Clinical trial results:
Investigation of once-weekly semaglutide s.c. dose-response in patients with type 2 diabetes and overweight - a participant- and investigator-blinded and sponsor open-label study.

Summary

EudraCT number	2022-000882-41
Trial protocol	HU GR PL
Global end of trial date	13 December 2023

Results information

Result version number	v1 (current)
This version publication date	27 December 2024
First version publication date	27 December 2024

Trial information

Trial identification

Sponsor protocol code	NN9535-4984

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05486065
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterise the dose-response curve of once weekly semaglutide s.c. for change in HbA1c from baseline to week 40 in patients with type 2 diabetes (T2D) and body mass index (BMI) ≥ 27 kg/m2 as an add-on to a stable dose of metformin.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 August 2022
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	Greece: 54
Country: Number of subjects enrolled	Hungary: 35
Country: Number of subjects enrolled	Poland: 33
Country: Number of subjects enrolled	United States: 123
Worldwide total number of subjects	245
EEA total number of subjects	122

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)	245
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 82 active sites in 4 countries, of which 75 sites enrolled subjects.

Pre-assignment

Screening details:

Subjects were randomized at a ratio of 3:1:3:1:3:1 to receive semaglutide (2 mg, 8 mg, 16 mg) or matching placebo.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Semaglutide 2.0 mg

Arm description:

Subjects received once-weekly subcutaneous (s.c.) injections of semaglutide (in a dose-escalation manner once in every 4 weeks [0-4 weeks: 0.29 mg; 5-8 weeks: 0.58 mg; 9-12 weeks: 1.06 mg], followed by the maintenance dose of 2 mg) till 40 weeks.

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

Dosage and administration details:

Subjects received once weekly s.c. injections of semaglutide for 40 weeks.

Arm title	Semaglutide 8.0 mg

Arm description:

Subjects received once-weekly s.c. injections of semaglutide (in a dose-escalation manner once in every 4 weeks [0-4 weeks: 0.29 mg; 5-8 weeks: 0.58 mg; 9-12 weeks: 1.06 mg; 13-16 weeks: 2.02 mg; 17-20 weeks: 4.03 mg], followed by the maintenance dose of 8 mg) till 40 weeks.

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

Dosage and administration details:

Subjects received once weekly s.c. injections of semaglutide for 40 weeks.

Arm title	Semaglutide 16.0 mg

Arm description:

Subjects received once-weekly s.c. injections of semaglutide (in a dose-escalation manner once in every 4 weeks [0-4 weeks: 0.29 mg; 5-8 weeks: 0.58 mg; 9-12 weeks: 1.06 mg; 13-16 weeks: 2.02 mg; 17-20 weeks: 4.03 mg; 21-24 weeks: 8.06 mg], followed by the maintenance dose of 16 mg) till 40 weeks.

Arm type	Experimental

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

Dosage and administration details:

Subjects received once weekly s.c. injections of semaglutide for 40 weeks.

Arm title	Placebo

Arm description:

Subjects received once-weekly s.c. injection of placebo matched to semaglutide for 40 weeks.

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

Dosage and administration details:

Subjects received once weekly s.c. injections of placebo matched to semaglutide for 40 weeks.

Number of subjects in period 1	Semaglutide 2.0 mg	Semaglutide 8.0 mg	Semaglutide 16.0 mg
Started	61	62	62
Full analysis set	61	62	62
Safety analysis set	60	60	62
Completed	56	54	55
Not completed	5	8	7
Consent withdrawn by subject	1	5	4
Physician decision	-	1	1
Failure to meet randomization criteria	-	-	-
Lost to follow-up	4	2	2

Number of subjects in period 1	Placebo
Started	60
Full analysis set	60
Safety analysis set	59
Completed	54
Not completed	6
Consent withdrawn by subject	3
Physician decision	-
Failure to meet randomization criteria	1
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Semaglutide 2.0 mg
Reporting group description:	
Subjects received once-weekly subcutaneous (s.c.) injections of semaglutide (in a dose-escalation manner once in every 4 weeks [0-4 weeks: 0.29 mg; 5-8 weeks: 0.58 mg; 9-12 weeks: 1.06 mg], followed by the maintenance dose of 2 mg) till 40 weeks.	
Reporting group title	Semaglutide 8.0 mg
Reporting group description:	
Subjects received once-weekly s.c. injections of semaglutide (in a dose-escalation manner once in every 4 weeks [0-4 weeks: 0.29 mg; 5-8 weeks: 0.58 mg; 9-12 weeks: 1.06 mg; 13-16 weeks: 2.02 mg; 17-20 weeks: 4.03 mg], followed by the maintenance dose of 8 mg) till 40 weeks.	
Reporting group title	Semaglutide 16.0 mg
Reporting group description:	
Subjects received once-weekly s.c. injections of semaglutide (in a dose-escalation manner once in every 4 weeks [0-4 weeks: 0.29 mg; 5-8 weeks: 0.58 mg; 9-12 weeks: 1.06 mg; 13-16 weeks: 2.02 mg; 17-20 weeks: 4.03 mg; 21-24 weeks: 8.06 mg], followed by the maintenance dose of 16 mg) till 40 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received once-weekly s.c. injection of placebo matched to semaglutide for 40 weeks.	

Reporting group values	Semaglutide 2.0 mg	Semaglutide 8.0 mg	Semaglutide 16.0 mg
Number of subjects	61	62	62
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	52.3	53.7	52.9
standard deviation	± 7.6	± 7.5	± 8.6
Sex: Female, Male Units: Subjects			
Female	27	33	25
Male	34	29	37
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	11	4
White	54	49	56
More than one race	0	0	2
Unknown or Not Reported	0	1	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	9	8	9
Not Hispanic or Latino	52	54	53
Unknown or Not Reported	0	0	0

Reporting group values	Placebo	Total	
Number of subjects	60	245	
Age categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	52.1		
standard deviation	± 9.5	-	
Sex: Female, Male Units: Subjects			
Female	35	120	
Male	25	125	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	3	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	4	25	
White	55	214	
More than one race	0	2	
Unknown or Not Reported	0	1	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	13	39	
Not Hispanic or Latino	47	206	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Semaglutide 2.0 mg
Reporting group description:	
Subjects received once-weekly subcutaneous (s.c.) injections of semaglutide (in a dose-escalation manner once in every 4 weeks [0-4 weeks: 0.29 mg; 5-8 weeks: 0.58 mg; 9-12 weeks: 1.06 mg], followed by the maintenance dose of 2 mg) till 40 weeks.	
Reporting group title	Semaglutide 8.0 mg
Reporting group description:	
Subjects received once-weekly s.c. injections of semaglutide (in a dose-escalation manner once in every 4 weeks [0-4 weeks: 0.29 mg; 5-8 weeks: 0.58 mg; 9-12 weeks: 1.06 mg; 13-16 weeks: 2.02 mg; 17-20 weeks: 4.03 mg], followed by the maintenance dose of 8 mg) till 40 weeks.	
Reporting group title	Semaglutide 16.0 mg
Reporting group description:	
Subjects received once-weekly s.c. injections of semaglutide (in a dose-escalation manner once in every 4 weeks [0-4 weeks: 0.29 mg; 5-8 weeks: 0.58 mg; 9-12 weeks: 1.06 mg; 13-16 weeks: 2.02 mg; 17-20 weeks: 4.03 mg; 21-24 weeks: 8.06 mg], followed by the maintenance dose of 16 mg) till 40 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received once-weekly s.c. injection of placebo matched to semaglutide for 40 weeks.	

Primary: Change in glycated haemoglobin (HbA1c)

End point title	Change in glycated haemoglobin (HbA1c)
End point description:	
Change in HbA1c from baseline (week 0) to end of treatment (week 40) is presented. Full analysis set included all randomised subjects. Here, "Overall Number of Subjects Analyzed" signifies those subjects who were evaluable for this outcome measure.	
End point type	Primary
End point timeframe:	
Baseline (week 0) and End of treatment (week 40)	

End point values	Semaglutide 2.0 mg	Semaglutide 8.0 mg	Semaglutide 16.0 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	57	56	54
Units: Percentage-point of HbA1c				
arithmetic mean (standard deviation)	-1.9 (± 1.1)	-1.8 (± 1.5)	-2.1 (± 1.5)	-1.1 (± 1.3)

Statistical analyses

Statistical analysis title	Semaglutide 2.0 mg - Placebo
Comparison groups	Semaglutide 2.0 mg v Placebo

Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.25
upper limit	-0.39

Statistical analysis title	Semaglutide 16.0 mg - Semaglutide 2.0 mg
Comparison groups	Semaglutide 2.0 mg v Semaglutide 16.0 mg
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2445
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.67
upper limit	0.17

Statistical analysis title	Semaglutide 8.0 mg vs Semaglutide 2.0 mg

Statistical analysis description:

The change in HbA1c from baseline was analysed using an ANCOVA (Analysis of Covariance) with randomised treatment and stratification factor, sex as fixed effect and baseline HbA1c as a covariate. Missing values were imputed using Jump to reference method.

Comparison groups	Semaglutide 2.0 mg v Semaglutide 8.0 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8305
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	0.47

Statistical analysis title	Semaglutide 16.0 mg - Semaglutide 8.0 mg
Comparison groups	Semaglutide 8.0 mg v Semaglutide 16.0 mg
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1678
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	0.13

Statistical analysis title	Semaglutide 8.0 mg vs Placebo
Comparison groups	Semaglutide 8.0 mg v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0003
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.19
upper limit	-0.35

Statistical analysis title	Sema 16.0 mg vs Placebo
Comparison groups	Semaglutide 16.0 mg v Placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-1.07

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.64

Secondary: Change in body weight

End point title	Change in body weight

End point description:

Change in body weight from baseline (week 0) to end of treatment (week 40) is presented. Full analysis set included all randomised subjects. Here, "Overall Number of Subjects Analyzed" signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline (week 0) and End of treatment (week 40)

End point values	Semaglutide 2.0 mg	Semaglutide 8.0 mg	Semaglutide 16.0 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	56	55	53
Units: Kilogram (kg)				
arithmetic mean (standard deviation)	-8.9 (± 8.5)	-10.1 (± 7.4)	-13.1 (± 8.4)	-2.3 (± 4.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment-emergent severe hypoglycaemic episodes

End point title	Number of treatment-emergent severe hypoglycaemic episodes

End point description:

Number of treatment-emergent severe Hypoglycaemic episodes are presented. Severe hypoglycaemic episodes (level 3) were defined as episodes that were associated with severe cognitive impairment requiring external assistance for recovery. On treatment observation period data are presented. On-treatment oberservation period is defined as time points from first drug date until the first date of end of data point sets (DPS1) or last administration of randomised treatment +63 days. DPS1 in trial is defined as all observed data points from randomisation until the first date of end of study visit or date of death or date of withdrawal of informed consent or date of last contact as defined by investigator for subjects that are lost to follow up. Safety analysis set included all subjects who are exposed to randomised treatment.

End point type	Secondary

End point timeframe:

From baseline (week 0) up to end of study (week 49)

End point values	Semaglutide 2.0 mg	Semaglutide 8.0 mg	Semaglutide 16.0 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	60	62	59
Units: Episodes				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment-emergent adverse events (TEAEs)

End point title	Number of treatment-emergent adverse events (TEAEs)

End point description:

AE is any untoward medical occurrence in a clinical study subjects that is temporally associated with use of investigational medicinal products (IMP), whether or not considered related to IMP. AE can therefore be any unfavourable & unintended sign, symptom or disease (new/exacerbated) temporally associated with use of IMP. TEAE was defined as event that had onset date (or increase in severity) during on-treatment observation period. On-treatment observation period is defined as time points from first drug date until first date of end of data point sets (DPS1) or last administration of randomised treatment +63 days. DPS1 in trial is defined as all observed data points from randomisation until first date of end of study visit or date of death or date of withdrawal of informed consent or contact as defined by investigator for subjects that are lost to follow up. Safety analysis set included all subjects who are exposed to randomised treatment.

End point type	Secondary

End point timeframe:

From baseline (week 0) up to end of study (week 49)

End point values	Semaglutide 2.0 mg	Semaglutide 8.0 mg	Semaglutide 16.0 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	60	62	59
Units: Events				
number (not applicable)	43	54	55	37

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline (week 0) up to end of study (week 49)

Adverse event reporting additional description:

AEs presented here are TEAEs. TEAE was defined as event that had onset date (or increase in severity) during on-treatment observation period. Safety analysis set included all subjects who are exposed to randomised treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26

Reporting groups

Reporting group title	Sema 16.0 mg

Reporting group description:

Subjects received once-weekly s.c. injections of semaglutide (in a dose-escalation manner once in every 4 weeks [0-4 weeks: 0.29 mg; 5-8 weeks: 0.58 mg; 9-12 weeks: 1.06 mg; 13-16 weeks: 2.02 mg; 17-20 weeks: 4.03 mg; 21-24 weeks: 8.06 mg], followed by the maintenance dose of 16 mg) till 40 weeks.

Reporting group title	Sema 2.0 mg

Reporting group description:

Subjects received once-weekly subcutaneous (s.c.) injections of semaglutide (in a dose-escalation manner once in every 4 weeks [0-4 weeks: 0.29 mg; 5-8 weeks: 0.58 mg; 9-12 weeks: 1.06 mg], followed by the maintenance dose of 2 mg) till 40 weeks.

Reporting group title	Placebo

Reporting group description:

Subjects received once-weekly s.c. injection of placebo matched to semaglutide for 40 weeks.

Reporting group title	Sema 8.0 mg

Reporting group description:

Subjects received once-weekly s.c. injections of semaglutide (in a dose-escalation manner once in every 4 weeks [0-4 weeks: 0.29 mg; 5-8 weeks: 0.58 mg; 9-12 weeks: 1.06 mg; 13-16 weeks: 2.02 mg; 17-20 weeks: 4.03 mg], followed by the maintenance dose of 8 mg) till 40 weeks.

Serious adverse events	Sema 16.0 mg	Sema 2.0 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 62 (1.61%)	4 / 60 (6.67%)	2 / 59 (3.39%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 62 (0.00%)	1 / 60 (1.67%)	0 / 59 (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			

Incisional hernia			
subjects affected / exposed	0 / 62 (0.00%)	1 / 60 (1.67%)	0 / 59 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 62 (0.00%)	1 / 60 (1.67%)	0 / 59 (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			
Cardiac failure chronic			
subjects affected / exposed	0 / 62 (0.00%)	0 / 60 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 62 (0.00%)	0 / 60 (0.00%)	1 / 59 (1.69%)
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 disorders			
Inguinal hernia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 60 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 62 (0.00%)	0 / 60 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 62 (1.61%)	0 / 60 (0.00%)	0 / 59 (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
Infections and infestations			
Vestibular neuronitis			

subjects affected / exposed	0 / 62 (0.00%)	1 / 60 (1.67%)	0 / 59 (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

Serious adverse events	Sema 8.0 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 60 (3.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Incisional hernia			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure chronic			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Inguinal hernia			

subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Vestibular neuronitis			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Sema 16.0 mg	Sema 2.0 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 62 (80.65%)	30 / 60 (50.00%)	29 / 59 (49.15%)
Investigations			
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 62 (0.00%)	0 / 60 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	3
Lipase increased			
subjects affected / exposed	3 / 62 (4.84%)	3 / 60 (5.00%)	1 / 59 (1.69%)
occurrences (all)	3	3	2
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 62 (0.00%)	1 / 60 (1.67%)	2 / 59 (3.39%)
occurrences (all)	0	1	2
Nervous system disorders			

Dizziness			
subjects affected / exposed	3 / 62 (4.84%)	2 / 60 (3.33%)	4 / 59 (6.78%)
occurrences (all)	3	2	5
Headache			
subjects affected / exposed	7 / 62 (11.29%)	2 / 60 (3.33%)	8 / 59 (13.56%)
occurrences (all)	9	6	23
Hyperaesthesia			
subjects affected / exposed	5 / 62 (8.06%)	0 / 60 (0.00%)	0 / 59 (0.00%)
occurrences (all)	6	0	0
Paraesthesia			
subjects affected / exposed	5 / 62 (8.06%)	0 / 60 (0.00%)	0 / 59 (0.00%)
occurrences (all)	5	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 62 (9.68%)	2 / 60 (3.33%)	2 / 59 (3.39%)
occurrences (all)	7	3	2
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	3 / 62 (4.84%)	2 / 60 (3.33%)	1 / 59 (1.69%)
occurrences (all)	3	3	1
Abdominal pain upper			
subjects affected / exposed	2 / 62 (3.23%)	5 / 60 (8.33%)	3 / 59 (5.08%)
occurrences (all)	3	5	4
Abdominal pain			
subjects affected / exposed	4 / 62 (6.45%)	3 / 60 (5.00%)	1 / 59 (1.69%)
occurrences (all)	4	3	1
Diarrhoea			
subjects affected / exposed	13 / 62 (20.97%)	9 / 60 (15.00%)	7 / 59 (11.86%)
occurrences (all)	19	29	56
Dry mouth			
subjects affected / exposed	0 / 62 (0.00%)	3 / 60 (5.00%)	0 / 59 (0.00%)
occurrences (all)	0	3	0
Dyspepsia			
subjects affected / exposed	5 / 62 (8.06%)	5 / 60 (8.33%)	1 / 59 (1.69%)
occurrences (all)	13	5	1
Eructation			

subjects affected / exposed	5 / 62 (8.06%)	3 / 60 (5.00%)	1 / 59 (1.69%)
occurrences (all)	8	3	2
Constipation			
subjects affected / exposed	12 / 62 (19.35%)	2 / 60 (3.33%)	3 / 59 (5.08%)
occurrences (all)	16	2	3
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 62 (4.84%)	1 / 60 (1.67%)	1 / 59 (1.69%)
occurrences (all)	3	1	1
Flatulence			
subjects affected / exposed	1 / 62 (1.61%)	2 / 60 (3.33%)	0 / 59 (0.00%)
occurrences (all)	1	2	0
Vomiting			
subjects affected / exposed	16 / 62 (25.81%)	11 / 60 (18.33%)	4 / 59 (6.78%)
occurrences (all)	32	16	4
Nausea			
subjects affected / exposed	23 / 62 (37.10%)	13 / 60 (21.67%)	9 / 59 (15.25%)
occurrences (all)	29	17	18
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 62 (3.23%)	0 / 60 (0.00%)	4 / 59 (6.78%)
occurrences (all)	2	0	6
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 62 (9.68%)	1 / 60 (1.67%)	2 / 59 (3.39%)
occurrences (all)	7	1	4
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 62 (1.61%)	1 / 60 (1.67%)	3 / 59 (5.08%)
occurrences (all)	1	1	3
Nasopharyngitis			
subjects affected / exposed	3 / 62 (4.84%)	3 / 60 (5.00%)	2 / 59 (3.39%)
occurrences (all)	3	4	3
Upper respiratory tract infection			
subjects affected / exposed	5 / 62 (8.06%)	1 / 60 (1.67%)	0 / 59 (0.00%)
occurrences (all)	5	1	0
Metabolism and nutrition disorders			

Dyslipidaemia			
subjects affected / exposed	2 / 62 (3.23%)	0 / 60 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 60 (0.00%)	4 / 59 (6.78%)
occurrences (all)	0	0	4
Hyperlipidaemia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 60 (0.00%)	4 / 59 (6.78%)
occurrences (all)	0	0	4

Non-serious adverse events	Sema 8.0 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 60 (80.00%)		
Investigations			
Glycosylated haemoglobin increased			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Lipase increased			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	6		
Headache			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	13		
Hyperaesthesia			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Abdominal pain upper			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	6		
Abdominal pain			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	20 / 60 (33.33%)		
occurrences (all)	30		
Dry mouth			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Dyspepsia			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Eructation			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Constipation			
subjects affected / exposed	8 / 60 (13.33%)		
occurrences (all)	11		
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Flatulence			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Vomiting			

subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	14 / 60 (23.33%) 26 25 / 60 (41.67%) 54		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 1 / 60 (1.67%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 0 / 60 (0.00%) 0		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 8 / 60 (13.33%) 8 1 / 60 (1.67%) 1 1 / 60 (1.67%) 1		
Metabolism and nutrition disorders Dyslipidaemia subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all) Hyperlipidaemia subjects affected / exposed occurrences (all)	 3 / 60 (5.00%) 3 1 / 60 (1.67%) 1 1 / 60 (1.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported