Clinical trial results:
Effect and safety of semaglutide 7.2 mg once-weekly in participants with obesity and type 2 diabetes

Summary

EudraCT number	2022-002235-60
Trial protocol	PT SK HU BG
Global end of trial date	13 December 2024

Results information

Result version number	v1 (current)
This version publication date	24 December 2025
First version publication date	24 December 2025

Trial information

Trial identification

Sponsor protocol code	NN9536-7545

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05649137
WHO universal trial number (UTN)	U1111-1279-0359

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Alle, 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	10 March 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to demonstrate the superiority of semaglutide s.c. 7.2 mg once weekly versus placebo as an adjunct to a reduced calorie diet and increased physical activity, with respect to relative change in body weight after 72 weeks, in adults with obesity and T2D and to demonstrate the superiority of semaglutide subcutaneously (s.c.) 7.2 milligrams (mg) once weekly versus placebo as an adjunct to a reduced calorie diet and increased physical activity, with respect to achieving body weight reduction greater than or equal to (>=) 5 percentage (%) after 72 weeks, in adults with obesity and type 2 diabetes (T2D).

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (Oct 2013) and International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, including archiving of essential documents (May 1996) and EN ISO 14155 Part 1 and 2 and Food and Drugs Administration (FDA) 21 Code of Federal Regulations (CFR) 312.120.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 January 2023
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	Bulgaria: 80
Country: Number of subjects enrolled	Canada: 32
Country: Number of subjects enrolled	Hungary: 76
Country: Number of subjects enrolled	Poland: 74
Country: Number of subjects enrolled	Portugal: 10
Country: Number of subjects enrolled	Slovakia: 61
Country: Number of subjects enrolled	United States: 125
Country: Number of subjects enrolled	South Africa: 54
Worldwide total number of subjects	512
EEA total number of subjects	301

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)	391
From 65 to 84 years	121
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted across 68 sites in 8 countries.

Pre-assignment

Screening details:

A total of 512 subjects were randomised in the study out of which 491 subjects completed the study. The study consisted of a 20-week dose escalation period followed by a 52-week maintenance period and a 9-week follow-up period.

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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Semaglutide 7.2 mg

Arm description:

Subjects received escalated dose of semaglutide s.c. (0.25, 0.5, 1.0, 1.7, and 2.4 mg) once weekly for 20 weeks followed by a maintenance dose of semaglutide 7.2 mg s.c. once weekly for 52 weeks.

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

Dosage and administration details:

Subjects received escalated dose of semaglutide s.c. (0.25, 0.5, 1.0, 1.7, and 2.4 mg) once weekly for 20 weeks followed by a maintenance dose of semaglutide 7.2 mg s.c. once weekly for 52 weeks.The subcutaneous injection was administered in the thigh, abdomen, or upper arm.

Arm title	Semaglutide 2.4 mg

Arm description:

Subjects received escalated dose of semaglutide s.c. (0.25, 0.5, 1.0, 1.7, and 2.4 mg) once weekly for 20 weeks followed by a maintenance dose of semaglutide 2.4 mg s.c. once weekly for 52 weeks.

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

Dosage and administration details:

Subjects received escalated dose of semaglutide s.c. (0.25, 0.5, 1.0, 1.7, and 2.4 mg) once weekly for 20 weeks followed by a maintenance dose of semaglutide 2.4 mg s.c. once weekly for 52 weeks. The subcutaneous injection was administered in the thigh, abdomen, or upper arm.

Arm title	Placebo

Arm description:

Subjects received matching placebo to semaglutide s.c. once a week for 72 weeks.

Arm type	Placebo

Investigational medicinal product name	Placebo matched to semaglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received matching placebo to semaglutide s.c. once a week for 72 weeks. The subcutaneous injection was administered in the thigh, abdomen, or upper arm.

Number of subjects in period 1	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo
Started	307	103	102
Full analysis set (FAS)	307	103	102
Safety analysis set (SAS)	307	103	102
Completed	295	100	96
Not completed	12	3	6
Physician decision	1	1	-
Consent withdrawn by subject	5	-	3
Death	4	1	1
Unspecified reason	-	1	-
Lost to follow-up	2	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Semaglutide 7.2 mg
Reporting group description:	
Subjects received escalated dose of semaglutide s.c. (0.25, 0.5, 1.0, 1.7, and 2.4 mg) once weekly for 20 weeks followed by a maintenance dose of semaglutide 7.2 mg s.c. once weekly for 52 weeks.	
Reporting group title	Semaglutide 2.4 mg
Reporting group description:	
Subjects received escalated dose of semaglutide s.c. (0.25, 0.5, 1.0, 1.7, and 2.4 mg) once weekly for 20 weeks followed by a maintenance dose of semaglutide 2.4 mg s.c. once weekly for 52 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received matching placebo to semaglutide s.c. once a week for 72 weeks.	

Reporting group values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo
Number of subjects	307	103	102
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)	237	73	81
From 65-84 years	70	30	21
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	57	58	55
standard deviation	± 10	± 10	± 10
Gender Categorical Units: Subjects			
Female	166	47	52
Male	141	56	50

Reporting group values	Total		
Number of subjects	512		
Age Categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	391		
From 65-84 years	121		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Units: Subjects			
Female	265		
Male	247		

End points

End points reporting groups

Reporting group title	Semaglutide 7.2 mg
Reporting group description:	
Subjects received escalated dose of semaglutide s.c. (0.25, 0.5, 1.0, 1.7, and 2.4 mg) once weekly for 20 weeks followed by a maintenance dose of semaglutide 7.2 mg s.c. once weekly for 52 weeks.	
Reporting group title	Semaglutide 2.4 mg
Reporting group description:	
Subjects received escalated dose of semaglutide s.c. (0.25, 0.5, 1.0, 1.7, and 2.4 mg) once weekly for 20 weeks followed by a maintenance dose of semaglutide 2.4 mg s.c. once weekly for 52 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received matching placebo to semaglutide s.c. once a week for 72 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 72) is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.	
End point type	Primary
End point timeframe:	
From baseline (week 0) to end of treatment (week 72)	

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	291	97	95	
Units: Percentage (%) of body weight				
arithmetic mean (standard deviation)	-13.5 (± 8.7)	-10.7 (± 8.1)	-4.0 (± 6.2)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Week 72 responses were analysed using an analysis of covariance model with randomised treatment as factor and baseline body weight as covariate.	
Comparison groups	Placebo v Semaglutide 7.2 mg

Number of subjects included in analysis	386
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-9.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.95
upper limit	-7.71

Primary: Greater than or equal to (>=) 5% body weight reduction (yes/no)

End point title	Greater than or equal to (>=) 5% body weight reduction (yes/no)

End point description:

Number of subjects with >= 5% body weight reduction (yes/no) is presented. Yes defines subjects who achieved body weight reduction >= 5% and no defines subjects who did not achieve body weight reduction >= 5%. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Primary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	291	97	95	
Units: Subjects				
Yes	251	73	33	
No	40	24	62	

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Week 72 responses were analysed using a binary regression model with randomized treatment as factor and baseline value as covariate.

Comparison groups	Semaglutide 7.2 mg v Placebo

Number of subjects included in analysis	386
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Binary regression model
Parameter estimate	Odds ratio (OR)
Point estimate	10.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.96
upper limit	16.87

Secondary: >= 10% body weight reduction (yes/no)

End point title	>= 10% body weight reduction (yes/no)

End point description:

Number of subjects who achieve body weight reduction >=10% is presented. Yes defines subjects who achieved body weight reduction >= 10% and no defines subjects who did not achieve body weight reduction >= 10%. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	291	97	95	
Units: Subjects				
Yes	183	50	11	
No	108	47	84	

Statistical analyses

No statistical analyses for this end point

Secondary: >=20% body weight reduction (yes/no)

End point title	>=20% body weight reduction (yes/no)

End point description:

Number of subjects who achieve body weight reduction >=20% is presented. Yes defines subjects who achieved body weight reduction >= 20% and no defines subjects who did not achieve body weight reduction >= 20%. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	291	97	95	
Units: Subjects				
Yes	62	14	2	
No	229	83	93	

Statistical analyses

No statistical analyses for this end point

Secondary: >= 15% body weight reduction (yes/no)

End point title	>= 15% body weight reduction (yes/no)

End point description:

Number of subjects who achieve body weight reduction >=15% is presented. Yes defines subjects who achieved body weight reduction >= 15% and no defines subjects who did not achieve body weight reduction >= 15%. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	291	97	95	
Units: Subjects				
Yes	120	28	7	
No	171	69	88	

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 72) is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	291	97	95	
Units: Centimetres (cm)				
arithmetic mean (standard deviation)	-12.6 (± 10.5)	-10.6 (± 8.4)	-6.5 (± 10.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in glycated haemoglobin (HbA1c)

End point title	Change in glycated haemoglobin (HbA1c)

End point description:

Change in HbA1c from baseline (week 0) to end of treatment (week 72) is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	288	96	94	
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-1.8 (± 1.2)	-1.7 (± 1.0)	-0.3 (± 1.3)	

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 72) is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	291	97	95	
Units: kilograms per metre square (kg/m^2)				
arithmetic mean (standard deviation)	-5.3 (± 3.8)	-4.1 (± 3.3)	-1.6 (± 2.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body weight

End point title	Change in body weight

End point description:

Change in body weight from baseline (week 0) to end of treatment (week 72) is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	291	97	95	
Units: kilograms (kg)				
arithmetic mean (standard deviation)	-14.9 (± 10.6)	-11.4 (± 8.9)	-4.6 (± 7.1)	

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 72) is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	291	97	95	
Units: Millimetres of mercury (mmHg)				
arithmetic mean (standard deviation)	-8 (± 13)	-7 (± 15)	-3 (± 13)	

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 72) is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	291	97	95	
Units: mmHg				
arithmetic mean (standard deviation)	-3 (± 9)	-3 (± 10)	-3 (± 9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in total cholesterol (millimoles per litre [mmol/L]) - ratio to baseline

End point title	Change in total cholesterol (millimoles per litre [mmol/L]) - ratio to baseline

End point description:

Change in total cholesterol in mmol/L from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	286	94	94	
Units: Ratio of total cholesterol				
geometric mean (geometric coefficient of variation)	0.96 (± 23.0)	0.96 (± 21.1)	0.97 (± 28.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in total cholesterol (milligrams per decilitre [mg/dL]) - ratio to baseline

End point title	Change in total cholesterol (milligrams per decilitre [mg/dL]) - ratio to baseline

End point description:

Change in total cholesterol in mg/dL from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	286	94	94	
Units: Ratio of total cholesterol				
geometric mean (geometric coefficient of variation)	0.96 (± 23.0)	0.96 (± 21.1)	0.97 (± 28.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in high-density lipoprotein (HDL) cholesterol (mmol/L) - ratio to baseline

End point title	Change in high-density lipoprotein (HDL) cholesterol (mmol/L) - ratio to baseline

End point description:

Change in HDL cholesterol in mmol/L from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	285	92	91	
Units: Ratio of HDL cholesterol				
geometric mean (geometric coefficient of variation)	1.10 (± 17.8)	1.06 (± 13.5)	1.07 (± 16.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in HDL cholesterol (mg/dL) - ratio to baseline

End point title	Change in HDL cholesterol (mg/dL) - ratio to baseline

End point description:

Change in HDL cholesterol in mg/dL from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	285	92	91	
Units: Ratio of HDL cholesterol				
geometric mean (geometric coefficient of variation)	1.10 (± 17.8)	1.06 (± 13.5)	1.07 (± 16.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in low-density lipoprotein (LDL) cholesterol (mmol/L) - ratio to baseline

End point title	Change in low-density lipoprotein (LDL) cholesterol (mmol/L) - ratio to baseline

End point description:

Change in LDL cholesterol in mmol/L from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	285	92	92	
Units: Ratio of LDL cholesterol				
geometric mean (geometric coefficient of variation)	0.99 (± 40.1)	0.95 (± 36.5)	0.97 (± 41.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in LDL cholesterol (mg/dL) - ratio to baseline

End point title	Change in LDL cholesterol (mg/dL) - ratio to baseline

End point description:

Change in LDL cholesterol in mg/dL from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	285	92	92	
Units: Ratio of LDL cholesterol				
geometric mean (geometric coefficient of variation)	0.99 (± 40.1)	0.95 (± 36.5)	0.97 (± 41.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in very-low-density lipoprotein (VLDL) cholesterol (mmol/L) - ratio to baseline

End point title	Change in very-low-density lipoprotein (VLDL) cholesterol (mmol/L) - ratio to baseline

End point description:

Change in VLDL cholesterol in mmol/L from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	286	94	93	
Units: Ratio of VLDL cholesterol				
geometric mean (geometric coefficient of variation)	0.72 (± 42.5)	0.81 (± 40.4)	0.90 (± 47.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in triglycerides (mmol/L) - ratio to baseline

End point title	Change in triglycerides (mmol/L) - ratio to baseline

End point description:

Change in triglycerides in mmol/L from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	286	94	94	
Units: Ratio of triglycerides				
geometric mean (geometric coefficient of variation)	0.71 (± 46.2)	0.80 (± 42.2)	0.87 (± 54.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in VLDL cholesterol (mg/dL) - ratio to baseline

End point title	Change in VLDL cholesterol (mg/dL) - ratio to baseline

End point description:

Change in VLDL cholesterol in mg/dL from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	286	94	93	
Units: Ratio of VLDL cholesterol				
geometric mean (geometric coefficient of variation)	0.72 (± 42.5)	0.81 (± 40.4)	0.90 (± 47.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in triglycerides (mg/dL) - ratio to baseline

End point title	Change in triglycerides (mg/dL) - ratio to baseline

End point description:

Change in triglycerides in mg/dL from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	286	94	94	
Units: Ratio of triglycerides				
geometric mean (geometric coefficient of variation)	0.71 (± 46.2)	0.80 (± 42.2)	0.87 (± 54.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in free fatty acids (mmol/L) - ratio to baseline

End point title	Change in free fatty acids (mmol/L) - ratio to baseline

End point description:

Change in free fatty acids in mmol/L from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	93	92	
Units: Ratio of free fatty acids				
geometric mean (geometric coefficient of variation)	0.74 (± 69.8)	0.81 (± 70.6)	0.98 (± 65.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in free fatty acids (mg/dL) - ratio to baseline

End point title	Change in free fatty acids (mg/dL) - ratio to baseline

End point description:

Change in free fatty acids in mg/dL from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	284	93	92	
Units: Ratio of free fatty acids				
geometric mean (geometric coefficient of variation)	0.74 (± 69.8)	0.81 (± 70.6)	0.98 (± 65.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting plasma glucose

End point title	Change in fasting plasma glucose

End point description:

Change in fasting plasma glucose from baseline (week 0) to end of treatment (week 72) is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	281	93	93	
Units: mg/dL				
arithmetic mean (standard deviation)	-59.6 (± 53.1)	-58.4 (± 46.3)	-20.2 (± 68.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in high-sensitivity c-reactive protein (hsCRP) - ratio to baseline

End point title	Change in high-sensitivity c-reactive protein (hsCRP) - ratio to baseline

End point description:

Change in hsCRP in mg/L from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	286	95	95	
Units: Ratio of hsCRP				
geometric mean (geometric coefficient of variation)	0.47 (± 166.7)	0.48 (± 121.1)	0.82 (± 96.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting serum insulin (picomoles per litre [pmol/L]) - ratio to baseline

End point title	Change in fasting serum insulin (picomoles per litre [pmol/L]) - ratio to baseline

End point description:

Change in fasting serum insulin in pmol/L from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	281	92	91	
Units: Ratio of fasting serum insulin				
geometric mean (geometric coefficient of variation)	0.77 (± 66.5)	0.90 (± 70.6)	0.87 (± 71.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: HbA1c < 7.0 % (53 millimoles per mole [mmol/mol])

End point title	HbA1c < 7.0 % (53 millimoles per mole [mmol/mol])

End point description:

Number of subjects with HbA1c less than (<) 7.0% (53 mmol/mol) from baseline (week 0) to end of treatment (week 72) is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	288	96	94	
Units: Subjects	235	75	27	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting serum insulin (milliinternational units per millilitre [mIU/mL]) - ratio to baseline

End point title	Change in fasting serum insulin (milliinternational units per millilitre [mIU/mL]) - ratio to baseline

End point description:

Change in fasting serum insulin in mIU/mL from baseline (week 0) to end of treatment (week 72) as ratio to baseline is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	281	92	91	
Units: Ratio of fasting serum insulin				
geometric mean (geometric coefficient of variation)	0.77 (± 66.5)	0.90 (± 70.6)	0.87 (± 71.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: HbA1c <= 6.5 % (48 mmol/mol)

End point title	HbA1c <= 6.5 % (48 mmol/mol)

End point description:

Number of subjects with HbA1c less than or equal to (<=) 6.5% (48 mmol/mol) from baseline (week 0) to end of treatment (week 72) is presented. Full analysis set included all randomised subjects. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	288	96	94	
Units: Subjects	209	64	15	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Adverse Events (AEs)

End point title	Number of Adverse Events (AEs)

End point description:

Number of AEs is reported. An AE is any untoward medical occurrence in a clinical study subject that is temporally associated with the use of investigational medicinal product (IMP), whether or not considered related to the IMP. Safety analysis set included all subjects who were exposed to at least one dose of randomised IMP.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of study (week 81)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	307	103	102	
Units: Events	1581	508	253	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in pulse

End point title	Change in pulse

End point description:

Change in pulse from baseline (week 0) to end of treatment (week 72) is presented. Safety analysis set included all subjects who were exposed to at least one dose of randomised IMP. Number of subjects analysed signifies subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 72)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	271	92	84	
Units: Beats per minute (bpm)				
arithmetic mean (standard deviation)	1 (± 10)	2 (± 10)	-4 (± 9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Serious Adverse Events (SAEs)

End point title	Number of Serious Adverse Events (SAEs)

End point description:

Number of SAEs is reported. An SAE is any untoward medical occurrence that fulfils at least one of the following criteria: results in death, is life threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect or important medical event. Safety analysis set included all subjects who were exposed to at least one dose of randomised IMP.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of study (week 81)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	307	103	102	
Units: Events	39	35	21	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment emergent severe or blood glucose confirmed symptomatic hypoglycaemic episodes

End point title	Number of treatment emergent severe or blood glucose confirmed symptomatic hypoglycaemic episodes

End point description:

Number of treatment emergent severe or blood glucose confirmed symptomatic hypoglycaemic episodes from baseline (week 0) to end of study (week 81) is presented. Safety analysis set included all subjects who were exposed to at least one dose of randomised IMP.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of study (week 81)

End point values	Semaglutide 7.2 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	307	103	102	
Units: Episodes	0	0	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From week 0 to week 81

Adverse event reporting additional description:

Safety analysis set included all participants who were exposed to at least one dose of randomised IMP. All presented AEs are treatment emergent AEs (TEAEs). A TEAE is defined as an adverse event which occured during the in-trial period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Semaglutide 7.2 mg

Reporting group description:

Subjects received escalated dose of semaglutide subcutaneously (s.c.) (0.25, 0.5, 1.0, 1.7, and 2.4 milligrams [mg]) once weekly for 20 weeks followed by a maintenance dose of semaglutide 7.2 mg s.c. once weekly for 52 weeks.

Reporting group title	Placebo

Reporting group description:

Subjects received matching placebo to semaglutide s.c. once a week for 72 weeks

Reporting group title	Semaglutide 2.4 mg

Reporting group description:

Subjects received escalated dose of semaglutide s.c. (0.25, 0.5, 1.0, 1.7, and 2.4 mg) once weekly for 20 weeks followed by a maintenance dose of semaglutide 2.4 mg s.c. once weekly for 52 weeks.

Serious adverse events	Semaglutide 7.2 mg	Placebo	Semaglutide 2.4 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 307 (9.77%)	10 / 102 (9.80%)	11 / 103 (10.68%)
number of deaths (all causes)	4	1	1
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			

subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 307 (0.33%)	1 / 102 (0.98%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cancer stage III			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian adenoma			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the tongue			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			

subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Reproductive system and breast disorders			
Postmenopausal haemorrhage			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Interstitial lung disease			

subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nasal septum deviation			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Intervertebral disc injury			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina unstable			
subjects affected / exposed	2 / 307 (0.65%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Acute left ventricular failure			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	2 / 307 (0.65%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 307 (0.33%)	3 / 102 (2.94%)	2 / 103 (1.94%)
occurrences causally related to treatment / all	0 / 1	0 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Anginal equivalent			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	2 / 307 (0.65%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiomyopathy			

subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nodal rhythm			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Bell's palsy			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral small vessel ischaemic disease			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Optic neuritis			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic encephalopathy			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			

subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iridocyclitis			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular oedema			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus paralytic			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatic mass			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Azotaemia			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	2 / 103 (1.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 307 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteolysis			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gangrene			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint abscess			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 307 (0.33%)	0 / 102 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Hyperphosphataemia			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperammonaemia			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 307 (0.00%)	0 / 102 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

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

Non-serious adverse events	Semaglutide 7.2 mg	Placebo	Semaglutide 2.4 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	187 / 307 (60.91%)	40 / 102 (39.22%)	64 / 103 (62.14%)
Nervous system disorders			
Headache			
subjects affected / exposed	22 / 307 (7.17%)	4 / 102 (3.92%)	8 / 103 (7.77%)
occurrences (all)	42	4	11
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	21 / 307 (6.84%)	5 / 102 (4.90%)	2 / 103 (1.94%)
occurrences (all)	34	5	3
Eye disorders			
Cataract			
subjects affected / exposed	9 / 307 (2.93%)	4 / 102 (3.92%)	6 / 103 (5.83%)
occurrences (all)	9	6	7
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	16 / 307 (5.21%)	3 / 102 (2.94%)	3 / 103 (2.91%)
occurrences (all)	19	3	4
Diarrhoea			
subjects affected / exposed	56 / 307 (18.24%)	9 / 102 (8.82%)	21 / 103 (20.39%)
occurrences (all)	98	13	35
Constipation			
subjects affected / exposed	45 / 307 (14.66%)	5 / 102 (4.90%)	19 / 103 (18.45%)
occurrences (all)	55	5	21
Dyspepsia			
subjects affected / exposed	25 / 307 (8.14%)	2 / 102 (1.96%)	4 / 103 (3.88%)
occurrences (all)	36	2	4
Eructation			
subjects affected / exposed	11 / 307 (3.58%)	1 / 102 (0.98%)	8 / 103 (7.77%)
occurrences (all)	13	1	9
Nausea			
subjects affected / exposed	89 / 307 (28.99%)	12 / 102 (11.76%)	29 / 103 (28.16%)
occurrences (all)	206	18	57
Vomiting			
subjects affected / exposed	51 / 307 (16.61%)	3 / 102 (2.94%)	14 / 103 (13.59%)
occurrences (all)	78	4	39
Skin and subcutaneous tissue disorders			
Sensitive skin			
subjects affected / exposed	18 / 307 (5.86%)	0 / 102 (0.00%)	2 / 103 (1.94%)
occurrences (all)	24	0	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	17 / 307 (5.54%)	3 / 102 (2.94%)	7 / 103 (6.80%)
occurrences (all)	18	3	8
Arthralgia			
subjects affected / exposed	16 / 307 (5.21%)	4 / 102 (3.92%)	4 / 103 (3.88%)
occurrences (all)	21	4	4
Infections and infestations			
COVID-19			
subjects affected / exposed	22 / 307 (7.17%)	7 / 102 (6.86%)	5 / 103 (4.85%)
occurrences (all)	22	7	6

Nasopharyngitis			
subjects affected / exposed	9 / 307 (2.93%)	8 / 102 (7.84%)	3 / 103 (2.91%)
occurrences (all)	10	9	3
Upper respiratory tract infection			
subjects affected / exposed	17 / 307 (5.54%)	5 / 102 (4.90%)	9 / 103 (8.74%)
occurrences (all)	21	5	9
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	21 / 307 (6.84%)	5 / 102 (4.90%)	8 / 103 (7.77%)
occurrences (all)	25	6	9

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2022	Key changes are listed below: - Editorial changes example spelling errors, punctuation or updates to more exact wording in order to improve readability. Wording related to a T2D indication had been removed including less strict requirements for T2D treatment - Discontinuation criteria line added. - Crosses corrected for contraceptive counselling, pharmacokinetic (PK) sampling, anti semaglutide antibodies, Columbia-Suicide Severity Rating Scale (C-SSRS) since last visit and administration of trial product. - Crosses corrected for contraceptive counselling, PK sampling, anti semaglutide antibodies, C-SSRS since last visit and administration of trial product. - Change in HbA1c changed to confirmatory secondary endpoint and estimands were updated accordingly. - Number of subjects increased to 500 and randomisation changed to 3:1:1. - Hepatic event text deleted. - Plan for Immunogenicity analyses changed. - HbA1c changed from primary to secondary endpoint. - Requirements updated for Canada, Germany, United States, South Africa.
07 March 2023	The key changes are listed below: - Editorial changes e.g. spelling errors, punctuation or updates to more exact wording to improve readability. - Biochemistry and haematology assessments added at visit (V)16. - Patient Health Questionnaire-9 (PHQ-9) and C-SSRS added to V8, V10, V14 and V18. Removed from V12. - Handout of PK diaries at V22 removed from flowchart. - Added that delaying dose escalation was allowed. - Calcitonin >= 100 nanograms per litre (ng/L) added as a discontinuation criterion. - Added direct bilirubin, amylase, calcitonin and lipase. - Criteria for hepatic laboratory outliers added. - Slovakia requirements added.
21 August 2023	The key changes are listed below: - Editorial changes e.g. spelling errors, punctuation or updates to more exact wording to improve readability. - Tobacco use assessment added at end-of treatment (V22) as new endpoint. - Removal of the potential risk of 'Neoplasms' (malignant and nonmalignant). - Update of the dosage and administration of, and transition to, the new drug-device combination product during the maintenance phase.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported