Clinical trial results:
Effect and safety of semaglutide 2.4 mg once-weekly in subjects with overweight or obesity and type 2 diabetes

Summary

EudraCT number	2017-003414-10
Trial protocol	GB DE ES GR
Global end of trial date	01 May 2020

Results information

Result version number	v2 (current)
This version publication date	02 July 2021
First version publication date	15 May 2021
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	NN9536-4374

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03552757
WHO universal trial number (UTN)	U1111-1200-8148
Other trial identifiers	JapicCTI: 183992

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsværd, Denmark, 2880
Public contact	Clinical Transparency Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Transparency Anchor and Disclosure (1452), 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	28 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 March 2020
Global end of trial reached?	Yes
Global end of trial date	01 May 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the effect of semaglutide subcutaneous (s.c.; under the skin) 2.4 milligram (mg) once-weekly versus semaglutide placebo I/II as an adjunct to a reduced-calorie diet and increased physical activity in subjects with overweight or obesity and type 2 diabetes (T2D) on body weight.

Protection of trial subjects:

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

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	04 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Arab Emirates: 38
Country: Number of subjects enrolled	Argentina: 62
Country: Number of subjects enrolled	Canada: 55
Country: Number of subjects enrolled	Germany: 70
Country: Number of subjects enrolled	Spain: 56
Country: Number of subjects enrolled	United Kingdom: 86
Country: Number of subjects enrolled	Greece: 47
Country: Number of subjects enrolled	India: 164
Country: Number of subjects enrolled	Japan: 125
Country: Number of subjects enrolled	Russian Federation: 96
Country: Number of subjects enrolled	United States: 361
Country: Number of subjects enrolled	South Africa: 50
Worldwide total number of subjects	1210
EEA total number of subjects	173

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)	953
From 65 to 84 years	257
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 149 sites in 12 countries as follows: Argentina (5 sites), Canada (10 sites), Germany (9 sites), Greece (6 sites), India (18 sites), Japan (12 sites), Russian Federation (9 sites), South Africa (6 sites), Spain (8 sites), United Arab Emirates (5 sites), United Kingdom (10 sites) and United States (51 sites).

Pre-assignment

Screening details:

Subjects were randomised in 1:1:1 ratio to receive either 'semaglutide 2.4 milligram (mg) and placebo II (placebo matched to semaglutide 1.0 mg) once weekly', 'semaglutide 1.0 mg and placebo I (placebo matched to semaglutide 2.4 mg) once weekly' or 'placebo I and placebo II once weekly'.

Period 1

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

Blinding implementation details:

Semaglutide and placebo were identical in appearance and were packed and labelled to fulfil the requirements for double-blind procedures.

Arms

Are arms mutually exclusive?	Yes
Arm title	Semaglutide 1.0 mg

Arm description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8 and 1.0 mg from week 9-68. Subjects also received once-weekly placebo I (placebo matched to semaglutide 2.4 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

Arm type	Active comparator
Investigational medicinal product name	Semaglutide B 1.34 mg/mL PDS290
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dosing was done once weekly with dose escalation every fourth week until semaglutide 1.0 mg was reached. Semaglutide was administered using a PDS290 pre-filled pen-injector containing semaglutide 1.34 mg/mL. Injection was done once weekly at the same day of the week (to the extent possible). Injections were administered in the thigh, abdomen or upper arm, and at any time of the day irrespective of meals.

Arm title	Semaglutide 2.4 mg

Arm description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8, 1.0 mg from week 9-12, 1.7 mg from week 13-16 and 2.4 mg from week 17-68. Subjects also received once-weekly placebo II (placebo matched to semaglutide 1.0 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

Arm type	Experimental

Investigational medicinal product name	Semaglutide B 1.0 mg/mL PDS290
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Semaglutide 1.0 mg/mL was only dispensed at the first dispensing visit to cover the 0.25 and 0.5 mg dose escalation purposes. Semaglutide was administered using a PDS290 pre-filled pen-injector containing semaglutide 1.0 mg/mL. Injection was done once weekly at the same day of the week (to the extent possible). Injections were administered in the thigh, abdomen or upper arm, and at any time of the day irrespective of meals.

Investigational medicinal product name	Semaglutide B 3.0 mg/mL PDS290
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dosing was done once weekly with dose escalation every fourth week until semaglutide 2.4 mg was reached. Semaglutide was administered using a PDS290 pre-filled pen-injector containing semaglutide 3.0 mg/mL. Injection was done once weekly at the same day of the week (to the extent possible). Injections were administered in the thigh, abdomen or upper arm, and at any time of the day irrespective of meals.

Arm title	Placebo

Arm description:

Subjects received once-weekly s.c placebo injections (both placebo I (placebo matched to semaglutide 1.0 mg) and placebo II (placebo matched to semaglutide 2.4 mg) for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

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

Dosage and administration details:

Placebo I (placebo matched to semaglutide 2.4 mg) was administered using a PDS290 pre-filled pen-injector by subjects in both ‘semaglutide 1.0 mg’ and ‘placebo’ groups. Injection was done once weekly at the same day of the week (to the extent possible). Injections were administered in the thigh, abdomen or upper arm, and at any time of the day irrespective of meals.

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

Dosage and administration details:

Placebo II (placebo matched to semaglutide 1.0 mg) was administered using a PDS290 pre-filled pen-injector by subjects in both ‘semaglutide 2.4 mg’ and ‘placebo’ groups. Injection was done once weekly at the same day of the week (to the extent possible). Injections were administered in the thigh, abdomen or upper arm, and at any time of the day irrespective of meals.

Number of subjects in period 1	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo
Started	403	404	403
Exposed	402	403	402
Full analysis set (FAS)	403	404	403
Safety analysis set (SAS)	402	403	402
Completed	390	391	383
Not completed	13	13	20
Adverse event, serious fatal	1	1	1
Consent withdrawn by subject	10	5	12
Lost to follow-up	2	7	7

Baseline characteristics

Reporting groups	
Reporting group title	Semaglutide 1.0 mg
Reporting group description:	
Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8 and 1.0 mg from week 9-68. Subjects also received once-weekly placebo I (placebo matched to semaglutide 2.4 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.	
Reporting group title	Semaglutide 2.4 mg
Reporting group description:	
Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8, 1.0 mg from week 9-12, 1.7 mg from week 13-16 and 2.4 mg from week 17-68. Subjects also received once-weekly placebo II (placebo matched to semaglutide 1.0 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.	
Reporting group title	Placebo
Reporting group description:	
Subjects received once-weekly s.c placebo injections (both placebo I (placebo matched to semaglutide 1.0 mg) and placebo II (placebo matched to semaglutide 2.4 mg) for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.	

Reporting group values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo
Number of subjects	403	404	403
Age Categorical Units: Subjects			
Adults (18-64 years)	320	316	317
From 65-84 years	83	88	86
Age Continuous Units: years			
arithmetic mean	56	55	55
standard deviation	± 10	± 11	± 11
Gender Categorical Units: Subjects			
Female	203	223	190
Male	200	181	213

Reporting group values	Total		
Number of subjects	1210		
Age Categorical Units: Subjects			
Adults (18-64 years)	953		
From 65-84 years	257		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical Units: Subjects			
Female	616		
Male	594		

End points

End points reporting groups

Reporting group title	Semaglutide 1.0 mg

Reporting group description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8 and 1.0 mg from week 9-68. Subjects also received once-weekly placebo I (placebo matched to semaglutide 2.4 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

Reporting group title	Semaglutide 2.4 mg

Reporting group description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8, 1.0 mg from week 9-12, 1.7 mg from week 13-16 and 2.4 mg from week 17-68. Subjects also received once-weekly placebo II (placebo matched to semaglutide 1.0 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

Reporting group title	Placebo

Reporting group description:

Subjects received once-weekly s.c placebo injections (both placebo I (placebo matched to semaglutide 1.0 mg) and placebo II (placebo matched to semaglutide 2.4 mg) for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

Primary: Change in body weight (%) - semaglutide 2.4 mg versus placebo

End point title	Change in body weight (%) - semaglutide 2.4 mg versus placebo[1]

End point description:

Change in body weight (%) from baseline (week 0) to week 68 is presented. Results are based on the data from both in-trial and on-treatment observation periods. In-trial observation period: the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact (week 75). On-treatment observation period: the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 2-week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least two consecutive missed doses. Number of subjects analysed = full analysis set (FAS) which comprised all randomised subjects. n = number of subjects with available data.

End point type	Primary

End point timeframe:

From baseline (week 0) to week 68

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	404	403		
Units: Percentage point of body weight				
arithmetic mean (standard deviation)				
In-trial observation period (n=388 & 376)	-9.9 (± 8.0)	-3.3 (± 5.5)		
On-treatment observation period (n=351 & 340)	-10.7 (± 7.8)	-3.1 (± 5.2)		

Statistical analyses

Statistical analysis title	Semaglutide 2.4 mg versus Placebo

Statistical analysis description:

Results are based on the data from in-trial observation period. Week 68 responses were analysed using an analysis of covariance model (ANCOVA) with randomised treatment, stratification groups (oral anti-diabetic (OAD) treatment status and HbA1c category at screening) and the interaction between stratification groups as factors and baseline body weight as covariate.

Comparison groups	Semaglutide 2.4 mg v Placebo
Number of subjects included in analysis	807
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-6.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.28
upper limit	-5.15

Notes:

[2] - 'Number of subjects included in analysis' is being erroneously displayed as 807. It should be read as "number of subjects with an observation at week 68 = 764".

Statistical analysis title	Semaglutide 2.4 mg versus Placebo

Statistical analysis description:

Results are based on the data from on-treatment observation period. 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 (MMRM) with randomised treatment, stratification groups (OAD treatment status and HbA1c category at screening) and the interaction between stratification groups as factors and baseline body weight as covariate, all nested within visit.

Comparison groups	Semaglutide 2.4 mg v Placebo
Number of subjects included in analysis	807
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001
Method	MMRM
Parameter estimate	Treatment difference
Point estimate	-7.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.56
upper limit	-6.58

Notes:

[3] - 'Number of subjects included in analysis' is being erroneously displayed as 807. It should be read as "number of subjects with an observation at week 68 = 633".

Primary: Subjects who achieve body weight reduction ≥5% from baseline (week 0) (yes/no) - semaglutide 2.4 mg versus placebo

End point title	Subjects who achieve body weight reduction ≥5% from baseline (week 0) (yes/no) - semaglutide 2.4 mg versus placebo[4]

End point description:

Number of subjects who achieved weight reduction ≥5% of their baseline body weight (yes/no) at week 68 is presented. Results are based on the data from both in-trial and on-treatment observation periods. In-trial observation period: the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. On-treatment observation period: the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 2 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least two consecutive missed doses. Number of subjects analysed = FAS which comprised all randomised subjects. n = number of subjects with available data.

End point type	Primary

End point timeframe:

After 68 weeks

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	404	403		
Units: Subjects				
In-trial observation period (n=388 & 376): Yes	267	107		
In-trial observation period (n=388 & 376): No	121	269		
On-treatment observation period (n=351 & 340): Yes	257	94		
On-treatment observation period (n=351 & 340): No	94	246		

Statistical analyses

Statistical analysis title	Semaglutide 2.4 mg versus Placebo

Statistical analysis description:

Results are based on the data from in-trial observation period. Week 68 responses were analysed using a binary logistic regression model with randomised treatment, stratification groups (OAD treatment status and HbA1c category at screening) and the interaction between stratification groups as factors and baseline body weight as covariate.

Comparison groups	Semaglutide 2.4 mg v Placebo

Number of subjects included in analysis	807
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.58
upper limit	6.64

Notes:

[5] - 'Number of subjects included in analysis' is being erroneously displayed as 807. It should be read as "number of subjects with an observation at week 68 = 764".

Statistical analysis title	Semaglutide 2.4 mg versus Placebo

Statistical analysis description:

Results are based on the data from on-treatment observation period. All responses prior to first discontinuation of treatment (or initiation of other anti-obesity medication or bariatric surgery) were included in a MMRM with randomised treatment, stratification groups (OAD treatment status and HbA1c category at screening) and the interaction between stratification groups as factors and baseline body weight as covariate, all nested within visit.

Comparison groups	Semaglutide 2.4 mg v Placebo
Number of subjects included in analysis	807
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	8.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.31
upper limit	11.97

Notes:

[6] - 'Number of subjects included in analysis' is being erroneously displayed as 807. It should be read as "number of subjects with an observation at week 68 = 633".

Secondary: Change in body weight (%) - semaglutide 2.4 mg versus semaglutide 1.0 mg

End point title	Change in body weight (%) - semaglutide 2.4 mg versus semaglutide 1.0 mg[7]

End point description:

Change in body weight (%) from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	380	388		
Units: Percentage point of body weight				
arithmetic mean (standard deviation)	-7.2 (± 6.6)	-9.9 (± 8.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects who achieve (yes/no): Body weight reduction ≥10% from baseline (week 0)

End point title	Subjects who achieve (yes/no): Body weight reduction ≥10% from baseline (week 0)

End point description:

Number of subjects who achieved weight reduction ≥10% of their baseline body weight (yes/no) at week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

After 68 weeks

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	380	388	376	
Units: Subjects				
Yes	109	177	31	
No	271	211	345	

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects who achieve (yes/no): Body weight reduction ≥15% from baseline (week 0)

End point title	Subjects who achieve (yes/no): Body weight reduction ≥15% from baseline (week 0)

End point description:

Number of subjects who achieved weight reduction ≥15% of their baseline body weight (yes/no) at week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

After 68 weeks

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	380	388	376	
Units: Subjects				
Yes	52	100	12	
No	328	288	364	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in waist circumference (cm)

End point title	Change in waist circumference (cm)

End point description:

Change in waist circumference from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	380	387	375	
Units: Centimetre (cm)				
arithmetic mean (standard deviation)	-6.9 (± 6.8)	-9.7 (± 8.1)	-4.3 (± 6.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in HbA1c (%)

End point title	Change in HbA1c (%)

End point description:

Change in glycated haemoglobin (HbA1c (%)) from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	376	381	374	
Units: Percentage point of HbA1c				
arithmetic mean (standard deviation)	-1.5 (± 1.1)	-1.7 (± 1.2)	-0.3 (± 1.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in HbA1c (mmol/mol)

End point title	Change in HbA1c (mmol/mol)

End point description:

Change in HbA1c (mmol/mol) from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	376	381	374	
Units: millimoles per mole (mmol/mol)				
arithmetic mean (standard deviation)	-16.9 (± 12.3)	-18.7 (± 13.0)	-3.4 (± 14.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Systolic blood pressure (mmHg)

End point title	Change in Systolic blood pressure (mmHg)

End point description:

Change in systolic blood pressure from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	379	387	376	
Units: Millimetre of mercury (mmHg)				
arithmetic mean (standard deviation)	-3 (± 15)	-4 (± 14)	0 (± 15)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in diastolic blood pressure (mmHg)

End point title	Change in diastolic blood pressure (mmHg)

End point description:

Change in diastolic blood pressure from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	379	387	376	
Units: Millimetre of mercury (mmHg)				
arithmetic mean (standard deviation)	-1 (± 9)	-2 (± 9)	-1 (± 9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body weight (kg)

End point title	Change in body weight (kg)

End point description:

Change in body weight (kg) from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	380	388	376	
Units: Kilogram (kg)				
arithmetic mean (standard deviation)	-7.1 (± 6.7)	-9.9 (± 8.5)	-3.4 (± 6.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in BMI (kg/sqm)

End point title	Change in BMI (kg/sqm)

End point description:

Change in body mass index (BMI) from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	380	388	376	
Units: kilogram per square meter (kg/m^2)				
arithmetic mean (standard deviation)	-2.6 (± 2.4)	-3.6 (± 3.1)	-1.2 (± 2.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting plasma glucose (FPG) (mg/dL)

End point title	Change in fasting plasma glucose (FPG) (mg/dL)

End point description:

Change in fasting plasma glucose (FPG) from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	367	375	370	
Units: milligrams per deciliter (mg/dL)				
arithmetic mean (standard deviation)	-36.5 (± 45.1)	-37.9 (± 45.9)	-2.3 (± 53.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting serum insulin (mIU/L)

End point title	Change in fasting serum insulin (mIU/L)

End point description:

Change in fasting serum insulin from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	352	360	351	
Units: Picomoles per litre (pmol/L)				
arithmetic mean (standard deviation)	0.94 (± 59.8)	0.90 (± 65.4)	0.93 (± 53.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in total cholesterol (mg/dL)

End point title	Change in total cholesterol (mg/dL)

End point description:

Change in total cholesterol (measured in milligram per decilitre (mg/dL)) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	372	380	373	
Units: Ratio of total cholesterol				
geometric mean (geometric coefficient of variation)	0.97 (± 20.1)	0.99 (± 17.9)	1.00 (± 18.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in high density lipoprotein (HDL) cholesterol (mg/dL)

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

End point description:

Change in high density lipoprotein (HDL; measured in mg/dL) from baseline (week 0) to week 68 is

presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	372	375	369	
Units: Ratio of HDL cholesterol				
geometric mean (geometric coefficient of variation)	1.06 (± 16.0)	1.07 (± 15.7)	1.04 (± 15.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in low density lipoprotein (LDL) cholesterol (mg/dL)

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

End point description:

Change in low density lipoprotein (LDL; measured in mg/dL) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	372	380	373	
Units: Ratio of LDL cholesterol				
geometric mean (geometric coefficient of variation)	0.99 (± 37.5)	1.00 (± 30.9)	1.00 (± 28.9)	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Change in very low density lipoprotein (VLDL; measured in mg/dL) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	372	380	373	
Units: Ratio of VLDL cholesterol				
geometric mean (geometric coefficient of variation)	0.82 (± 42.1)	0.80 (± 42.0)	0.92 (± 40.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in free fatty acids (FFA)

End point title	Change in free fatty acids (FFA)

End point description:

Change in free fatty acids (measured in mg/dL) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	353	361	354	
Units: Ratio of free fatty acids				
geometric mean (geometric coefficient of variation)	0.85 (± 61.4)	0.84 (± 68.7)	1.01 (± 62.3)	

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 (measured in mg/dL) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	372	380	373	
Units: Ratio of triglycerides				
geometric mean (geometric coefficient of variation)	0.81 (± 44.5)	0.79 (± 43.8)	0.92 (± 44.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in high sensitivity C-Reactive Protein (hsCRP) (mg/L)

End point title	Change in high sensitivity C-Reactive Protein (hsCRP) (mg/L)

End point description:

Change in high sensitivity C-reactive protein (hsCRP; measured in milligram per ilitre (mg/L)) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	372	380	373	
Units: Ratio of hsCRP				
geometric mean (geometric coefficient of variation)	0.59 (± 115.7)	0.50 (± 125.7)	0.84 (± 90.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasminogen Activator Inhibitor-1 (PAI-1) Activity (AU/mL)

End point title	Plasminogen Activator Inhibitor-1 (PAI-1) Activity (AU/mL)

End point description:

Change in Plasminogen Activator Inhibitor-1 (PAI-1; measured in arbritary units per millilitre (AU/mL)) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	334	353	336	
Units: Ratio of PAI-1 activity				
geometric mean (geometric coefficient of variation)	1.21 (± 73.7)	1.06 (± 80.8)	1.42 (± 68.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Short Form 36 v2.0 acute (SF-36) (physical functioning score)

End point title	Change in Short Form 36 v2.0 acute (SF-36) (physical functioning score)

End point description:

SF-36 is a 36-item patient-reported survey of patient health that measures the subject's overall health-related quality of life (HRQoL). SF-36v2™ questionnaire measured 8 domains of functional health and well-being as well as 2 component summary scores (physical component summary and mental

component summary). This endpoint shows results for 'physical functioning domain'. The 0-100 scale scores from the SF-36 were converted to norm-based scores to enable a direct interpretation in relation to the distribution of the scores in the 2009 U.S. general population. In the metric of norm-based scores, 50 and 10 corresponds to the mean and standard deviation respectively. Change from week 0 in the domain scores were evaluated at week 68. A positive change score indicates an improvement since baseline. Results are based on the data from in-trial observation period. This endpoint was evaluated based on the FAS. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

Baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	370	376	365	
Units: Score on a scale				
arithmetic mean (standard deviation)	2.1 (± 6.8)	2.8 (± 7.7)	0.8 (± 7.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in SF-36 (all scores except physical functioning)

End point title	Change in SF-36 (all scores except physical functioning)

End point description:

SF-36 is a 36-item patient-reported survey of patient health that measures the subject's overall health-related quality of life (HRQoL). SF-36v2™ questionnaire measured 8 domains of functional health and well-being as well as 2 component summary scores (physical component summary & mental component summary). This endpoint shows results for all the domains, except physical functioning. The 0-100 scale scores from the SF-36 were converted to norm-based scores to enable a direct interpretation in relation to the distribution of the scores in the 2009 U.S. general population. In the metric of norm-based scores, 50 and 10 corresponds to the mean and standard deviation respectively. 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. Results are based on data from in-trial observation period. Analysis population=FAS. No. of subjects analysed=No. of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	370	376	365	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Role-Physical	0.6 (± 6.9)	0.8 (± 7.4)	0.0 (± 7.1)	
Bodily Pain	0.4 (± 8.3)	0.3 (± 9.0)	-0.4 (± 8.6)	
General Health	1.7 (± 7.2)	2.2 (± 7.3)	0.6 (± 7.5)	

Vitality	-0.1 (± 7.8)	0.8 (± 7.9)	-0.9 (± 7.9)	
Social Functioning	-0.3 (± 6.6)	0.2 (± 6.6)	-0.7 (± 7.4)	
Role-Emotional	-0.4 (± 7.3)	-0.4 (± 7.7)	-1.1 (± 7.8)	
Mental Health	-0.9 (± 7.5)	-0.4 (± 6.9)	-1.6 (± 7.5)	
Physical component summary	1.9 (± 6.4)	2.3 (± 7.2)	0.9 (± 6.6)	
Mental component summary	-1.4 (± 7.4)	-0.9 (± 6.9)	-1.8 (± 7.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in IWQOL-Lite for CT (physical function domain (5-items) score)

End point title	Change in IWQOL-Lite for CT (physical function domain (5-items) score)

End point description:

The Impact of Weight on Quality of Life Clinical Trials Version (IWQOL-Lite-CT) is designed to assess the impact of changes in weight on patients' quality of life within the context of clinical trials. IWQOL-Lite-CT is a 20-item questionnaire-based instrument used to assess the impact of body weight changes on subject's overall health-related quality of life (HRQoL). All IWQOL-Lite-CT composite scores range from 0 to 100, with higher scores reflecting better levels of functioning. This endpoint shows results for 'physical function domain'. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	369	376	365	
Units: Score on a scale				
arithmetic mean (standard deviation)	8.5 (± 18.8)	11.4 (± 20.8)	4.9 (± 20.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in IWQOL-Lite for CT (all scores except physical function)

End point title	Change in IWQOL-Lite for CT (all scores except physical function)

End point description:

The Impact of Weight on Quality of Life Clinical Trials Version (IWQOL-Lite-CT) is designed to assess the impact of changes in weight on patients' quality of life within the context of clinical trials. IWQOL-Lite-CT is a 20-item questionnaire-based instrument used to assess the impact of body weight changes on subject's overall health-related quality of life (HRQoL). All IWQOL-Lite-CT composite scores range from 0 to 100, with higher scores reflecting better levels of functioning. This endpoint shows results for

'physical and psychosocial domains, and for total'. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	369	376	365	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Physical	7.6 (± 18.0)	11.0 (± 19.6)	4.4 (± 19.1)	
Psychosocial	8.6 (± 15.7)	9.6 (± 16.7)	5.6 (± 16.5)	
Total	8.2 (± 14.8)	10.1 (± 15.9)	5.2 (± 15.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects who achieve (yes/no): Responder definition value for SF-36 physical functioning score

End point title	Subjects who achieve (yes/no): Responder definition value for SF-36 physical functioning score

End point description:

Number of subjects experiencing a meaningful within subject improvement in SF-36 Physical function after 68 weeks was determined by two thresholds. The default generic responder threshold of 4.3 is for general population. The threshold of 3.7 is for overweight/obese population in the study and calculated using patient global rating anchor questionnaires to reflect subjects' own perspective based on Food and Drug Administration (FDA) recommendations. In the reported data, number of subjects who have achieved an improvement in score >/= to threshold are inferred as "Yes" and who have not achieved an improvement in score >/= to threshold are inferred as "No". The endpoint was evaluated based on in-trial observation period which is the uninterrupted time interval from randomization (week 0) to last trial related subject-site contact. The endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

After 68 weeks

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	370	376	365	
Units: Subjects				
Yes (with threshold 4.3)	88	111	68	
No (with threshold 4.3)	282	265	297	
Yes (with threshold 3.7)	130	158	102	
No (with threshold 3.7)	240	218	263	

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects who achieve (yes/no): Responder definition value for IWQOL-Lite for CT physical function domain (5-items) score

End point title	Subjects who achieve (yes/no): Responder definition value for IWQOL-Lite for CT physical function domain (5-items) score

End point description:

Number of subjects experiencing a meaningful within subject improvement in IWQOL-Lite-CT physical function after 68 weeks was determined by two thresholds. The preliminary responder threshold 20 was based on earlier studies. The threshold of 14.6 is for the overweight/obese population in the study and calculated using patient global rating anchor questionnaires to reflect subjects' own perspective based on FDA recommendations. In the reported data, number of subjects who have achieved an improvement in score >/= to threshold are inferred as "Yes" and who have not achieved an improvement in score >/= to threshold are inferred as "No". The endpoint was evaluated based on in-trial observation period which was the uninterrupted time interval from randomization (week 0) to last trial related subject-site contact. The endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

After 68 weeks

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	369	376	365	
Units: Subjects				
number (not applicable)				
Yes (with threshold 20)	107	131	83	
No (with threshold 20)	262	245	282	
Yes (with threshold 14.6)	144	160	113	
No (with threshold 14.6)	225	216	252	

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects who achieve (yes/no): HbA1c <7.0% (53 mmol/mol)

End point title	Subjects who achieve (yes/no): HbA1c <7.0% (53 mmol/mol)

End point description:

Number of subjects who achieved HbA1c <7% (yes/no) at week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

After 68 weeks

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	376	381	374	
Units: Subjects				
number (not applicable)				
Yes	272	299	99	
No	104	82	275	

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects who achieve (yes/no): HbA1c ≤6.5% (48 mmol/mol)

End point title	Subjects who achieve (yes/no): HbA1c ≤6.5% (48 mmol/mol)

End point description:

Number of subjects who achieved HbA1c ≤6.5% (yes/no) at week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

After 68 weeks

End point values	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	376	381	374	
Units: Subjects				
Yes	226	257	58	
No	150	124	316	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment-emergent adverse events (TEAEs) - semaglutide 2.4 mg versus placebo

End point title	Number of treatment-emergent adverse events (TEAEs) - semaglutide 2.4 mg versus placebo[8]

End point description:

Adverse events (AEs) with onset during the on-treatment observation period were defined as treatment-emergent AEs (TEAEs). On-treatment observation period: the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 7 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least seven consecutive missed doses. This endpoint was evaluated based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 75

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	402		
Units: Events	2197	1388		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of serious adverse events (SAEs) - semaglutide 2.4 mg versus placebo

End point title	Number of serious adverse events (SAEs) - semaglutide 2.4 mg versus placebo[9]

End point description:

Serious adverse event (SAE) results are based on the on-treatment observation period, which was defined as the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 7 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least seven consecutive missed doses. This endpoint was evaluated based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 75

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	402		
Units: Events	71	53		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment emergent severe or blood glucose confirmed symptomatic hypoglycaemia episodes - semaglutide 2.4 mg versus placebo

End point title	Number of treatment emergent severe or blood glucose confirmed symptomatic hypoglycaemia episodes - semaglutide 2.4 mg versus placebo[10]

End point description:

Hypoglycaemic episodes with onset during the on-treatment observation period were considered treatment-emergent. On-treatment observation period was defined as the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 7 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least 7 consecutive missed doses. Severe hypoglycaemia: An episode requiring assistance of another person to actively administer carbohydrate, glucagon or take other corrective actions. plasma glucose (PG) concentrations may not be available during an event, but neurological recovery following the return of PG to normal is considered sufficient evidence that the event was induced by a low PG concentration. Blood glucose (BG) confirmed symptomatic hypoglycaemia: An episode that is BG confirmed by PG value <3.1 mmol/L (56 mg/dL) with symptoms consistent with hypoglycaemia.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 75

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	402		
Units: Episodes	51	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in pulse (bpm) - semaglutide 2.4 mg versus placebo

End point title	Change in pulse (bpm) - semaglutide 2.4 mg versus placebo[11]

End point description:

Change in pulse from baseline (week 0) to week 68 is presented. Results are based on the data from on-treatment observation period, which was defined as the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 2 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least two consecutive missed doses. This endpoint was evaluated based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	351	340		
Units: Beats/minute				
arithmetic mean (standard deviation)	2 (± 9)	0 (± 9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in amylase (U/L) - semaglutide 2.4 mg versus placebo

End point title	Change in amylase (U/L) - semaglutide 2.4 mg versus

End point description:

Change in amylase (units/litre) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from on-treatment observation period, which was defined as the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 2 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least two consecutive missed doses. This endpoint was evaluated based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	350	338		
Units: Ratio of amylase				
geometric mean (geometric coefficient of variation)	1.24 (± 28.3)	1.06 (± 25.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in lipase (U/L) - semaglutide 2.4 mg versus placebo

End point title	Change in lipase (U/L) - semaglutide 2.4 mg versus placebo[13]

End point description:

Change in lipase (units/litre) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from on-treatment observation period, which was defined as the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 2 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least two consecutive missed doses. This endpoint was evaluated based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	350	338		
Units: Ratio of lipase				
geometric mean (geometric coefficient of variation)	1.41 (± 57.2)	0.99 (± 51.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in calcitonin - semaglutide 2.4 mg versus placebo

End point title	Change in calcitonin - semaglutide 2.4 mg versus placebo[14]

End point description:

Change in calcitonin (nanogram/litre) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from on-treatment observation period, which was defined as the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 2 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least two consecutive missed doses. This endpoint was

evaluated based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 68

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

End point values	Semaglutide 2.4 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	339		
Units: Ratio of calcitonin				
geometric mean (geometric coefficient of variation)	0.94 (± 60.3)	0.96 (± 38.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Week 0 to week 75. Results are based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment.

Adverse event reporting additional description:

All presented AEs are treatment-emergent (i.e., TEAEs).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	Semaglutide 1.0 mg

Reporting group description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8 and 1.0 mg from week 9-68. Subjects also received once-weekly placebo I (placebo matched to semaglutide 2.4 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

Reporting group title	Semaglutide 2.4 mg

Reporting group description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8, 1.0 mg from week 9-12, 1.7 mg from week 13-16 and 2.4 mg from week 17-68. Subjects also received once-weekly placebo II (placebo matched to semaglutide 1.0 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

Reporting group title	Placebo

Reporting group description:

Subjects received once-weekly s.c placebo injections (both placebo I (placebo matched to semaglutide 1.0 mg) and placebo II (placebo matched to semaglutide 2.4 mg) for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

Serious adverse events	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 402 (7.71%)	40 / 403 (9.93%)	37 / 402 (9.20%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Adenocarcinoma of colon			

subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Gastric cancer			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer stage IV			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal lymphoma			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Gastrointestinal stromal tumour			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Hepatocellular carcinoma			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Keratinising squamous cell carcinoma of nasopharynx			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myeloid leukaemia			

subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Neuroendocrine tumour			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Prostate cancer			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	2 / 402 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cancer			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Vascular disorders			
Aortic rupture			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Hypertension			
subjects affected / exposed	0 / 402 (0.00%)	2 / 403 (0.50%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive urgency			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Surgical and medical procedures			

Cardiac pacemaker replacement			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Sperm aspiration			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stent placement			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroidectomy			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
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 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Immunisation reaction			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Reproductive system and breast disorders			
Uterine polyp			

subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 402 (0.25%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Cervical vertebral fracture			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Fall			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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

Hip fracture			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Humerus fracture			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Joint dislocation			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament rupture			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Lisfranc fracture			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 402 (0.00%)	2 / 403 (0.50%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Skin laceration			

subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Spinal compression fracture			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Subdural haematoma			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Traumatic haemothorax			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Upper limb fracture			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 402 (0.50%)	1 / 403 (0.25%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			

subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Atrial fibrillation			
subjects affected / exposed	2 / 402 (0.50%)	2 / 403 (0.50%)	2 / 402 (0.50%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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 acute			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
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 failure congestive			
subjects affected / exposed	1 / 402 (0.25%)	1 / 403 (0.25%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 402 (0.25%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral artery thrombosis			

subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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 infarction			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Hyperaesthesia			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemic encephalopathy			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Ischaemic stroke			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal epidural haematoma			

subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Syncope			
subjects affected / exposed	1 / 402 (0.25%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 402 (0.75%)	0 / 403 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Diverticular perforation			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			

subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Gastric ulcer			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Gastritis			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	2 / 402 (0.50%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Vomiting			

subjects affected / exposed	0 / 402 (0.00%)	2 / 403 (0.50%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 402 (0.25%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-alcoholic steatohepatitis			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 402 (0.50%)	2 / 403 (0.50%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder outlet obstruction			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Stag horn calculus			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Ureterolithiasis			

subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	2 / 402 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Neuropathic arthropathy			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Pain in extremity			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Spondylolisthesis			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Trigger finger			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchitis			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 402 (0.50%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic abscess			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Diverticulitis			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	3 / 402 (0.75%)	3 / 403 (0.74%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	1 / 3	2 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Joint abscess			

subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
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	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 402 (0.25%)	1 / 403 (0.25%)	2 / 402 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Postoperative wound infection			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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 tract infection			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Sepsis			

subjects affected / exposed	3 / 402 (0.75%)	0 / 403 (0.00%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Viral infection			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection staphylococcal			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Decreased appetite			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Dehydration			
subjects affected / exposed	2 / 402 (0.50%)	1 / 403 (0.25%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			

subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Hyponatraemia			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (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
Ketoacidosis			
subjects affected / exposed	0 / 402 (0.00%)	1 / 403 (0.25%)	0 / 402 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lactic acidosis			
subjects affected / exposed	1 / 402 (0.25%)	0 / 403 (0.00%)	0 / 402 (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
Obesity			
subjects affected / exposed	0 / 402 (0.00%)	0 / 403 (0.00%)	1 / 402 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Semaglutide 1.0 mg	Semaglutide 2.4 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	261 / 402 (64.93%)	284 / 403 (70.47%)	190 / 402 (47.26%)
Nervous system disorders			
Headache			
subjects affected / exposed	33 / 402 (8.21%)	31 / 403 (7.69%)	20 / 402 (4.98%)
occurrences (all)	48	40	27
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	19 / 402 (4.73%)	28 / 403 (6.95%)	4 / 402 (1.00%)
occurrences (all)	26	29	4
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	9 / 402 (2.24%)	24 / 403 (5.96%)	11 / 402 (2.74%)
occurrences (all)	12	30	13
Constipation			
subjects affected / exposed	51 / 402 (12.69%)	70 / 403 (17.37%)	22 / 402 (5.47%)
occurrences (all)	70	82	26
Diarrhoea			
subjects affected / exposed	88 / 402 (21.89%)	86 / 403 (21.34%)	48 / 402 (11.94%)
occurrences (all)	157	141	66
Dyspepsia			
subjects affected / exposed	27 / 402 (6.72%)	25 / 403 (6.20%)	5 / 402 (1.24%)
occurrences (all)	27	30	5
Flatulence			
subjects affected / exposed	21 / 402 (5.22%)	16 / 403 (3.97%)	7 / 402 (1.74%)
occurrences (all)	25	21	9
Nausea			
subjects affected / exposed	128 / 402 (31.84%)	135 / 403 (33.50%)	37 / 402 (9.20%)
occurrences (all)	196	248	45
Vomiting			
subjects affected / exposed	54 / 402 (13.43%)	86 / 403 (21.34%)	11 / 402 (2.74%)
occurrences (all)	93	186	12
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	24 / 402 (5.97%)	23 / 403 (5.71%)	20 / 402 (4.98%)
occurrences (all)	27	29	20
Back pain			
subjects affected / exposed	28 / 402 (6.97%)	27 / 403 (6.70%)	14 / 402 (3.48%)
occurrences (all)	30	30	15
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	21 / 402 (5.22%)	11 / 403 (2.73%)	12 / 402 (2.99%)
occurrences (all)	25	12	14
Nasopharyngitis			
subjects affected / exposed	47 / 402 (11.69%)	68 / 403 (16.87%)	59 / 402 (14.68%)
occurrences (all)	69	115	92
Upper respiratory tract infection			
subjects affected / exposed	37 / 402 (9.20%)	42 / 403 (10.42%)	38 / 402 (9.45%)
occurrences (all)	54	48	50
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	29 / 402 (7.21%)	38 / 403 (9.43%)	15 / 402 (3.73%)
occurrences (all)	33	41	17

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 July 2018	Inclusion of genetic biosamples for future analysis for applicable countries. Removal of discontinuation criteria for trial products for subjects enrolled in violation with exclusion/inclusion criteria. Removal of classification of risks, inclusion of a reference to the investigator's brochure. Removal of persistent criteria from exploratory endpoint regarding micro/macro albuminuria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33667417

http://www.ncbi.nlm.nih.gov/pubmed/32441473

http://www.ncbi.nlm.nih.gov/pubmed/30122305