2 / 52 (3.85%)
occurrences (all)	3	12	2
Hypoaesthesia			
subjects affected / exposed	3 / 61 (4.92%)	1 / 120 (0.83%)	1 / 52 (1.92%)
occurrences (all)	3	1	2
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	1 / 61 (1.64%)	1 / 120 (0.83%)	3 / 52 (5.77%)
occurrences (all)	1	1	3
Vertigo			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Eyelid disorder			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Glaucoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	3 / 52 (5.77%)
occurrences (all)	0	0	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 61 (14.75%)	7 / 120 (5.83%)	6 / 52 (11.54%)
occurrences (all)	14	9	6
Nausea			
subjects affected / exposed	2 / 61 (3.28%)	5 / 120 (4.17%)	1 / 52 (1.92%)
occurrences (all)	2	6	1
Abdominal pain			
subjects affected / exposed	2 / 61 (3.28%)	3 / 120 (2.50%)	1 / 52 (1.92%)
occurrences (all)	3	4	1
Abdominal pain lower			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	1 / 61 (1.64%)	2 / 120 (1.67%)	3 / 52 (5.77%)
occurrences (all)	1	2	4
Duodenal ulcer			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			

subjects affected / exposed	1 / 61 (1.64%)	3 / 120 (2.50%)	2 / 52 (3.85%)
occurrences (all)	2	3	2
Oesophagitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	1 / 61 (1.64%)	3 / 120 (2.50%)	2 / 52 (3.85%)
occurrences (all)	1	5	2
Vomiting			
subjects affected / exposed	3 / 61 (4.92%)	7 / 120 (5.83%)	2 / 52 (3.85%)
occurrences (all)	3	8	3
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 61 (4.92%)	4 / 120 (3.33%)	5 / 52 (9.62%)
occurrences (all)	3	4	7
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	0 / 61 (0.00%)	1 / 120 (0.83%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 61 (8.20%)	9 / 120 (7.50%)	8 / 52 (15.38%)
occurrences (all)	5	9	9
Back pain			
subjects affected / exposed	5 / 61 (8.20%)	13 / 120 (10.83%)	1 / 52 (1.92%)
occurrences (all)	7	13	1

Myalgia			
subjects affected / exposed	4 / 61 (6.56%)	5 / 120 (4.17%)	4 / 52 (7.69%)
occurrences (all)	4	7	4
Pain in extremity			
subjects affected / exposed	1 / 61 (1.64%)	5 / 120 (4.17%)	5 / 52 (9.62%)
occurrences (all)	1	5	7
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	10 / 61 (16.39%)	11 / 120 (9.17%)	8 / 52 (15.38%)
occurrences (all)	14	13	13
Bronchitis			
subjects affected / exposed	4 / 61 (6.56%)	4 / 120 (3.33%)	2 / 52 (3.85%)
occurrences (all)	5	4	2
Gastroenteritis			
subjects affected / exposed	3 / 61 (4.92%)	9 / 120 (7.50%)	1 / 52 (1.92%)
occurrences (all)	3	13	1
Influenza			
subjects affected / exposed	4 / 61 (6.56%)	5 / 120 (4.17%)	1 / 52 (1.92%)
occurrences (all)	8	5	2
Nasopharyngitis			
subjects affected / exposed	14 / 61 (22.95%)	32 / 120 (26.67%)	15 / 52 (28.85%)
occurrences (all)	25	48	21
Pharyngitis			
subjects affected / exposed	1 / 61 (1.64%)	2 / 120 (1.67%)	3 / 52 (5.77%)
occurrences (all)	1	2	5
Pulpitis dental			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	4 / 61 (6.56%)	2 / 120 (1.67%)	4 / 52 (7.69%)
occurrences (all)	8	3	4
Tonsillitis			
subjects affected / exposed	3 / 61 (4.92%)	5 / 120 (4.17%)	3 / 52 (5.77%)
occurrences (all)	3	5	4
Tooth abscess			

subjects affected / exposed	0 / 61 (0.00%)	2 / 120 (1.67%)	3 / 52 (5.77%)
occurrences (all)	0	2	3
Urinary tract infection			
subjects affected / exposed	3 / 61 (4.92%)	6 / 120 (5.00%)	2 / 52 (3.85%)
occurrences (all)	3	9	2
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 61 (0.00%)	0 / 120 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1

Non-serious adverse events	Norditropin/Somapacitan	Norditropin/No treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 51 (72.55%)	11 / 16 (68.75%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 51 (7.84%)	0 / 16 (0.00%)	
occurrences (all)	4	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 51 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	7	0	
Injection site bruising			
subjects affected / exposed	3 / 51 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	3	0	
Oedema peripheral			
subjects affected / exposed	3 / 51 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	3	0	
Chills			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	
Pain			
subjects affected / exposed	1 / 51 (1.96%)	3 / 16 (18.75%)	
occurrences (all)	1	3	
Pyrexia			
subjects affected / exposed	2 / 51 (3.92%)	1 / 16 (6.25%)	
occurrences (all)	2	2	

Immune system disorders			
Allergy to plants			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 51 (7.84%)	0 / 16 (0.00%)	
occurrences (all)	5	0	
Dyspnoea			
subjects affected / exposed	1 / 51 (1.96%)	2 / 16 (12.50%)	
occurrences (all)	2	2	
Oropharyngeal pain			
subjects affected / exposed	2 / 51 (3.92%)	0 / 16 (0.00%)	
occurrences (all)	3	0	
Respiratory tract congestion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Blood testosterone decreased			
subjects affected / exposed	3 / 51 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	3	0	
Thyroxine free decreased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 51 (1.96%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Contusion			
subjects affected / exposed	2 / 51 (3.92%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Foot fracture			

subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 51 (13.73%)	1 / 16 (6.25%)	
occurrences (all)	16	1	
Dizziness			
subjects affected / exposed	3 / 51 (5.88%)	2 / 16 (12.50%)	
occurrences (all)	7	3	
Hypoaesthesia			
subjects affected / exposed	3 / 51 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	3	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 51 (3.92%)	0 / 16 (0.00%)	
occurrences (all)	4	0	
Vertigo			
subjects affected / exposed	4 / 51 (7.84%)	0 / 16 (0.00%)	
occurrences (all)	4	0	
Eye disorders			
Eyelid disorder			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Glaucoma			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Visual impairment			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 51 (9.80%)	2 / 16 (12.50%)	
occurrences (all)	10	2	

Nausea			
subjects affected / exposed	4 / 51 (7.84%)	1 / 16 (6.25%)	
occurrences (all)	15	1	
Abdominal pain			
subjects affected / exposed	2 / 51 (3.92%)	1 / 16 (6.25%)	
occurrences (all)	3	2	
Abdominal pain lower			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Dental caries			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Duodenal ulcer			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	3 / 51 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	4	0	
Oesophagitis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	3 / 51 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	3	0	
Vomiting			
subjects affected / exposed	4 / 51 (7.84%)	1 / 16 (6.25%)	
occurrences (all)	6	2	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			

Dysuria			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nocturia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	1 / 51 (1.96%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 51 (13.73%)	0 / 16 (0.00%)	
occurrences (all)	9	0	
Back pain			
subjects affected / exposed	1 / 51 (1.96%)	2 / 16 (12.50%)	
occurrences (all)	1	2	
Myalgia			
subjects affected / exposed	2 / 51 (3.92%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	2 / 51 (3.92%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	6 / 51 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	8	0	
Bronchitis			
subjects affected / exposed	1 / 51 (1.96%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Gastroenteritis			
subjects affected / exposed	1 / 51 (1.96%)	1 / 16 (6.25%)	
occurrences (all)	1	2	
Influenza			
subjects affected / exposed	5 / 51 (9.80%)	0 / 16 (0.00%)	
occurrences (all)	6	0	
Nasopharyngitis			

subjects affected / exposed	12 / 51 (23.53%)	1 / 16 (6.25%)	
occurrences (all)	20	1	
Pharyngitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Pulpitis dental			
subjects affected / exposed	2 / 51 (3.92%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Sinusitis			
subjects affected / exposed	3 / 51 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	4	0	
Tonsillitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Tooth abscess			
subjects affected / exposed	1 / 51 (1.96%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	3 / 51 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	6	0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 51 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 January 2015	Updates based on comments received on the protocol during End of Phase 2 meetings with US Food and drug administration (FDA) and Pharmaceuticals and Medical Devices Agency, Japan (PMDA): FDA: Primary analysis to be based on intention-to-treat principle; Additional antibody and PK sampling to align with the time points for immunogenicity assessments as recommended in the FDA Immunogenicity guideline of February 2013; Inclusion of subjects with diabetes. PMDA: Patients with diabetes mellitus will be excluded at sites in Japan. Application of Japanese guidelines for the diagnosis of adult growth hormone deficiency (AGHD) for patients included at sites in Japan. Changes to subect information-informed consent (SI-IC): specification of discontinuation of trial drug, and withdrawal and termination of the trial; Urine sample was deleted and eye examination was added. Full title was added.
29 January 2015	Based on feedback from Ethics Committee, clarifications and feedback from investigators: Alternative test for adrenocorticotropic hormone (ACTH) stimulation test (limited availability in some countries). Impact on inclusion criterion regarding serum levels of free thyroxine (T4) and the patient informed consent form. Process for local tolerability assessments includes external review of photos by a dermatologist. Clarification of follow-up process after last patient last visit (LPLV) if 2 consecutive positive antibody results. Ethics Committee, Germany: 2 additional exclusion criteria added, applicable to Germany only. These criteria cover exclusion of patients committed to an institution and persons employed with the sponsor/CRO/trial centre. Novo Nordisk: Clarifications when and how deviation from the titration schedule should be handled; adrenal insufficient patients on stable replacement therapy for 3 months the option of re-screening.
24 September 2015	This amendment was implemented due to recruitment difficulties and more flexibility was needed in the inclusion/exclusion criteria, and titration visit schedule. Allowed visits 1a and 1b to be combined into one visit. Request from FDA to ensure that electrocardiograms (ECGs) were performed at time of mean Cmax. Changes to SI-IC: Information added that replacement therapy could be initiated if low thyroid or adrenal function or testosterone levels. Text on evidence of intracranial tumour growth was rephrased (‘no evidence of intracranial tumour growth since removal of the tumour’).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported