Clinical trial results:
Effect and safety of semaglutide 2.4 mg once weekly on weight management in adolescents with overweight or obesity

Summary

EudraCT number	2018-002431-18
Trial protocol	GB AT BE IE HR
Global end of trial date	28 March 2022

Results information

Result version number	v1 (current)
This version publication date	03 September 2022
First version publication date	03 September 2022

Trial information

Trial identification

Sponsor protocol code	NN9536-4451

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04102189
WHO universal trial number (UTN)	U1111-1215-7560

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Office (2834), 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-001441-PIP03-17
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	18 May 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the effect of semaglutide subcutaneously (s.c.) once-weekly versus semaglutide placebo as an adjunct to a reduced-calorie diet and increased physical activity on weight management in adolescents (ages 12 to less than [<18] years) with overweight or obesity

Protection of trial subjects:

This trial was conducted in accordance with the principles of the Declaration of Helsinki (2013), International Council for Harmonisation (ICH) Good Clinical Practice, including the archiving of essential documents (2016), and US Food and Drug Administration (FDA) 21 Code of Federal Regulations (CFR) 312.120. The FDA 21 CFR, parts 312, 50, and 56 were followed.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	07 October 2019
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	Austria: 11
Country: Number of subjects enrolled	Belgium: 24
Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	Croatia: 16
Country: Number of subjects enrolled	Ireland: 4
Country: Number of subjects enrolled	Mexico: 18
Country: Number of subjects enrolled	Russian Federation: 55
Country: Number of subjects enrolled	United States: 51
Worldwide total number of subjects	201
EEA total number of subjects	55

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	201
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 37 sites in 8 countries, as follows: Austria (3), Belgium (4), Croatia (3), Ireland (1), Mexico (1), Russia (7), Great Britain (6), United States (12).

Pre-assignment

Screening details:

Subjects were randomised 2:1 to receive either semaglutide s.c. once weekly or semaglutide placebo s.c. once weekly for a dose escalation period of 16 weeks and a maintenance period of 52 weeks. This was followed by a 7-week follow-up period after 'end of treatment' due to the long half-life of semaglutide.

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 clinical study group and the investigator were blinded throughout the trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Semaglutide 2.4 mg

Arm description:

Subjects received once weekly s.c. injection of semaglutide for 68 weeks. Subjects initially received 0.25 mg of semaglutide and the dose was then escalated once in 4 weeks for 16 weeks until the target dose of 2.4 mg was reached which was maintained for a period of 52 weeks: 0.25 mg (week 1 to week 4), 0.5 mg (week 5 to week 8), 1.0 mg (week 9 to week 12), 1.7 mg (week 13 to week 16) and 2.4 mg (week 17 to week 68). The treatment was an adjunct to a reduced-calorie diet and increased physical activity.

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

Dosage and administration details:

Subjects initially received 0.25 mg of semaglutide and the dose was then escalated once in 4 weeks for 16 weeks until the target dose of 2.4 mg was reached which was maintained for a period of 52 weeks: 0.25 mg (week 1 to week 4), 0.5 mg (week 5 to week 8), 1.0 mg (week 9 to week 12), 1.7 mg (week 13 to week 16) and 2.4 mg (week 17 to week 68). Injections were administered in the thigh, abdomen or upper arm at any time of day irrespective of meals.

Arm title	Placebo

Arm description:

Subjects received once weekly s.c. injection of semaglutide matching placebo for 68 weeks. The treatment was an adjunct to a reduced-calorie diet and increased physical activity.

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

Dosage and administration details:

Subjects received once weekly s.c. injection of semaglutide matching placebo for 68 weeks. Injections were administered in the thigh, abdomen or upper arm at any time of day irrespective of meals.

Number of subjects in period 1	Semaglutide 2.4 mg	Placebo
Started	134	67
Treated	133	67
Completed	132	64
Not completed	2	3
Consent withdrawn by subject	1	2
Lost to follow-up	1	-
Withdrawal by parent/guardian	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Semaglutide 2.4 mg
Reporting group description:	
Subjects received once weekly s.c. injection of semaglutide for 68 weeks. Subjects initially received 0.25 mg of semaglutide and the dose was then escalated once in 4 weeks for 16 weeks until the target dose of 2.4 mg was reached which was maintained for a period of 52 weeks: 0.25 mg (week 1 to week 4), 0.5 mg (week 5 to week 8), 1.0 mg (week 9 to week 12), 1.7 mg (week 13 to week 16) and 2.4 mg (week 17 to week 68). The treatment was an adjunct to a reduced-calorie diet and increased physical activity.	
Reporting group title	Placebo
Reporting group description:	
Subjects received once weekly s.c. injection of semaglutide matching placebo for 68 weeks. The treatment was an adjunct to a reduced-calorie diet and increased physical activity.	

Reporting group values	Semaglutide 2.4 mg	Placebo	Total
Number of subjects	134	67	201
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	134	67	201
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	15.5	15.3	
standard deviation	± 1.5	± 1.6	-
Gender Categorical			
Units: Subjects			
Female	84	41	125
Male	50	26	76

End points

End points reporting groups

Reporting group title	Semaglutide 2.4 mg

Reporting group description:

Subjects received once weekly s.c. injection of semaglutide for 68 weeks. Subjects initially received 0.25 mg of semaglutide and the dose was then escalated once in 4 weeks for 16 weeks until the target dose of 2.4 mg was reached which was maintained for a period of 52 weeks: 0.25 mg (week 1 to week 4), 0.5 mg (week 5 to week 8), 1.0 mg (week 9 to week 12), 1.7 mg (week 13 to week 16) and 2.4 mg (week 17 to week 68). The treatment was an adjunct to a reduced-calorie diet and increased physical activity.

Reporting group title	Placebo

Reporting group description:

Subjects received once weekly s.c. injection of semaglutide matching placebo for 68 weeks. The treatment was an adjunct to a reduced-calorie diet and increased physical activity.

Primary: Change in body mass index (BMI) from baseline

End point title	Change in body mass index (BMI) from baseline

End point description:

Change in percentage of BMI from baseline at week 68 is presented. Full analysis set (FAS) included all randomised subjects according to the intention-to-treat principle. 'Number of Subjects Analyzed' signifies number or subjects evaluable for this endpoint. Data is presented for in-trial period: the in-trial period was defined as the uninterrupted time interval from randomisation to last contact with trial site.

End point type	Primary

End point timeframe:

Baseline (week 0), week 68

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	62		
Units: Percentage of BMI				
arithmetic mean (standard deviation)	-16.2 (± 12.9)	-0.1 (± 8.6)		

Statistical analyses

Statistical analysis title	Semaglutide 2.4 mg vesrus Placebo

Statistical analysis description:

Week 68 responses were analysed using an analysis of covariance model with randomised treatment, stratification groups (sex and tanner stage at baseline)
and the interaction between stratification groups as factors and baseline BMI as covariate. All subjects in FAS (201 subjects) contributed to the analysis.

Comparison groups	Placebo v Semaglutide 2.4 mg

Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-16.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.27
upper limit	-13.23

Secondary: Subjects achieving equal to or above 5% reduction of body weight from baseline (yes/no)

End point title	Subjects achieving equal to or above 5% reduction of body weight from baseline (yes/no)

End point description:

Number of subjects who achieved equal to or above 5% reduction in body weight from baseline to 68 weeks is presented. In the reported data, 'Yes' infers the number of subjects who achieved equal to or above 5% weight reduction, whereas 'No' infers the number of subjects who have not achieved equal to or above 5% weight reduction. FAS included all randomised subjects according to the intention-to-treat principle. 'Number of Subjects Analyzed' signifies number or subjects evaluable for this endpoint. Data is presented for in-trial period: the in-trial period was defined as the uninterrupted time interval from randomisation to last contact with trial site.

End point type	Secondary

End point timeframe:

Baseline (week 0) to week 68

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	62		
Units: Subjects				
Yes	95	11		
No	36	51		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline (week 0) to week 75

Adverse event reporting additional description:

All presented adverse events (AEs) are treatment-emergent (i.e., TEAEs). TEAEs: AEs with if onset of event occurred in on-treatment period . On-treatment period: interval from first to last trial product administration plus 7 weeks. Safety analysis set included all randomised subjects exposed to at least 1 dose of randomised treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Semaglutide 2.4 mg

Reporting group description:

Subjects were initiated at a once-weekly dose of 0.25 mg semaglutide s.c. and followed a fixed-dose escalation regimen, with dose increases every 4 weeks (to doses of 0.5, 1.0, 1.7 and 2.4 mg/week) until maintenance dose (2.4 mg) was reached in dose escalation period of 16 weeks. Subjects continued the maintenance dose of semaglutide 2.4 mg in maintenance period of 52 weeks. Subjects were followed up for 7 weeks after the 'end of treatment'.

Reporting group title	Placebo

Reporting group description:

Subjects received semaglutide placebo once weekly for dose escalation period of 16 weeks followed by a maintenance period of 52 weeks. Subjects were followed up for 7 weeks after the 'end of treatment'.

Serious adverse events	Semaglutide 2.4 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 133 (11.28%)	6 / 67 (8.96%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian germ cell teratoma benign			
subjects affected / exposed	0 / 133 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Transaminases increased			
subjects affected / exposed	1 / 133 (0.75%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural			

complications			
Contusion			
subjects affected / exposed	0 / 133 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 133 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural constipation			
subjects affected / exposed	1 / 133 (0.75%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention postoperative			
subjects affected / exposed	1 / 133 (0.75%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 133 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension headache			
subjects affected / exposed	0 / 133 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 133 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			

subjects affected / exposed	1 / 133 (0.75%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 133 (0.75%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 133 (0.75%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	3 / 133 (2.26%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	1 / 133 (0.75%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Sleep apnoea syndrome			
subjects affected / exposed	1 / 133 (0.75%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 133 (0.75%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Appendicitis			
subjects affected / exposed	2 / 133 (1.50%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 133 (0.75%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 133 (0.75%)	0 / 67 (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	Semaglutide 2.4 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	90 / 133 (67.67%)	40 / 67 (59.70%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 133 (0.75%)	4 / 67 (5.97%)	
occurrences (all)	1	4	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 133 (1.50%)	4 / 67 (5.97%)	
occurrences (all)	2	4	
Nervous system disorders			
Dizziness			
subjects affected / exposed	10 / 133 (7.52%)	2 / 67 (2.99%)	
occurrences (all)	13	3	
Headache			
subjects affected / exposed	22 / 133 (16.54%)	11 / 67 (16.42%)	
occurrences (all)	52	20	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	4 / 133 (3.01%)	5 / 67 (7.46%)	
occurrences (all)	4	5	
Pyrexia			
subjects affected / exposed	5 / 133 (3.76%)	5 / 67 (7.46%)	
occurrences (all)	5	5	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	20 / 133 (15.04%)	4 / 67 (5.97%)	
occurrences (all)	31	4	
Abdominal pain upper			
subjects affected / exposed	11 / 133 (8.27%)	8 / 67 (11.94%)	
occurrences (all)	19	11	
Constipation			
subjects affected / exposed	8 / 133 (6.02%)	1 / 67 (1.49%)	
occurrences (all)	8	1	
Diarrhoea			
subjects affected / exposed	29 / 133 (21.80%)	13 / 67 (19.40%)	
occurrences (all)	54	19	
Nausea			
subjects affected / exposed	56 / 133 (42.11%)	12 / 67 (17.91%)	
occurrences (all)	127	29	
Vomiting			
subjects affected / exposed	48 / 133 (36.09%)	7 / 67 (10.45%)	
occurrences (all)	105	18	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 133 (1.50%)	4 / 67 (5.97%)	
occurrences (all)	3	7	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 133 (3.01%)	4 / 67 (5.97%)	
occurrences (all)	5	4	
Skin and subcutaneous tissue disorders			
Acne			

subjects affected / exposed	4 / 133 (3.01%)	4 / 67 (5.97%)	
occurrences (all)	4	4	
Infections and infestations			
COVID-19			
subjects affected / exposed	15 / 133 (11.28%)	10 / 67 (14.93%)	
occurrences (all)	16	10	
Gastroenteritis			
subjects affected / exposed	9 / 133 (6.77%)	2 / 67 (2.99%)	
occurrences (all)	9	2	
Nasopharyngitis			
subjects affected / exposed	16 / 133 (12.03%)	7 / 67 (10.45%)	
occurrences (all)	21	12	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 133 (6.02%)	3 / 67 (4.48%)	
occurrences (all)	8	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35797460