Clinical trial results:
Efficacy and safety of oral semaglutide 50 mg once daily in subjects with overweight or obesity

Summary

EudraCT number	2020-002953-11
Trial protocol	FI FR DK
Global end of trial date	12 May 2023

Results information

Result version number	v1 (current)
This version publication date	23 May 2024
First version publication date	23 May 2024

Trial information

Trial identification

Sponsor protocol code	NN9932-4737

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1253-1670

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 May 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 March 2023
Global end of trial reached?	Yes
Global end of trial date	12 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm superior efficacy on body weight reduction of oral semaglutide 50 mg once daily versus placebo as an adjunct to reduced-calorie diet and increased physical activity in subjects with overweight or obesity

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and International Council for Harmonisation (ICH) Good Clinical Practice, including archiving of essential documents, and 21 Code of Federal Regulations (CFR) 312.120.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 September 2021
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: 40
Country: Number of subjects enrolled	Germany: 55
Country: Number of subjects enrolled	Denmark: 26
Country: Number of subjects enrolled	Finland: 67
Country: Number of subjects enrolled	France: 51
Country: Number of subjects enrolled	Japan: 60
Country: Number of subjects enrolled	Poland: 60
Country: Number of subjects enrolled	Russian Federation: 80
Country: Number of subjects enrolled	United States: 228
Worldwide total number of subjects	667
EEA total number of subjects	259

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)	587
From 65 to 84 years	80
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 50 sites in 9 countries as follows: Canada (5 sites), Denmark (3 sites), Finland (3 sites), France (5 sites), Germany (7 sites), Japan (3 sites), Poland (5 sites), Russia (8 sites) and United States (11 sites).

Pre-assignment

Screening details:

The trial included an initial 16-week dose-escalation period and a 52-week dose maintenance period. Subjects were randomized in 1:1 ratio either to receive oral semaglutide 50 mg or placebo. The treatment is an adjunct to reduced-calorie diet and increased physical activity.

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	Oral semaglutide 50 mg

Arm description:

Subjects received oral dose of semaglutide tablet once daily for 68 weeks. Subjects initially received 3 milligrams (mg) of semaglutide and the dose was then escalated once in 4 weeks until the target dose of 50 mg was reached: 3 mg (week 1 to week 4); 7 mg (week 5 to week 8); 14 mg (week 9 to week 12); 25 mg (week 13 to week 16) and 50 mg (week 17 to week 68).

Arm type	Experimental
Investigational medicinal product name	Oral semaglutide 50 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Once-daily tablet of oral semaglutide was administered for 4 weeks with escalating doses (3 mg, 7 mg, 14 mg, and 25 mg), followed by a maintenance period of 52 weeks with a dose of 50 mg.

Arm title	Placebo

Arm description:

Subjects received oral dose of placebo matched to semaglutide tablet once daily for 68 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Once-daily tablet of oral semaglutide placebo was administered for 4 weeks with escalating doses (3 mg, 7 mg, 14 mg, and 25 mg), followed by a maintenance period of 52 weeks with a dose of 50 mg.

Number of subjects in period 1	Oral semaglutide 50 mg	Placebo
Started	334	333
Completed	320	307
Not completed	14	26
Consent withdrawn by subject	10	11
Physician decision	-	1
Lost to follow-up	4	14

Baseline characteristics

Reporting groups	
Reporting group title	Oral semaglutide 50 mg
Reporting group description:	
Subjects received oral dose of semaglutide tablet once daily for 68 weeks. Subjects initially received 3 milligrams (mg) of semaglutide and the dose was then escalated once in 4 weeks until the target dose of 50 mg was reached: 3 mg (week 1 to week 4); 7 mg (week 5 to week 8); 14 mg (week 9 to week 12); 25 mg (week 13 to week 16) and 50 mg (week 17 to week 68).	
Reporting group title	Placebo
Reporting group description:	
Subjects received oral dose of placebo matched to semaglutide tablet once daily for 68 weeks.	

Reporting group values	Oral semaglutide 50 mg	Placebo	Total
Number of subjects	334	333	667
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)	0	0	0
Adults (18-64 years)	294	293	587
From 65-84 years	40	40	80
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	49	50	
standard deviation	± 13	± 12	-
Gender Categorical Units: Subjects			
Female	247	238	485
Male	87	95	182

End points

End points reporting groups

Reporting group title	Oral semaglutide 50 mg

Reporting group description:

Subjects received oral dose of semaglutide tablet once daily for 68 weeks. Subjects initially received 3 milligrams (mg) of semaglutide and the dose was then escalated once in 4 weeks until the target dose of 50 mg was reached: 3 mg (week 1 to week 4); 7 mg (week 5 to week 8); 14 mg (week 9 to week 12); 25 mg (week 13 to week 16) and 50 mg (week 17 to week 68).

Reporting group title	Placebo

Reporting group description:

Subjects received oral dose of placebo matched to semaglutide tablet once daily for 68 weeks.

Primary: Relative change in body weight

End point title	Relative change in body weight

End point description:

Relative change in body weight from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from both in-trial and on-treatment observation periods. In-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. The on-treatment period was from the date of first trial product administration to the date of last trial product administration excluding potential off-treatment time intervals of more than 3 consecutive days. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint. Number analyzed (n)= number of subjects evaluable for defined row.

End point type	Primary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	295		
Units: Percentage (%) of body weight				
arithmetic mean (standard deviation)				
In-trial (n= 317, 295)	-15.8 (± 10.3)	-2.2 (± 7.2)		
On-treatment (n= 277, 245)	-17.0 (± 9.8)	-2.0 (± 7.3)		

Statistical analyses

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	Oral semaglutide 50 mg v Placebo

Number of subjects included in analysis	612
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-15.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.07
upper limit	-14.18

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 68 responses were analysed using an analysis of covariance model (ANCOVA) with randomised treatment as factor and baseline body weight as covariate.

Comparison groups	Oral semaglutide 50 mg v Placebo
Number of subjects included in analysis	612
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-12.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.15
upper limit	-11.33

Primary: Achievement of body weight reduction greater than or equal to 5% (Yes/No)

End point title	Achievement of body weight reduction greater than or equal to 5% (Yes/No)

End point description:

Number of subjects who achieved weight loss greater than or equal to 5% of their baseline body weight (yes/no) at end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from both in-trial and on-treatment observation periods. In-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. The on-treatment period was from the date of first trial product administration to the date of last trial product administration excluding potential off-treatment time intervals of more than 3 consecutive days. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint. Number analyzed (n)= number of subjects evaluable for defined row.

End point type	Primary

End point timeframe:

At end-of-treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	295		
Units: Subjects				
In-trial: Yes (n= 317, 295)	269	76		
In-trial: No (n= 317, 295)	48	219		
On-treatment: Yes (n= 277, 245)	247	60		
On-treatment: No (n= 277, 245)	30	185		

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Week 68 responses were analysed using a binary logistic regression model with randomised treatment as factor and baseline body weight as covariate.

Comparison groups	Oral semaglutide 50 mg v Placebo
Number of subjects included in analysis	612
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	55.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	32.98
upper limit	92.41

Notes:

[1] - Hypothetical estimand

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 68 responses were analysed using a binary logistic regression model with randomised treatment as factor and baseline body weight as covariate.

Comparison groups	Oral semaglutide 50 mg v Placebo
Number of subjects included in analysis	612
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	12.62

Confidence interval	
level	95 %
sides	2-sided
lower limit	8.5
upper limit	18.74

Notes:

[2] - Treatment policy estimand

Secondary: Achievement of body weight reduction greater than or equal to 15% (Yes/No)

End point title	Achievement of body weight reduction greater than or equal to 15% (Yes/No)

End point description:

Number of subjects who achieved weight loss greater than or equal (≥) 15% (Yes/No) at end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

At end-of-treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	295		
Units: Subjects				
Yes	170	17		
No	147	278		

Statistical analyses

No statistical analyses for this end point

Secondary: Achievement of body weight reduction greater than or equal to 10% (Yes/No)

End point title	Achievement of body weight reduction greater than or equal to 10% (Yes/No)

End point description:

Number of subjects who achieved weight loss greater than or equal ≥10% (Yes/No) at end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

At end-of-treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	295		
Units: Subjects				
Yes	220	35		
No	97	260		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in waist circumference

End point title	Change in waist circumference

End point description:

Change in waist circumference from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	295		
Units: Centimeter (cm)				
arithmetic mean (standard deviation)	-13.4 (± 10.0)	-2.8 (± 7.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Achievement of body weight reduction greater than or equal to 20% (Yes/No)

End point title	Achievement of body weight reduction greater than or equal to 20% (Yes/No)

End point description:

Number of subjects who achieved weight loss greater than or equal (≥) 20% (Yes/No) at end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period

which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

At end-of-treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	295		
Units: Subjects				
Yes	107	8		
No	210	287		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body mass index (BMI)

End point title	Change in body mass index (BMI)

End point description:

Change in BMI from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	295		
Units: Kilogram per meter square (kg/m^2)				
arithmetic mean (standard deviation)	-5.9 (± 4.0)	-0.9 (± 2.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Impact of Weight on Quality of Life-Lite-Clinical Trials Version (IWQOL-Lite-CT) physical function

End point title	Change in Impact of Weight on Quality of Life-Lite-Clinical Trials Version (IWQOL-Lite-CT) physical function

End point description:

The IWQOL-Lite-CT is a 20-item, obesity-specific patient-reported outcome (PRO) instrument developed for use in obesity clinical trials. It assesses 2 primary domains of obesity-related health-related quality of life (HRQoL): physical (7 items), and psychosocial (13 items). A 5-item subset of the physical domain, the physical-function composite is also supported. Items in the physical-function composite describe physical impacts related to general and specific physical activities. All items in the physical domain are rated on either a 5-point frequency ("never" to "always") scale or a 5-point truth ("not at all true" to "completely true") scale. Total score of IWQOL-Lite-CT composite ranges from 0 to 100, with higher scores reflecting better quality of life. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	298	278		
Units: Score on a scale				
arithmetic mean (standard deviation)	14.5 (± 20.2)	5.0 (± 19.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Short Form-36 (SF-36) Physical Function

End point title	Change in Short Form-36 (SF-36) Physical Function

End point description:

The short form 36 (SF-36) form, assesses participants' health-related quality of life (HRQoL) on eight domains of functional health and well-being as well as two component summary scores (physical component summary and mental component summary). In the metric of norm-based scores, 50 and 10 corresponds to the mean and standard deviation, respectively, for the 2009 US general population. Change from week 0 in the domain scores and component summary scores were evaluated at week 68. A positive change score indicates an improvement since baseline. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end-of-treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	303	280		
Units: Score on a scale				
arithmetic mean (standard deviation)	2.4 (± 5.7)	-0.0 (± 5.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting serum insulin

End point title	Change in fasting serum insulin

End point description:

Change in fasting serum insulin (measured in picomoles per liter (pmol/L)) from baseline (week 0) to end-of-treatment (week 68) is presented as ratio to baseline. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	260		
Units: Ratio of fasting serum insulin				
geometric mean (geometric coefficient of variation)	0.67 (± 71.4)	0.94 (± 55.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting plasma glucose (FPG)

End point title	Change in fasting plasma glucose (FPG)

End point description:

Change in FPG from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313	292		
Units: Milligrams per deciliter (mg/dL)				
arithmetic mean (standard deviation)	-10.3 (± 12.7)	-1.8 (± 10.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in glycosylated haemoglobin (HbA1c)

End point title	Change in glycosylated haemoglobin (HbA1c)

End point description:

Change in HbA1c from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	286		
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-0.2 (± 0.3)	0.1 (± 0.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in diastolic blood pressure

End point title	Change in diastolic blood pressure

End point description:

Change in diastolic blood pressure from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	295		
Units: Millimeter of mercury (mmHg)				
arithmetic mean (standard deviation)	-2 (± 9)	-1 (± 10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in systolic blood pressure

End point title	Change in systolic blood pressure

End point description:

Change in systolic blood pressure from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	295		
Units: Millimeter of mercury (mmHg)				
arithmetic mean (standard deviation)	-7 (± 14)	-1 (± 14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in free fatty acids

End point title	Change in free fatty acids

End point description:

Change in free fatty acids (measured in Milligrams per deciliter (mg/dL)) from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	260		
Units: Ratio of free fatty acids				
geometric mean (geometric coefficient of variation)	0.87 (± 71.7)	1.00 (± 80.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in triglycerides

End point title	Change in triglycerides

End point description:

Change in triglycerides from (measured in milligrams per deciliter (mg/dL)) baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312	288		
Units: Ratio of triglycerides				
geometric mean (geometric coefficient of variation)	0.77 (± 38.4)	0.96 (± 37.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in very low density lipoprotein (VLDL) cholesterol

End point title	Change in very low density lipoprotein (VLDL) cholesterol

End point description:

Change in very low density lipoprotein (VLDL) cholesterol (measured in milligrams per deciliter (mg/dL)) from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312	288		
Units: Ratio of VLDL cholesterol				
geometric mean (geometric coefficient of variation)	0.77 (± 38.3)	0.96 (± 37.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in low density lipoprotein (LDL) cholesterol

End point title	Change in low density lipoprotein (LDL) cholesterol

End point description:

Change in low density lipoprotein (LDL) cholesterol (measured in milligrams per deciliter (mg/dL)) from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	286		
Units: Ratio of LDL cholesterol				
geometric mean (geometric coefficient of variation)	0.98 (± 25.8)	1.03 (± 26.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in high density lipoprotein (HDL) cholesterol

End point title	Change in high density lipoprotein (HDL) cholesterol

End point description:

Change in high density lipoprotein (HDL) cholesterol (measured in milligrams per deciliter (mg/dL)) from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	286		
Units: Ratio of HDL cholesterol				
geometric mean (geometric coefficient of variation)	1.05 (± 16.6)	1.01 (± 15.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in total cholesterol

End point title	Change in total cholesterol

End point description:

Change in total cholesterol (measured in milligrams per deciliter (mg/dL)) from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313	288		
Units: Ratio of total cholesterol				
geometric mean (geometric coefficient of variation)	0.97 (± 17.1)	1.01 (± 16.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment emergent adverse events

End point title	Number of treatment emergent adverse events

End point description:

Number of treatment emergent adverse events from baseline (week 0) to end-of-study (week 75) is presented. An adverse event is any untoward medical occurrence in a clinical trial subject that is temporally associated with the use of an investigational medicinal product (IMP), whether or not considered related to the IMP. Treatment emergent adverse events (TEAEs): events that had onset date during on-treatment period, time period in which subjects was considered exposed to trial product. The endpoint was evaluated based on the data from on-treatment period. The on-treatment period was from the date of first trial product administration to the date of last trial product administration excluding potential off-treatment time intervals. A time point is considered on-treatment if any dose was administered within the prior 49 days.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end-of-study (week 75)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	333		
Units: Events				
number (not applicable)	2500	1577		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of serious adverse events

End point title	Number of serious adverse events

End point description:

Number of serious adverse events from baseline (week 0) to end-of-study (week 75) is presented. A serious adverse event (SAE) was defined as any event that resulted in any of the following: death, life-threatening experience, in-patient hospitalisation or prolongation of existing hospitalisation, persistent or significant disability or incapacity, congenital anomaly or birth defect or important medical event. The endpoint was evaluated based on the data from on-treatment period. The on-treatment period was from the date of first trial product administration to the date of last trial product administration excluding potential off-treatment time intervals. A time point is considered on-treatment if any dose was administered within the prior 49 days.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end-of-study (week 75)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	333		
Units: Events				
number (not applicable)	44	48		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in high sensitivity C-reactive protein (hsCRP)

End point title	Change in high sensitivity C-reactive protein (hsCRP)

End point description:

Change in high sensitivity C-reactive protein (measured in Milligrams per liter (mg/L)) from baseline (week 0) to end-of-treatment (week 68) is presented. The endpoint was evaluated based on the data from in-trial period which was defined as the uninterrupted time interval from the date of randomisation to the date of last contact with the study site. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 68)

End point values	Oral semaglutide 50 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	314	288		
Units: Ratio of hsCRP				
geometric mean (geometric coefficient of variation)	0.42 (± 129.9)	0.85 (± 117.9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline (week 0) to end-of-study (week 75)

Adverse event reporting additional description:

All the presented adverse events (AEs) are treatment emergent adverse events (TEAEs). Treatment emergent adverse events (TEAEs): events that had onset date during on-treatment period, time period in which participants was considered exposed to trial product.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received oral dose of placebo matched to semaglutide tablet once daily for 68 weeks.

Reporting group title	Oral semaglutide 50 mg

Reporting group description:

Subjects received oral dose of semaglutide tablet once daily for 68 weeks. Subjects initially received 3 milligrams (mg) of semaglutide and the dose was then escalated once in 4 weeks until the target dose of 50 mg was reached: 3 mg (week 1 to week 4); 7 mg (week 5 to week 8); 14 mg (week 9 to week 12); 25 mg (week 13 to week 16) and 50 mg (week 17 to week 68).

Serious adverse events	Placebo	Oral semaglutide 50 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 333 (8.71%)	32 / 334 (9.58%)	
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)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
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	1 / 333 (0.30%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			

subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Gastric bypass			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus operation			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (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			
Chest pain			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent stenosis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			

subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 333 (0.30%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Adjustment disorder with depressed mood			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
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			
Foot fracture			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			

subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	2 / 333 (0.60%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			

subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Foreign body sensation in eyes			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diverticulum intestinal			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal angiodysplasia			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric panniculitis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			

subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (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	0 / 333 (0.00%)	4 / 334 (1.20%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
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			
Back pain			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	2 / 333 (0.60%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	4 / 333 (1.20%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periarthritis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 333 (0.00%)	2 / 334 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 333 (0.30%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 333 (0.30%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abscess limb			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 333 (0.60%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-acute COVID-19 syndrome			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 334 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval abscess			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	0 / 333 (0.00%)	1 / 334 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Oral semaglutide 50 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	242 / 333 (72.67%)	292 / 334 (87.43%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	22 / 333 (6.61%)	10 / 334 (2.99%)	
occurrences (all)	24	12	
Nervous system disorders			
Dizziness			
subjects affected / exposed	15 / 333 (4.50%)	27 / 334 (8.08%)	
occurrences (all)	18	33	
Headache			
subjects affected / exposed	29 / 333 (8.71%)	46 / 334 (13.77%)	
occurrences (all)	36	80	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	20 / 333 (6.01%)	24 / 334 (7.19%)	
occurrences (all)	23	28	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	16 / 333 (4.80%)	25 / 334 (7.49%)	
occurrences (all)	19	26	
Abdominal pain			
subjects affected / exposed	16 / 333 (4.80%)	22 / 334 (6.59%)	
occurrences (all)	19	27	
Abdominal pain upper			
subjects affected / exposed	12 / 333 (3.60%)	31 / 334 (9.28%)	
occurrences (all)	16	44	
Constipation			

subjects affected / exposed	50 / 333 (15.02%)	92 / 334 (27.54%)	
occurrences (all)	71	123	
Diarrhoea			
subjects affected / exposed	56 / 333 (16.82%)	89 / 334 (26.65%)	
occurrences (all)	70	169	
Dyspepsia			
subjects affected / exposed	17 / 333 (5.11%)	47 / 334 (14.07%)	
occurrences (all)	19	64	
Eructation			
subjects affected / exposed	7 / 333 (2.10%)	32 / 334 (9.58%)	
occurrences (all)	7	42	
Flatulence			
subjects affected / exposed	13 / 333 (3.90%)	19 / 334 (5.69%)	
occurrences (all)	15	22	
Gastrooesophageal reflux disease			
subjects affected / exposed	11 / 333 (3.30%)	29 / 334 (8.68%)	
occurrences (all)	12	35	
Nausea			
subjects affected / exposed	51 / 333 (15.32%)	173 / 334 (51.80%)	
occurrences (all)	64	331	
Vomiting			
subjects affected / exposed	12 / 333 (3.60%)	80 / 334 (23.95%)	
occurrences (all)	13	154	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	9 / 333 (2.70%)	23 / 334 (6.89%)	
occurrences (all)	9	25	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	38 / 333 (11.41%)	22 / 334 (6.59%)	
occurrences (all)	42	26	
Back pain			
subjects affected / exposed	24 / 333 (7.21%)	16 / 334 (4.79%)	
occurrences (all)	37	19	
Infections and infestations			

COVID-19			
subjects affected / exposed	115 / 333 (34.53%)	119 / 334 (35.63%)	
occurrences (all)	121	127	
Gastroenteritis			
subjects affected / exposed	10 / 333 (3.00%)	18 / 334 (5.39%)	
occurrences (all)	10	22	
Influenza			
subjects affected / exposed	18 / 333 (5.41%)	26 / 334 (7.78%)	
occurrences (all)	21	37	
Nasopharyngitis			
subjects affected / exposed	49 / 333 (14.71%)	38 / 334 (11.38%)	
occurrences (all)	73	54	
Sinusitis			
subjects affected / exposed	18 / 333 (5.41%)	12 / 334 (3.59%)	
occurrences (all)	24	13	
Upper respiratory tract infection			
subjects affected / exposed	20 / 333 (6.01%)	19 / 334 (5.69%)	
occurrences (all)	29	26	
Urinary tract infection			
subjects affected / exposed	6 / 333 (1.80%)	19 / 334 (5.69%)	
occurrences (all)	6	27	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	24 / 333 (7.21%)	56 / 334 (16.77%)	
occurrences (all)	26	61	

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