Clinical trial results:
Effect of liraglutide for weight management in paediatric subjects with Prader-Willi Syndrome. A randomised, placebo controlled, parallel group, multi-centre, multi-national trial with a 16-week double-blind period and 36-week open-label period

Summary

EudraCT number	2014-004415-37
Trial protocol	IT FR NL
Global end of trial date	19 November 2020

Results information

Result version number	v1 (current)
This version publication date	02 June 2021
First version publication date	02 June 2021

Trial information

Trial identification

Sponsor protocol code	NN8022-4179

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02527200
WHO universal trial number (UTN)	U1111-1162-7884

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Transparency and Medical Writing Office (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Transparency and Medical Writing Office (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000128-PIP02-09
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 November 2020
Global end of trial reached?	Yes
Global end of trial date	19 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of liraglutide versus placebo on weight loss in paediatric subjects with obesity and PWS at 16 weeks and versus no treatment at 52 weeks.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (64th World Medical Association (WMA) general assembly; October 2013), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, including archiving of essential documents, 21 US Code of Federal Regulations (CFR) 312.120 and US Food and Drug Administration (FDA) 21 CFR 314.126.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 November 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	Turkey: 12
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	56
EEA total number of subjects	19

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)	24
Adolescents (12-17 years)	32
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 20 sites in 8 countries as follows: Australia (2), Canada (1), France (7), Italy (2), Netherlands (1), New Zealand (1), Turkey (3), United States (3).

Pre-assignment

Screening details:

This trial has part A & part B. Part A was conducted in adolescents (≥12-<18 years, Tanner stage 2−5) with Prader-Willi Syndrome (PWS) and obesity. Part B was conducted in children [≥6-12 years, Tanner stage below 2 (defined as Tanner stage 1 with or without premature adrenarche)] with PWS and obesity. Entry into part A and part B was sequential.

Period 1

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

Blinding implementation details:

The trial was 'double-blind' for the first 16 weeks followed by an 'open-label' period of 36 weeks.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A+B: Liraglutide 3.0 mg

Arm description:

Subjects received once daily subcutaneous (under the skin) injection of liraglutide for 52 weeks (open label for 16 weeks and double-blinded for 36 weeks) in a dose escalating manner. For both part A and part B (for children with body weight ≥45 kg): dosing was initiated with liraglutide 0.6 mg daily for one week and increased in weekly dosage steps of 0.6 mg until a maximum tolerated dose (MTD) (as judged by the Investigator) or a dose of 3.0 mg liraglutide was reached, i.e., 0.6 mg (week 1), 1.2 mg (week 2), 1.8 mg (week 3), 2.4 mg (week 4) and 3.0 mg (week 5 to week 52). For Part B children with body weight <45 kg: dosing was initiated with liraglutide 0.3 mg daily for one week and increased to 0.6 mg after the first week. Thereafter, the dose was increased in weekly steps of 0.6 mg until an MTD (as judged by the Investigator) or a dose of 2.4 mg liraglutide was reached. i.e., 0.3 mg (week 1), 0.6 mg (week 2), 1.2 mg (week 3), 1.8 mg (week 4), 2.4 mg (week 5 to week 52).

Arm type	Experimental
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	
Other name	Saxenda
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received once daily subcutaneous injection of liraglutide (0.3 mg, 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg or 3.0 mg) for 52 weeks either in the abdomen, thigh, or upper arm.

Arm title	Part A+B: Placebo

Arm description:

Subjects received once daily subcutaneous injection of liraglutide matching placebo for 16 weeks (open label).

Arm type	Placebo

Investigational medicinal product name	Liraglutide placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received once daily subcutaneous injection of liraglutide matching placebo (0.3 mg, 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg or 3.0 mg) for 16 weeks either in the abdomen, thigh, or upper arm.

Number of subjects in period 1	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo
Started	37	19
Safety analysis set	37	19
Full analysis set	36	19
Completed	32	16
Not completed	5	3
Unclassified	-	1
Lost to follow-up	1	-
Withdrawal by parent/guardian	4	2

Baseline characteristics

Reporting groups	
Reporting group title	Part A+B: Liraglutide 3.0 mg

Reporting group description:

Subjects received once daily subcutaneous (under the skin) injection of liraglutide for 52 weeks (open label for 16 weeks and double-blinded for 36 weeks) in a dose escalating manner. For both part A and part B (for children with body weight ≥45 kg): dosing was initiated with liraglutide 0.6 mg daily for one week and increased in weekly dosage steps of 0.6 mg until a maximum tolerated dose (MTD) (as judged by the Investigator) or a dose of 3.0 mg liraglutide was reached, i.e., 0.6 mg (week 1), 1.2 mg (week 2), 1.8 mg (week 3), 2.4 mg (week 4) and 3.0 mg (week 5 to week 52). For Part B children with body weight <45 kg: dosing was initiated with liraglutide 0.3 mg daily for one week and increased to 0.6 mg after the first week. Thereafter, the dose was increased in weekly steps of 0.6 mg until an MTD (as judged by the Investigator) or a dose of 2.4 mg liraglutide was reached. i.e., 0.3 mg (week 1), 0.6 mg (week 2), 1.2 mg (week 3), 1.8 mg (week 4), 2.4 mg (week 5 to week 52).

Reporting group title	Part A+B: Placebo

Reporting group description:

Subjects received once daily subcutaneous injection of liraglutide matching placebo for 16 weeks (open label).

Reporting group values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Total
Number of subjects	37	19	56
Age Categorical Units: Subjects			
Children (2-11 years)	17	7	24
Adolescents (12-17 years)	20	12	32
Gender Categorical Units: Subjects			
Female	22	7	29
Male	15	12	27

End points

End points reporting groups

Reporting group title	Part A+B: Liraglutide 3.0 mg

Reporting group description:

Subjects received once daily subcutaneous (under the skin) injection of liraglutide for 52 weeks (open label for 16 weeks and double-blinded for 36 weeks) in a dose escalating manner. For both part A and part B (for children with body weight ≥45 kg): dosing was initiated with liraglutide 0.6 mg daily for one week and increased in weekly dosage steps of 0.6 mg until a maximum tolerated dose (MTD) (as judged by the Investigator) or a dose of 3.0 mg liraglutide was reached, i.e., 0.6 mg (week 1), 1.2 mg (week 2), 1.8 mg (week 3), 2.4 mg (week 4) and 3.0 mg (week 5 to week 52). For Part B children with body weight <45 kg: dosing was initiated with liraglutide 0.3 mg daily for one week and increased to 0.6 mg after the first week. Thereafter, the dose was increased in weekly steps of 0.6 mg until an MTD (as judged by the Investigator) or a dose of 2.4 mg liraglutide was reached. i.e., 0.3 mg (week 1), 0.6 mg (week 2), 1.2 mg (week 3), 1.8 mg (week 4), 2.4 mg (week 5 to week 52).

Reporting group title	Part A+B: Placebo

Reporting group description:

Subjects received once daily subcutaneous injection of liraglutide matching placebo for 16 weeks (open label).

Subject analysis set title	Part A: Liraglutide
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received once daily subcutaneous injection of liraglutide for 52 weeks. Dosing was initiated with liraglutide 0.6 mg daily for one week and increased in weekly dosage steps of 0.6 mg until a MTD (as judged by the Investigator) or a dose of 3.0 mg liraglutide was reached, i.e., 0.6 mg (week 1), 1.2 mg (week 2), 1.8 mg (week 3), 2.4 mg (week 4) and 3.0 mg (week 5 to week 52).

Subject analysis set title	Part A: Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received once daily subcutaneous injection of liraglutide matching placebo for 16 weeks.

Subject analysis set title	Part B: Liraglutide
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received once daily subcutaneous injection of liraglutide for 52 weeks. For children with body weight ≥ 45 kg; dosing was initiated with liraglutide 0.6 mg daily for one week and increased in weekly dosage steps of 0.6 mg until a MTD (as judged by the Investigator) or a dose of 3.0 mg liraglutide was reached, i.e., 0.6 mg (week 1), 1.2 mg (week 2), 1.8 mg (week 3), 2.4 mg (week 4) and 3.0 mg (week 5 to week 52). For children with body weight <45 kg: dosing was initiated with liraglutide 0.3 mg daily for one week and increased to 0.6 mg after the first week. Thereafter, the dose was increased in weekly steps of 0.6 mg until an MTD (as judged by the Investigator) or a dose of 2.4 mg liraglutide was reached. i.e., 0.3 mg (week 1), 0.6 mg (week 2), 1.2 mg (week 3), 1.8 mg (week 4), 2.4 mg (week 5 to week 52).

Subject analysis set title	Part B: Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received once daily subcutaneous injection of liraglutide matching placebo for 16 weeks.

Primary: Change in body mass index (BMI) standard deviation score (SDS) from baseline to 16 weeks

End point title	Change in body mass index (BMI) standard deviation score (SDS) from baseline to 16 weeks

End point description:

Change in BMI SDS from baseline to week 16 is presented. BMI SDS also called Z-scores, was calculated using the following formula: Z=[(y / M)^L - 1] / S*L; where L, M and S are median (M), Box-cox power (L) and variation coefficient (S) of children/adolescents', y= individual BMI. BMI provided for each sex and age. For each subject, a standard deviation score Z (SDS) was calculated based on age and sex referring to the values L, M and S. Possible values range from -3 to +3, a negative score being beneficial. Results are based on the FAS which included all randomised subjects who received at least

one dose of trial product and had any post-randomisation data. Number of subjects analysed = Number of subjects who contributed to the analysis.

End point type	Primary

End point timeframe:

From baseline (week 0) to 16 weeks

End point values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Part A: Liraglutide	Part A: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	34	19	18	12
Units: SDS score				
arithmetic mean (standard deviation)	-0.33 (± 0.49)	-0.29 (± 0.32)	-0.18 (± 0.21)	-0.18 (± 0.23)

End point values	Part B: Liraglutide	Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	7		
Units: SDS score				
arithmetic mean (standard deviation)	-0.50 (± 0.65)	-0.48 (± 0.39)		

Statistical analyses

Statistical analysis title	Part A: Liraglutide 0.3 mg - Placebo

Statistical analysis description:

Analysis of in-trial data with missing observations imputed from the placebo arm based on a jump to reference multiple (x1000) imputation approach. Responses at week 16 were analysed using an analysis of covariance model with treatment, sex, region, baseline glycaemic category, stratification factor for Tanner stage and interaction between baseline glycaemic category and stratification factor for Tanner stage as fixed effects, baseline BMI SDS, age as covariates.

Comparison groups	Part A: Liraglutide v Part A: Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3787
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.09

Statistical analysis title	Part B: Liraglutide 0.3 mg - Placebo

Statistical analysis description:

Analysis of in-trial data with missing observations imputed from the placebo arm based on a jump to reference multiple (x1000) imputation approach. Responses at week 16 were analysed using an analysis of covariance model with treatment, sex, region, baseline glycaemic category, stratification factor for Tanner stage and interaction between baseline glycaemic category and stratification factor for Tanner stage as fixed effects, baseline BMI SDS, age as covariates.

Comparison groups	Part B: Liraglutide v Part B: Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.9008
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	0.93

Notes:

[1] - The "number of subjects included in analysis" is being erroneously displayed as 23. It should be read as 'Number of observed subjects with an assessment' = 22.

Statistical analysis title	Part A+B: Liraglutide 0.3 mg - Placebo

Statistical analysis description:

Analysis of in-trial data with missing observations imputed from the placebo arm based on a jump to reference multiple (x1000) imputation approach. Responses at week 16 were analysed using an analysis of covariance model with treatment, sex, region, baseline glycaemic category, stratification factor for Tanner stage and interaction between baseline glycaemic category and stratification factor for Tanner stage as fixed effects, baseline BMI SDS, age as covariates.

Comparison groups	Part A+B: Liraglutide 3.0 mg v Part A+B: Placebo
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.595
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.15

Notes:

[2] - The "number of subjects included in analysis" is being erroneously displayed as 53. It should be read as 'Number of observed subjects with an assessment' = 52.

Primary: Change in body mass index (BMI) standard deviation score (SDS) from baseline to 52 weeks

End point title	Change in body mass index (BMI) standard deviation score (SDS) from baseline to 52 weeks

End point description:

Change in BMI SDS from baseline to week 52 is presented. BMI SDS also called Z-scores, was calculated using the following formula: Z=[(y / M)^L - 1] / S*L; where L, M and S are median (M), Box-cox power

(L) and variation coefficient (S) of children/adolescents', y= individual BMI. BMI provided for each sex and age. For each subject, a standard deviation score Z (SDS) was calculated based on age and sex referring to the values L, M and S. Possible values range from -3 to +3, a negative score being beneficial. Results are based on the FAS which included all randomised subjects who received at least one dose of trial product and had any post-randomisation data. Number of subjects analysed = Number of subjects who contributed to the analysis.

End point type	Primary

End point timeframe:

From baseline (week 0) to 52 weeks

End point values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Part A: Liraglutide	Part A: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	11	17	11
Units: SDS score				
arithmetic mean (standard deviation)	-0.27 (± 0.37)	-0.13 (± 0.25)	-0.27 (± 0.37)	-0.13 (± 0.25)

End point values	Part B: Liraglutide	Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	7		
Units: SDS score				
arithmetic mean (standard deviation)	-0.79 (± 1.21)	-0.71 (± 0.68)		

Statistical analyses

Statistical analysis title	Part A: Liraglutide 0.3 mg - Placebo

Statistical analysis description:

Analysis of in-trial data with missing observations imputed from the placebo arm based on a jump to reference multiple (x1000) imputation approach. Responses at week 52 were analysed using an analysis of covariance model with treatment, sex, region, baseline glycaemic category, stratification factor for Tanner stage and interaction between baseline glycaemic category and stratification factor for Tanner stage as fixed effects, baseline BMI SDS, age as covariates.

Comparison groups	Part A: Liraglutide v Part A: Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5665
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.34

Statistical analysis title	Part B: Liraglutide 0.3 mg - Placebo

Statistical analysis description:

Analysis of in-trial data with missing observations imputed from the placebo arm based on a jump to reference multiple (x1000) imputation approach. Responses at week 52 were analysed using an analysis of covariance model with treatment, sex, region, baseline glycaemic category, stratification factor for Tanner stage and interaction between baseline glycaemic category and stratification factor for Tanner stage as fixed effects, baseline BMI SDS, age as covariates.

Comparison groups	Part B: Liraglutide v Part B: Placebo
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8761
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	0.76

Statistical analysis title	Part A+B: Liraglutide 0.3 mg - Placebo

Statistical analysis description:

Analysis of in-trial data with missing observations imputed from the placebo arm based on a jump to reference multiple (x1000) imputation approach. Responses at week 52 were analysed using an analysis of covariance model with treatment, sex, region, baseline glycaemic category, stratification factor for Tanner stage and interaction between baseline glycaemic category and stratification factor for Tanner stage as fixed effects, baseline BMI SDS, age as covariates.

Comparison groups	Part A+B: Liraglutide 3.0 mg v Part A+B: Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.5189
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	0.26

Notes:

[3] - The "number of subjects included in analysis" is being erroneously displayed as 28. It should be read as 'Number of observed subjects with an assessment' = 49.

Secondary: Percent of subjects achieving ≥ 5% reduction in baseline BMI

End point title	Percent of subjects achieving ≥ 5% reduction in baseline BMI

End point description:

Percentage of subjects achieving more than or equal to (≥) 5% reduction in their baseline (week 0) BMI at weeks 16 and 52 is presented. In below table, 'Yes' infers percentage of subjects who achieved ≥ 5% reduction in their baseline (week 0) BMI at weeks 16 and 52 and 'No' infers percentage of subjects who did not achieve ≥ 5% reduction in their baseline (week 0) BMI at weeks 16 and 52. Results are based on the FAS which included all randomised subjects who received at least one dose of trial product and had any post-randomisation data. Number of subjects analysed = Number of subjects who contributed to the analysis. n = number of subjects from the respective arms analysed for specific timepoints. At week 16: n= 34, 19, 18, 12, 16, 7 are the number of subjects from the respective arms analysed for week 16. At week 52: n= 31, 18, 17, 11, 14, 7 are the number of subjects from the respective arms analysed for week 52.

End point type	Secondary

End point timeframe:

At weeks 16 and 52

End point values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Part A: Liraglutide	Part A: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	34	19	18	12
Units: Percentage of subjects				
number (not applicable)				
At Week 16: Yes	32.4	26.3	27.8	8.3
At Week 16: No	67.6	73.7	72.2	91.7
At Week 52: Yes	32.3	27.8	29.4	18.2
At Week 52: No	67.7	72.2	70.6	81.8

End point values	Part B: Liraglutide	Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	7		
Units: Percentage of subjects				
number (not applicable)				
At Week 16: Yes	37.5	57.1		
At Week 16: No	62.5	42.9		
At Week 52: Yes	35.7	42.9		
At Week 52: No	64.3	57.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of subjects achieving ≥ 10% reduction in baseline BMI

End point title	Percent of subjects achieving ≥ 10% reduction in baseline BMI

End point description:

Percentage of subjects achieving ≥ 10% reduction in their baseline (week 0) BMI at weeks 16 and 52 is presented. In below table, 'Yes' infers percentage of subjects who achieved ≥ 10% reduction in their baseline (week 0) BMI at weeks 16 and 52 and 'No' infers percentage of subjects who did not achieve ≥

10% reduction in their baseline (week 0) BMI at weeks 16 and 52. Results are based on the FAS which included all randomised subjects who received at least one dose of trial product and had any post-randomisation data. Number of subjects analysed = Number of subjects who contributed to the analysis. n = number of subjects from the respective arms analysed for specific timepoints. At week 16: n= 34, 19, 18, 12, 16, 7 are the number of subjects from the respective arms analysed for week 16. At week 52: n= 31, 18, 17, 11, 14, 7 are the number of subjects from the respective arms analysed for week 52.

End point type	Secondary

End point timeframe:

At weeks 16 and 52

End point values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Part A: Liraglutide	Part A: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	34	19	18	12
Units: Percent of subjects				
number (not applicable)				
At Week 16: Yes	2.9	5.3	0	0
At Week 16: No	97.1	94.7	100	100
At Week 52: Yes	12.9	11.1	11.8	0
At Week 52: No	87.1	88.9	88.2	100

End point values	Part B: Liraglutide	Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	7		
Units: Percent of subjects				
number (not applicable)				
At Week 16: Yes	6.3	14.3		
At Week 16: No	93.8	85.7		
At Week 52: Yes	14.3	28.6		
At Week 52: No	85.7	71.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in BMI

End point title	Change in BMI

End point description:

Change in body mass index (BMI) from baseline to week 16 and week 52 is presented. Results are based on the FAS which included all randomised subjects who received at least one dose of trial product and had any post-randomisation data. Number of subjects analysed = Number of subjects who contributed to the analysis. n = number of subjects from the respective arms analysed for specific timepoints. At week 16: n= 34, 19, 18, 12, 16, 7 are the number of subjects from the respective arms analysed for week 16. At week 52: n= 31, 18, 17, 11, 14, 7 are the number of subjects from the respective arms analysed for week 52.

End point type	Secondary

End point timeframe:

From baseline (week 0) to 16 and 52 weeks

End point values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Part A: Liraglutide	Part A: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	34	19	18	12
Units: kilogram per metre square (kg/m^2)				
arithmetic mean (standard deviation)				
Week 16	-1.0 (± 1.4)	-1.1 (± 1.6)	-0.9 (± 1.4)	-0.8 (± 1.6)
Week 52	-0.7 (± 2.7)	-0.4 (± 2.3)	-0.8 (± 2.2)	-0.1 (± 2.1)

End point values	Part B: Liraglutide	Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	7		
Units: kilogram per metre square (kg/m^2)				
arithmetic mean (standard deviation)				
Week 16	-1.1 (± 1.5)	-1.5 (± 1.7)		
Week 52	-0.6 (± 3.3)	-0.7 (± 2.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Body weight (kilogram (kg))

End point title	Change in Body weight (kilogram (kg)

End point description:

Change in body weight (kg) from baseline to week 16 and week 52 is presented. Results are based on the FAS which included all randomised subjects who received at least one dose of trial product and had any post-randomisation data. Number of subjects analysed = Number of subjects who contributed to the analysis. n = number of subjects from the respective arms analysed for specific timepoints. At week 16: n= 34, 19, 18, 12, 16, 7 are the number of subjects from the respective arms analysed for week 16. At week 52: n= 31, 18, 17, 11, 14, 7 are the number of subjects from the respective arms analysed for week 52.

End point type	Secondary

End point timeframe:

From baseline (week 0) to 16 and 52 weeks

End point values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Part A: Liraglutide	Part A: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	34	19	18	12
Units: kilograms (kg)				
arithmetic mean (standard deviation)				
Week 16	-1.2 (± 3.0)	-1.0 (± 4.2)	-1.7 (± 3.6)	-1.1 (± 5.0)
Week 52	1.1 (± 6.5)	2.3 (± 5.6)	-0.4 (± 6.3)	1.9 (± 6.0)

End point values	Part B: Liraglutide	Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	7		
Units: kilograms (kg)				
arithmetic mean (standard deviation)				
Week 16	-0.6 (± 2.2)	-1.0 (± 2.7)		
Week 52	3.0 (± 6.6)	2.8 (± 5.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Body weight (pounds (lb))

End point title	Change in Body weight (pounds (lb))

End point description:

Change in body weight (lb) from baseline to week 16 and week 52 is presented. Results are based on the FAS which included all randomised subjects who received at least one dose of trial product and had any post-randomisation data. Number of subjects analysed = Number of subjects who contributed to the analysis. n = number of subjects from the respective arms analysed for specific timepoints. At week 16: n= 34, 19, 18, 12, 16, 7 are the number of subjects from the respective arms analysed for week 16. At week 52: n= 31, 18, 17, 11, 14, 7 are the number of subjects from the respective arms analysed for week 52.

End point type	Secondary

End point timeframe:

From baseline (week 0) to 16 and 52 weeks

End point values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Part A: Liraglutide	Part A: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	34	19	18	12
Units: pounds (lb)				
arithmetic mean (standard deviation)				
Week 16	-2.6 (± 6.6)	-2.3 (± 9.2)	-3.7 (± 7.8)	-2.4 (± 11.0)
Week 52	2.5 (± 14.4)	5.0 (± 12.3)	-0.9 (± 13.9)	4.3 (± 13.2)

End point values	Part B: Liraglutide	Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	7		
Units: pounds (lb)				
arithmetic mean (standard deviation)				
Week 16	-1.4 (± 4.8)	-2.1 (± 5.9)		
Week 52	6.7 (± 14.4)	6.2 (± 11.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Body weight (percentage (%))

End point title	Change in Body weight (percentage (%))

End point description:

Change in body weight (percentage (%)) from baseline to week 16 and week 52 is presented. Results are based on the FAS which included all randomised subjects who received at least one dose of trial product and had any post-randomisation data. Number of subjects analysed = Number of subjects who contributed to the analysis. n = number of subjects from the respective arms analysed for specific timepoints. At week 16: n= 34, 19, 18, 12, 16, 7 are the number of subjects from the respective arms analysed for week 16. At week 52: n= 31, 18, 17, 11, 14, 7 are the number of subjects from the respective arms analysed for week 52.

End point type	Secondary

End point timeframe:

From baseline (week 0) to 16 and 52 weeks

End point values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Part A: Liraglutide	Part A: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	34	19	18	12
Units: percentage of body weight				
arithmetic mean (standard deviation)				
Week 16	-1.4 (± 3.9)	-1.2 (± 4.3)	-1.7 (± 3.8)	-0.7 (± 3.7)
Week 52	2.6 (± 9.9)	3.3 (± 6.9)	-0.4 (± 6.5)	2.3 (± 5.7)

End point values	Part B: Liraglutide	Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	7		
Units: percentage of body weight				
arithmetic mean (standard deviation)				

Week 16	-1.1 (± 4.1)	-2.2 (± 5.5)		
Week 52	6.3 (± 12.1)	4.9 (± 8.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in hyperphagia score: total score and hyperphagic behaviour, drive and severity score

End point title	Change in hyperphagia score: total score and hyperphagic behaviour, drive and severity score

End point description:

Change in hyperphagia score (hyperphagia total score and hyperphagic behaviour, drive and severity score respectively), from baseline to week 16 and week 52 is presented. Hyperphagia, is assessed using the hyperphagia questionnaire. It contains 13 questions. Out of 13 questions 11 questions are categorised into 3 domains (behaviour, drive and severity) scores. 2 questions are considered as additional questions. The total score is the sum of all the 3 domain scores. Total score ranges from 0 to 36, with higher score indicating a worse outcome. Results are based on the FAS which included all randomised subjects who received at least one dose of trial product and had any post-randomisation data. Number of subjects analysed = Number of subjects who contributed to the analysis.

End point type	Secondary

End point timeframe:

From baseline (week 0) to 16 and 52 weeks

End point values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Part A: Liraglutide	Part A: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	36	19	19	12
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 16:Hyperphagia behaviour score	-1.0 (± 2.97)	-2.0 (± 3.48)	-0.8 (± 2.01)	-1.7 (± 4.14)
Week 16:Hyperphagia drive score	-1.3 (± 2.87)	-1.3 (± 2.69)	-0.9 (± 2.80)	-0.9 (± 2.61)
Week 16:Hyperphagia severity score	-0.4 (± 1.59)	-0.2 (± 2.12)	-0.6 (± 1.54)	-0.3 (± 2.46)
Week 16:Hyperphagia total score	-2.7 (± 6.34)	-3.5 (± 5.63)	-2.4 (± 5.55)	-2.9 (± 5.79)
Week 52:Hyperphagia behaviour score	-0.8 (± 3.82)	-1.3 (± 3.00)	-0.9 (± 3.20)	-0.6 (± 2.62)
Week 52:Hyperphagia drive score	-1.7 (± 3.41)	-0.8 (± 3.06)	-2.2 (± 2.90)	-0.5 (± 2.42)
Week 52:Hyperphagia severity score	-0.9 (± 2.27)	-1.1 (± 2.26)	-1.3 (± 1.81)	-0.9 (± 2.51)
Week 52:Hyperphagia total score	-3.4 (± 8.23)	-3.1 (± 6.77)	-4.4 (± 6.57)	-2.1 (± 6.11)

End point values	Part B: Liraglutide	Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	7		
Units: score on a scale				
arithmetic mean (standard deviation)				

Week 16:Hyperphagia behaviour score	-1.2 (± 3.83)	-2.6 (± 2.07)		
Week 16:Hyperphagia drive score	-1.8 (± 2.97)	-2.0 (± 2.89)		
Week 16:Hyperphagia severity score	-0.1 (± 1.65)	0.1 (± 1.46)		
Week 16:Hyperphagia total score	-3.1 (± 7.28)	-4.4 (± 5.65)		
Week 52:Hyperphagia behaviour score	-0.7 (± 4.63)	-2.6 (± 3.65)		
Week 52:Hyperphagia drive score	-1.1 (± 3.99)	-1.4 (± 4.45)		
Week 52:Hyperphagia severity score	-0.4 (± 2.73)	-1.4 (± 1.82)		
Week 52:Hyperphagia total score	-2.1 (± 10.11)	-5.4 (± 8.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in systolic and diastolic blood pressure

End point title	Change in systolic and diastolic blood pressure

End point description:

Change in systolic blood pressure (SBP) and diastolic blood pressure (DBP) from baseline to week 16 and week 52 is presented. Results are based on the FAS which included all randomised subjects who received at least one dose of trial product and had any post-randomisation data. Number of subjects analysed = Number of subjects who contributed to the analysis. n = number of subjects from the respective arms analysed for specific timepoints. At week 16: n= 33, 19, 18, 12, 15, 7 are the number of subjects from the respective arms analysed for week 16. At week 52: n= 30, 16, 17, 11, 13, 5 are the number of subjects from the respective arms analysed for week 52.

End point type	Secondary

End point timeframe:

From baseline (week 0) to 16 and 52 weeks

End point values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Part A: Liraglutide	Part A: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	33	19	18	12
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
Week 16: SBP	-1 (± 13)	-1 (± 11)	-5 (± 15)	-2 (± 13)
Week 16: DBP	0 (± 9)	0 (± 11)	-1 (± 10)	0 (± 7)
Week 52: SBP	-1 (± 11)	5 (± 11)	-5 (± 6)	4 (± 12)
Week 52: DBP	0 (± 11)	4 (± 12)	-3 (± 9)	5 (± 13)

End point values	Part B: Liraglutide	Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	7		
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
Week 16: SBP	2 (± 9)	2 (± 6)		

Week 16: DBP	1 (± 8)	-1 (± 17)		
Week 52: SBP	4 (± 15)	7 (± 8)		
Week 52: DBP	4 (± 13)	1 (± 7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in glucose metabolism: glycosylated haemoglobin (HbA1c)

End point title	Change in glucose metabolism: glycosylated haemoglobin (HbA1c)

End point description:

Change in HbA1c from baseline to week 16 and week 52 is presented. Results are based on the FAS which included all randomised subjects who received at least one dose of trial product and had any post-randomisation data. Number of subjects analysed = Number of subjects who contributed to the analysis. n = number of subjects from the respective arms analysed for specific timepoints. At week 16: n= 29, 19, 16, 12, 13, 7 are the number of subjects from the respective arms analysed for week 16. At week 52: n= 28, 14, 16, 9, 12, 5 are the number of subjects from the respective arms analysed for week 52.

End point type	Secondary

End point timeframe:

From baseline (week 0) to 16 and 52 weeks

End point values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Part A: Liraglutide	Part A: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	29	19	16	12
Units: Percentage point of HbA1c				
arithmetic mean (standard deviation)				
Week 16	-0.2 (± 0.2)	-0.1 (± 0.3)	-0.2 (± 0.1)	0 (± 0.3)
Week 52	-0.2 (± 0.3)	0.1 (± 0.3)	-0.2 (± 0.2)	0.1 (± 0.3)

End point values	Part B: Liraglutide	Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	7		
Units: Percentage point of HbA1c				
arithmetic mean (standard deviation)				
Week 16	-0.2 (± 0.3)	-0.2 (± 0.3)		
Week 52	-0.2 (± 0.4)	-0.1 (± 0.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in glucose metabolism: fasting plasma glucose (FPG)

End point title	Change in glucose metabolism: fasting plasma glucose (FPG)

End point description:

Change in FPG from baseline to week 16 and week 52 is presented. Results are based on the FAS which included all randomised subjects who received at least one dose of trial product and had any post-randomisation data. Number of subjects analysed = Number of subjects who contributed to the analysis. n = number of subjects from the respective arms analysed for specific timepoints. At week 16: n= 31, 16, 18, 11, 13, 5 are the number of subjects from the respective arms analysed for week 16. At week 52: n= 27, 14, 15, 9, 12, 5 are the number of subjects from the respective arms analysed for week 52.

End point type	Secondary

End point timeframe:

From baseline (week 0) to 16 and 52 weeks

End point values	Part A+B: Liraglutide 3.0 mg	Part A+B: Placebo	Part A: Liraglutide	Part A: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	31	16	18	11
Units: Millimoles per litre (mmol/L)				
arithmetic mean (standard deviation)				
Week 16	-0.2 (± 0.5)	0.1 (± 0.4)	-0.2 (± 0.5)	0.1 (± 0.5)
Week 52	0 (± 0.6)	0.2 (± 0.7)	0 (± 0.7)	0.3 (± 0.8)

End point values	Part B: Liraglutide	Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	5		
Units: Millimoles per litre (mmol/L)				
arithmetic mean (standard deviation)				
Week 16	-0.1 (± 0.5)	0.2 (± 0.4)		
Week 52	0 (± 0.4)	0 (± 0.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Weeks 0-54.
Results are based on SAS which included all subjects exposed to at least one dose of trial product. All presented adverse events (AEs) are treatment emergent adverse events (TEAEs). TEAE was an event that occurred during on-treatment period.

Adverse event reporting additional description:

On treatment period: AEs are included with an onset date on or after first day of trial product administration and any of following dates, whichever came first: 14 days after last day on trial product, or Follow-up visit (week 54) for subjects with trial product discontinuation, or Last study visit (subjects withdrawn without follow-up visit).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	Part A+B: Liraglutide 3.0 mg

Reporting group description:

Subjects received once daily subcutaneous injection of liraglutide for 52 weeks (open label for 16 weeks and double-blinded for 36 weeks) in a dose escalating manner. For both part A and part B (for children with body weight ≥45 kg): dosing was initiated with liraglutide 0.6 mg daily for one week and increased in weekly dosage steps of 0.6 mg until a MTD (as judged by the Investigator) or a dose of 3.0 mg liraglutide was reached, i.e., 0.6 mg (week 1), 1.2 mg (week 2), 1.8 mg (week 3), 2.4 mg (week 4) and 3.0 mg (week 5 to week 52). For Part B children with body weight <45 kg: dosing was initiated with liraglutide 0.3 mg daily for one week and increased to 0.6 mg after the first week. Thereafter, the dose was increased in weekly steps of 0.6 mg until an MTD (as judged by the Investigator) or a dose of 2.4 mg liraglutide was reached. i.e., 0.3 mg (week 1), 0.6 mg (week 2), 1.2 mg (week 3), 1.8 mg (week 4), 2.4 mg (week 5 to week 52).

Reporting group title	Placebo

Reporting group description:

Subjects received once daily subcutaneous injection of liraglutide matching placebo for 16 weeks (open label).

Serious adverse events	Part A+B: Liraglutide 3.0 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 37 (8.11%)	1 / 19 (5.26%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Arthrodesis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal operation			

subjects affected / exposed	1 / 37 (2.70%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Hyperthermia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Staphylococcal infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	Part A+B: Liraglutide 3.0 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 37 (81.08%)	14 / 19 (73.68%)	
Surgical and medical procedures			
Pain prophylaxis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	3 / 37 (8.11%)	0 / 19 (0.00%)	
occurrences (all)	3	0	
Injection site bruising			
subjects affected / exposed	2 / 37 (5.41%)	1 / 19 (5.26%)	
occurrences (all)	2	1	
Injection site haematoma			
subjects affected / exposed	3 / 37 (8.11%)	1 / 19 (5.26%)	
occurrences (all)	4	1	
Malaise			
subjects affected / exposed	1 / 37 (2.70%)	2 / 19 (10.53%)	
occurrences (all)	1	2	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 37 (5.41%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 37 (8.11%)	1 / 19 (5.26%)	
occurrences (all)	3	1	
Oropharyngeal pain			
subjects affected / exposed	4 / 37 (10.81%)	1 / 19 (5.26%)	
occurrences (all)	5	1	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Psychiatric disorders			
Aggression			
subjects affected / exposed	2 / 37 (5.41%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 37 (2.70%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Glycosylated haemoglobin increased			

subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Insulin-like growth factor decreased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Thyroxine free decreased			
subjects affected / exposed	2 / 37 (5.41%)	0 / 19 (0.00%)	
occurrences (all)	3	0	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	2 / 37 (5.41%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Fall			
subjects affected / exposed	3 / 37 (8.11%)	0 / 19 (0.00%)	
occurrences (all)	4	0	
Hip fracture			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Ligament sprain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 37 (10.81%)	3 / 19 (15.79%)	
occurrences (all)	11	6	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	9 / 37 (24.32%)	3 / 19 (15.79%)	
occurrences (all)	20	3	
Abdominal pain upper			
subjects affected / exposed	4 / 37 (10.81%)	0 / 19 (0.00%)	
occurrences (all)	8	0	

Abdominal rigidity			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	3 / 37 (8.11%)	0 / 19 (0.00%)	
occurrences (all)	4	0	
Diarrhoea			
subjects affected / exposed	17 / 37 (45.95%)	2 / 19 (10.53%)	
occurrences (all)	92	4	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 37 (5.41%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	2 / 37 (5.41%)	0 / 19 (0.00%)	
occurrences (all)	3	0	
Vomiting			
subjects affected / exposed	5 / 37 (13.51%)	0 / 19 (0.00%)	
occurrences (all)	7	0	
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Precocious puberty			
subjects affected / exposed	2 / 37 (5.41%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	1 / 37 (2.70%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Pain in extremity			
subjects affected / exposed	2 / 37 (5.41%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Ear infection viral			
subjects affected / exposed	1 / 37 (2.70%)	1 / 19 (5.26%)	
occurrences (all)	3	1	
Gastroenteritis			
subjects affected / exposed	4 / 37 (10.81%)	0 / 19 (0.00%)	
occurrences (all)	6	0	
Influenza			
subjects affected / exposed	4 / 37 (10.81%)	3 / 19 (15.79%)	
occurrences (all)	6	5	
Nasopharyngitis			
subjects affected / exposed	5 / 37 (13.51%)	1 / 19 (5.26%)	
occurrences (all)	8	1	
Pharyngitis			
subjects affected / exposed	1 / 37 (2.70%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Rhinitis			
subjects affected / exposed	3 / 37 (8.11%)	0 / 19 (0.00%)	
occurrences (all)	3	0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 37 (8.11%)	2 / 19 (10.53%)	
occurrences (all)	3	2	
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Hypernatraemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 October 2015	Following changes were made in this amendment: • A new exclusion criterion of "Suggestive history of, or significant risk of gastroparesis (e.g. marked abdominal bloating post meal, history of vomiting, severe constipation), as judged by the Investigators" was included. • The order of definitions for hip and waist circumference in Section 8.4.1.2 was changed to align with electronic data capture (EDC) standards. • Systolic and diastolic blood pressure text specifying cuff size when measuring blood pressure was deleted, as it referred to an adult population. • The text for calcium measurement in Section 8.5.7 was corrected due to an error in writing. Albumin corrected calcium was collected instead of the ionised form.
24 January 2018	Following changes were made in this amendment: • The starting dose and dose escalation for part B were adjusted based on the results of the safety and PK data from the NN8022-4181 trial and part A of NN8022-4179. Dosing was changed for part B such that: a) Children with a body weight < 45 kilograms (kg), initiated dose titration with 0.3 milligrams per day (mg/day) and had a maximum dose of 2.4 mg/day or maximum tolerated dose (MTD). b) Children with body weight ≥ 45 kg, initiated dose titration at 0.6 mg/day, with a maximum dose of 3.0 mg/day or MTD • Clarification and alignment with the Paediatric Investigational Plan of inclusion criterion 4 and related text regarding Tanner staging throughout the protocol • Alignment of number of subjects completing the trial and definition of evaluable subjects with wording from the Paediatric Investigational Plan (Sections 6.1 and 6.6) • To be in alignment with the Novo Nordisk recommendation to use patient centric language, "obese children" was changed to "children with obesity" throughout the protocol. • The option of local testing for adrenal insufficiency was added to facilitate the inclusion of subjects with missing documentation of test results
09 April 2020	Following changes were made in this amendment: Section 6.1 related to number of subjects and Section 12.6 related to product overdose were updated
20 July 2020	Following sections were updated for number of subjects in this amendment: • Section 1 (Summary); • Section 6.1 (Number of subjects); • Section 6.6 (Subject replacement); • Section 17.1 (Sample size calculation).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported