



Clinical trial results:

Two-year effect and safety of semaglutide 2.4 mg once-weekly in subjects with overweight or obesity

Summary

EudraCT number	2017-003726-32
Trial protocol	HU ES IT
Global end of trial date	23 March 2021

Results information

Result version number	v1 (current)
This version publication date	31 March 2022
First version publication date	31 March 2022

Trial information

Trial identification

Sponsor protocol code	NN9536-4378
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03693430
WHO universal trial number (UTN)	U1111-1202-1740

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)	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	17 August 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	23 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the two-year effect of semaglutide subcutaneous (s.c) 2.4 milligram (mg) once weekly versus semaglutide placebo as an adjunct to a reduced-calorie diet and increased physical activity in subjects with overweight or obesity on body weight.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (2016) and US Food and Drug Administration (FDA) 21 Code of Federal Regulations (CFR) 312.120.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 October 2018
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	Canada: 51
Country: Number of subjects enrolled	Spain: 50
Country: Number of subjects enrolled	Hungary: 35
Country: Number of subjects enrolled	Italy: 45
Country: Number of subjects enrolled	United States: 123
Worldwide total number of subjects	304
EEA total number of subjects	130

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)	285
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 41 sites in 5 countries as follows: Canada (9 sites), Hungary (6 sites), Italy (5 sites), Spain (6 sites), and United States (15 sites).

Pre-assignment

Screening details:

Subjects were randomized in a 1:1 manner to receive treatment with semaglutide 2.4 milligram (mg) or placebo once weekly as an adjunct to a reduced-calorie diet and increased physical activity. The trial has a 104 weeks treatment period (16 weeks of dose escalation period and 88 weeks of maintenance dose).

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Semaglutide 2.4 mg

Arm description:

Subjects received once-weekly s.c. injection of semaglutide in 16 week dose escalation period with dose escalation (0.25 mg, 0.5 mg, 1.0 mg and 1.7 mg) every fourth week until maintenance dose of 2.4 mg of semaglutide was reached. Treatment was continued on the maintenance dose of 2.4 mg once weekly for an additional 88 weeks until week 104.

Arm type	Experimental
Investigational medicinal product name	Semaglutide
Investigational medicinal product code	
Other name	PDS290
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received once-weekly s.c injection of semaglutide in 16 week dose escalation period with dose escalation (0.25 mg, 0.5 mg, 1.0 mg and 1.7 mg) every fourth week until maintenance dose of 2.4 mg of semaglutide was reached. Treatment was continued on the maintenance dose of 2.4 mg once weekly for an additional 88 weeks until week 104.

Arm title	Placebo
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Arm description:

Subjects received once-weekly s.c. injection of placebo matched to semaglutide for 104 weeks.

Arm type	Placebo
Investigational medicinal product name	Semaglutide 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 placebo matched to semaglutide for 104 weeks.

Number of subjects in period 1	Semaglutide 2.4 mg	Placebo
Started	152	152
Full analysis set (FAS)	152	152
Safety analysis set (SAS)	152	152
Completed	148	134
Not completed	4	18
Consent withdrawn by subject	-	4
Death	1	-
Lost to follow-up	3	14

Baseline characteristics

Reporting groups

Reporting group title	Semaglutide 2.4 mg
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Reporting group description:

Subjects received once-weekly s.c. injection of semaglutide in 16 week dose escalation period with dose escalation (0.25 mg, 0.5 mg, 1.0 mg and 1.7 mg) every fourth week until maintenance dose of 2.4 mg of semaglutide was reached. Treatment was continued on the maintenance dose of 2.4 mg once weekly for an additional 88 weeks until week 104.

Reporting group title	Placebo
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Reporting group description:

Subjects received once-weekly s.c. injection of placebo matched to semaglutide for 104 weeks.

Reporting group values	Semaglutide 2.4 mg	Placebo	Total
Number of subjects	152	152	304
Age Categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	47 ± 12	47 ± 10	-
Gender Categorical Units: Subjects			
Female	123	113	236
Male	29	39	68

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 in 16 week dose escalation period with dose escalation (0.25 mg, 0.5 mg, 1.0 mg and 1.7 mg) every fourth week until maintenance dose of 2.4 mg of semaglutide was reached. Treatment was continued on the maintenance dose of 2.4 mg once weekly for an additional 88 weeks until week 104.	
Reporting group title	Placebo
Reporting group description: Subjects received once-weekly s.c. injection of placebo matched to semaglutide for 104 weeks.	
Subject analysis set title	Semaglutide 2.4 mg
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received once-weekly s.c injection of semaglutide in 16 week dose escalation period with dose escalation (0.25 mg, 0.5 mg, 1.0 mg and 1.7 mg) every fourth week until maintenance dose of 2.4 mg of semaglutide was reached. Treatment was continued on the maintenance dose of 2.4 mg once weekly for an additional 88 weeks until week 104.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received once-weekly s.c. injection of placebo matched to semaglutide for 104 weeks.	

Primary: Change in body weight (%)

End point title	Change in body weight (%)
End point description: Percentage change in body weight for both in-trial and on-treatment observation period from baseline (week 0) to week 104 is presented. The endpoint was evaluated based on the data from both in-trial and on-treatment periods. In-trial observation period: the uninterrupted time interval from randomisation to last contact with trial site. On-treatment observation period: the interval from first to last trial product administration plus 2 weeks of follow-up and excluding any period of temporary treatment interruption defined as >2 consecutive missed doses (corresponding to >2 weeks off-treatment). The FAS included all randomised subjects according to the intention-to-treat principle. Overall Number of Subjects Analyzed = subjects with available data for this endpoint and Number Analyzed = subjects with available data for each specified category.	
End point type	Primary
End point timeframe: From baseline (week 0) to week 104	

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	128		
Units: Percentage change				
arithmetic mean (standard deviation)				
In-trial observation period	-15.9 (± 12.3)	-1.9 (± 8.9)		
On-treatment observation period (n= 132, 109)	-17.3 (± 11.9)	-2.0 (± 8.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Week 104 responses were analysed using an analysis of covariance model with randomised treatment as factor and baseline body weight as covariate. Missing observations were multiple (x1000) imputed from retrieved subjects of the same randomised treatment arm.	
Comparison groups	Semaglutide 2.4 mg v Placebo
Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-12.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.33
upper limit	-9.77

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
All responses prior to first discontinuation of treatment (or initiation of other anti-obesity medication or bariatric surgery) were included in a mixed model for repeated measurements with randomised treatment as factor and baseline body weight as covariate, all nested within visit.	
Comparison groups	Semaglutide 2.4 mg v Placebo
Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	< 0.0001
Method	MMRM (Mixed model repeated measurement)
Parameter estimate	Treatment difference
Point estimate	-16.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.64
upper limit	-13.45

Notes:

[1] - The number of subjects in this analysis is auto-calculated by the system. The actual number of subjects in the analysis are 211.

Primary: Subjects who achieve (yes/no): Body weight reduction equal to or above

5%

End point title	Subjects who achieve (yes/no): Body weight reduction equal to or above 5%
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End point description:

Number of subjects who achieved greater than or equal to (\geq) 5% weight loss at 104 weeks is presented. In the reported data, 'Yes' infers the number of subjects who have achieved \geq 5% weight loss, whereas 'No' infers the number of subjects who have not achieved \geq 5% weight loss. The endpoint was evaluated based on the data from both in-trial and on-treatment periods. In-trial observation period: the uninterrupted time interval from randomisation to last contact with trial site. On-treatment observation period: the interval from first to last trial product administration plus 2 weeks of follow-up and excluding any period of temporary treatment interruption defined as >2 consecutive missed doses (corresponding to >2 weeks off-treatment). The FAS included all randomised subjects according to the intention-to-treat principle. Overall Number of Subjects Analyzed= subjects with available data for this endpoint and Number Analyzed= subjects with available data for each specified category.

End point type	Primary
End point timeframe:	
From baseline (week 0) to week 104	

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	128		
Units: Subjects				
In-trial observation period: Yes	111	44		
In-trial observation period: No	33	84		
On-treatment observation period: Yes (n= 132, 109)	110	38		
On-treatment observation period: No (n= 132, 109)	22	71		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Treatment policy estimand.	
Comparison groups	Semaglutide 2.4 mg v Placebo
Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.95
upper limit	8.42

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Hypothetical estimand.	
Comparison groups	Semaglutide 2.4 mg v Placebo
Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	< 0.0001
Method	MMRM
Parameter estimate	Odds ratio (OR)
Point estimate	18.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.04
upper limit	32.49

Notes:

[2] - The number of subjects in this analysis is auto-calculated by the system. The actual number of subjects in the analysis are 211.

Secondary: Subjects who achieve (yes/no): Body weight reduction equal to or above 10% from baseline (week 0)

End point title	Subjects who achieve (yes/no): Body weight reduction equal to or above 10% from baseline (week 0)
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End point description:

Number of subjects who achieved $\geq 10\%$ weight loss at 104 weeks is presented. In the reported data, 'Yes' infers the number of subjects who have achieved $\geq 10\%$ weight loss, whereas 'No' infers the number of subjects who have not achieved $\geq 10\%$ weight loss. The endpoint was evaluated based on the data from in-trial observation period. In-trial observation period: the uninterrupted time interval from randomisation to last contact with trial site. The FAS included all randomised subjects according to the intention-to-treat principle. Overall Number of Subjects Analyzed = subjects with available data for this endpoint.

End point type	Secondary
End point timeframe:	
After 104 weeks	

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	128		
Units: Subjects				
Yes	89	17		
No	55	111		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects who achieve (yes/no): Body weight reduction equal to or above 15% from baseline (week 0)

End point title	Subjects who achieve (yes/no): Body weight reduction equal to or above 15% from baseline (week 0)
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End point description:

Number of subjects who achieved $\geq 15\%$ weight loss at 154 weeks is presented. In the reported data, 'Yes' infers the number of subjects who have achieved $\geq 15\%$ weight loss, whereas 'No' infers the number of subjects who have not achieved $\geq 15\%$ weight loss. The endpoint was evaluated based on the data from in-trial observation period. In-trial observation period: the uninterrupted time interval from randomisation to last contact with trial site. The FAS included all randomised subjects according to the intention-to-treat principle. Overall Number of Subjects Analyzed = subjects with available data for this endpoint.

End point type	Secondary
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End point timeframe:

After 104 weeks

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	128		
Units: Subjects				
Yes	75	9		
No	69	119		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in: Waist circumference (cm)

End point title	Change in: Waist circumference (cm)
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End point description:

Change in waist circumference from baseline (week 0) to week 104 is presented. The endpoint was evaluated based on the data from in-trial observation period. In-trial observation period: the uninterrupted time interval from randomisation to last contact with trial site. The FAS included all randomised subjects according to the intention-to-treat principle. Overall Number of Subjects Analyzed = subjects with available data for this endpoint.

End point type	Secondary
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End point timeframe:

From baseline (week 0) to week 104

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	126		
Units: Centimetre (cm)				
arithmetic mean (standard deviation)	-15.2 (± 12.4)	-4.3 (± 9.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in: Systolic blood pressure (mmHg)

End point title	Change in: Systolic blood pressure (mmHg)
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End point description:

Change in systolic blood pressure from baseline (week 0) to week 104 is presented. The endpoint was evaluated based on the data from in-trial observation period. In-trial observation period: the uninterrupted time interval from randomisation to last contact with trial site. The FAS included all randomised subjects according to the intention-to-treat principle. Overall Number of Subjects Analyzed = subjects with available data for this endpoint.

End point type	Secondary
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End point timeframe:

From baseline (week 0) to week 104

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	125		
Units: Millimetre of mercury (mmHg)				
arithmetic mean (standard deviation)	-6 (± 13)	-1 (± 15)		

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 111

Adverse event reporting additional description:

All AEs mentioned here are TEAE defined as an event that had onset date (or increase in severity) on or after the first day of exposure to randomised treatment and no later than the date of last dose + 7 weeks. Results are based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Subjects received once-weekly s.c. injection of placebo matched to semaglutide for 104 weeks.

Reporting group title	Semaglutide 2.4 mg
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Reporting group description:

Subjects received once-weekly s.c injection of semaglutide in 16 week dose escalation period with dose escalation (0.25 mg, 0.5 mg, 1.0 mg and 1.7 mg) every fourth week until maintenance dose of 2.4 mg of semaglutide was reached. Treatment was continued on the maintenance dose of 2.4 mg once weekly for an additional 88 weeks until week 104.

Serious adverse events	Placebo	Semaglutide 2.4 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 152 (11.84%)	12 / 152 (7.89%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign uterine neoplasm			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	2 / 152 (1.32%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			

subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer metastatic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Thyroidectomy			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Panic disorder			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Jaw fracture			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			

subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Arnold-Chiari malformation			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cervical cord compression			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension headache			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroesophageal reflux disease			

subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 152 (0.00%)	2 / 152 (1.32%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	1 / 152 (0.66%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			

subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 152 (1.32%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic abscess			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			

subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (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	Placebo	Semaglutide 2.4 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	117 / 152 (76.97%)	141 / 152 (92.76%)	
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	1 / 152 (0.66%)	10 / 152 (6.58%)	
occurrences (all)	1	10	
Vascular disorders			
Hypertension			
subjects affected / exposed	14 / 152 (9.21%)	6 / 152 (3.95%)	
occurrences (all)	14	6	
Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 152 (5.26%)	13 / 152 (8.55%)	
occurrences (all)	12	16	
Headache			
subjects affected / exposed	16 / 152 (10.53%)	16 / 152 (10.53%)	
occurrences (all)	31	36	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 152 (1.32%)	8 / 152 (5.26%)	
occurrences (all)	3	10	
Fatigue			
subjects affected / exposed	8 / 152 (5.26%)	11 / 152 (7.24%)	
occurrences (all)	8	12	

Injection site bruising subjects affected / exposed occurrences (all)	8 / 152 (5.26%) 11	5 / 152 (3.29%) 8	
Gastrointestinal disorders			
Abdominal distension subjects affected / exposed occurrences (all)	9 / 152 (5.92%) 13	15 / 152 (9.87%) 22	
Abdominal pain subjects affected / exposed occurrences (all)	4 / 152 (2.63%) 14	20 / 152 (13.16%) 32	
Abdominal pain upper subjects affected / exposed occurrences (all)	10 / 152 (6.58%) 13	22 / 152 (14.47%) 23	
Constipation subjects affected / exposed occurrences (all)	17 / 152 (11.18%) 26	47 / 152 (30.92%) 62	
Diarrhoea subjects affected / exposed occurrences (all)	36 / 152 (23.68%) 51	53 / 152 (34.87%) 108	
Dyspepsia subjects affected / exposed occurrences (all)	7 / 152 (4.61%) 12	20 / 152 (13.16%) 24	
Eructation subjects affected / exposed occurrences (all)	1 / 152 (0.66%) 2	17 / 152 (11.18%) 21	
Flatulence subjects affected / exposed occurrences (all)	10 / 152 (6.58%) 11	20 / 152 (13.16%) 25	
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	6 / 152 (3.95%) 6	15 / 152 (9.87%) 19	
Nausea subjects affected / exposed occurrences (all)	33 / 152 (21.71%) 53	81 / 152 (53.29%) 213	
Vomiting			

subjects affected / exposed occurrences (all)	7 / 152 (4.61%) 8	46 / 152 (30.26%) 78	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	8 / 152 (5.26%) 10	8 / 152 (5.26%) 8	
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	11 / 152 (7.24%) 12	8 / 152 (5.26%) 8	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Osteoarthritis subjects affected / exposed occurrences (all)	11 / 152 (7.24%) 20 19 / 152 (12.50%) 20 8 / 152 (5.26%) 9	14 / 152 (9.21%) 20 15 / 152 (9.87%) 17 9 / 152 (5.92%) 10	
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) COVID-19 subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	8 / 152 (5.26%) 9 6 / 152 (3.95%) 6 4 / 152 (2.63%) 4 16 / 152 (10.53%) 19 23 / 152 (15.13%) 31	8 / 152 (5.26%) 9 15 / 152 (9.87%) 16 20 / 152 (13.16%) 28 20 / 152 (13.16%) 23 24 / 152 (15.79%) 33	

Sinusitis			
subjects affected / exposed	9 / 152 (5.92%)	8 / 152 (5.26%)	
occurrences (all)	9	8	
Upper respiratory tract infection			
subjects affected / exposed	23 / 152 (15.13%)	20 / 152 (13.16%)	
occurrences (all)	30	31	
Urinary tract infection			
subjects affected / exposed	6 / 152 (3.95%)	12 / 152 (7.89%)	
occurrences (all)	7	19	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 152 (3.95%)	17 / 152 (11.18%)	
occurrences (all)	6	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 July 2018	Inclusion of the Control of Eating Questionnaire (CoEQ) as an exploratory endpoint.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported