Clinical trial results:
Multiple dose trial examining dose range, escalation and efficacy of oral semaglutide in subjects with type 2 diabetes

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2012-004994-16
Trial protocol	SE IT DE GB BG AT ES DK
Global end of trial date	11 December 2014

Results information

Result version number	v1 (current)
This version publication date	27 July 2016
First version publication date	27 July 2016

Trial information

Trial identification

Sponsor protocol code	NN9924-3790

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01923181
WHO universal trial number (UTN)	U1111-1136-4716

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Global Clinical Registry (GCR,1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Global Clinical Registry (GCR,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	01 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 December 2014
Global end of trial reached?	Yes
Global end of trial date	11 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy on glycaemic control of oral semaglutide in a SNAC formulation against placebo in subjects with T2D

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013) and International Conference on Harmonisation (ICH) Good Clinical Practice (1996) and 21 Code of Federal Regulations (CFR) 312.120 (2013).

Background therapy:

The trial medication was given as add-on to previous metformin therapy or as monotherapy if subject was treated with diet and exercise alone.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	02 December 2013
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	Spain: 44
Country: Number of subjects enrolled	Sweden: 28
Country: Number of subjects enrolled	United Kingdom: 62
Country: Number of subjects enrolled	Austria: 38
Country: Number of subjects enrolled	Bulgaria: 33
Country: Number of subjects enrolled	Denmark: 25
Country: Number of subjects enrolled	Germany: 37
Country: Number of subjects enrolled	Italy: 33
Country: Number of subjects enrolled	Canada: 35
Country: Number of subjects enrolled	Israel: 51
Country: Number of subjects enrolled	Malaysia: 33
Country: Number of subjects enrolled	Serbia: 26
Country: Number of subjects enrolled	South Africa: 16
Country: Number of subjects enrolled	United States: 171
Worldwide total number of subjects	632
EEA total number of subjects	300

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)	479
From 65 to 84 years	152
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 100 sites in 14 countries as follows: Austria: 6 sites; Bulgaria: 3 sites; Canada: 6 sites; Denmark: 6 sites; Germany: 6 sites; Israel: 6 sites; Italy: 4 sites; Malaysia: 4 sites; Serbia: 1 site; South Africa: 3 sites; Spain: 5 sites; Sweden: 3 sites; United Kingdom: 8 sites; United States: 39 sites.

Pre-assignment

Screening details:

Subjects attended a screening visit in order to assess their eligibility, which took place within 2 weeks prior to the randomisation visit. Subjects were randomised once all inclusion and exclusion criteria were confirmed. At this visit, data about the subjects already on metformin was documented, based on which the randomisation was stratified.

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:

The study was partially blinded, where oral semaglutide and oral placebo arms were double-blinded, whereas subcutaneous (sc) semaglutide active comparator arm was open-labelled. An internal oral GLP-1 safety committee was constituted to perform ongoing blinded safety surveillance and in case this committee recommended unblinding of any data for further analysis, an independent ad hoc safety group was established to maintain the blinding.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

The subjects in this arm were administered with placebo tablets once daily orally for 26 weeks. The placebo tablets did not contain sodium N-(8-[2-hydroxybenzoyl] amino) caprylate (SNAC).

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

Dosage and administration details:

The doses were administered according to the following rules: Fasting for at least 6 hours (e.g., in the morning following an overnight fast) before tablet ingestion. Water and oral concomitant medication was allowed up to 2 hours prior to dosing. Intake of maximum 120 mL of water was allowed when swallowing the tablet. Subjects were required to abstain from food and fluid intake for at least 30 minutes after ingestion of oral placebo tablet. Oral concomitant medication was allowed to be taken 2 hours post-dosing. If taken with food, concomitant medication was allowed to be administered 30 minutes after ingestion of the placebo tablet.

Arm title	Sema 2.5 mg

Arm description:

The subjects in this group were administered with 2.5 mg of oral semaglutide once daily for 26 weeks. The semaglutide 2.5 mg tablet contained a fixed dose of 300 mg SNAC.

Arm type	Experimental

Investigational medicinal product name	Semaglutide 2.5 mg
Investigational medicinal product code	
Other name	SEMAGLUTIDE
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The doses were administered according to the following rules: Fasting for at least 6 hours (e.g., in the morning following an overnight fast) before tablet ingestion. Water and oral concomitant medication was allowed up to 2 hours prior to dosing. Intake of maximum 120 mL of water was allowed when swallowing the tablet. Subjects were required to abstain from food and fluid intake for at least 30 minutes after ingestion of oral semaglutide tablet. Oral concomitant medication was allowed to be taken 2 hours post-dosing. If taken with food, concomitant medication was allowed to be administered 30 minutes after ingestion of the semaglutide tablet.

Arm title	Sema 5 mg

Arm description:

The subjects in this group were administered with once daily oral doses of 2.5 mg semaglutide for 4 weeks, then 5 mg of semaglutide for 22 weeks. The maintenance dose was 5 mg for subjects in this group. The semaglutide 5 mg tablet contained a fixed dose of 300 mg SNAC.

Arm type	Experimental
Investigational medicinal product name	Semaglutide 5.0 mg
Investigational medicinal product code	
Other name	SEMAGLUTIDE
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The doses were administered according to the following rules: Fasting for at least 6 hours (e.g., in the morning following an overnight fast) before tablet ingestion. Water and oral concomitant medication was allowed up to 2 hours prior to dosing. Intake of maximum 120 mL of water was allowed when swallowing the tablet. Subjects were required to abstain from food and fluid intake for at least 30 minutes after ingestion of oral semaglutide tablet. Oral concomitant medication was allowed to be taken 2 hours post-dosing. If taken with food, concomitant medication was allowed to be administered 30 minutes after ingestion of the semaglutide tablet.

Arm title	Sema 10 mg

Arm description:

The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 4 weeks, then 10 mg of semaglutide for 22 weeks. The maintenance dose was 10 mg for subjects in this group. The semaglutide 10 mg tablet contained a fixed dose of 300 mg SNAC.

Arm type	Experimental
Investigational medicinal product name	Semaglutide 10 mg
Investigational medicinal product code	
Other name	SEMAGLUTIDE
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The doses were administered according to the following rules: Fasting for at least 6 hours (e.g., in the morning following an overnight fast) before tablet ingestion. Water and oral concomitant medication was allowed up to 2 hours prior to dosing. Intake of maximum 120 mL of water was allowed when swallowing the tablet. Subjects were required to abstain from food and fluid intake for at least 30 minutes after ingestion of oral semaglutide tablet. Oral concomitant medication was allowed to be taken 2 hours post-dosing. If taken with food, concomitant medication was allowed to be administered 30 minutes after ingestion of the semaglutide tablet.

Arm title	Sema 20 mg

Arm description:

The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 4 weeks, then 10 mg for 4 weeks, then 20 mg for 18 weeks. The maintenance dose was 20 mg for subjects in this group. The semaglutide 20 mg tablet contained a fixed dose of 300 mg SNAC.

Arm type	Experimental

Investigational medicinal product name	Semaglutide 20 mg
Investigational medicinal product code	
Other name	SEMAGLUTIDE
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The doses were administered according to the following rules: Fasting for at least 6 hours (e.g., in the morning following an overnight fast) before tablet ingestion. Water and oral concomitant medication was allowed up to 2 hours prior to dosing. Intake of maximum 120 mL of water was allowed when swallowing the tablet. Subjects were required to abstain from food and fluid intake for at least 30 minutes after ingestion of oral semaglutide tablet. Oral concomitant medication was allowed to be taken 2 hours post-dosing. If taken with food, concomitant medication was allowed to be administered 30 minutes after ingestion of the semaglutide tablet.

Arm title	Sema 40 mg

Arm description:

The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 4 weeks, then 10 mg for 4 weeks, then 20 mg for 4 weeks, then 40 mg for 14 weeks. The maintenance dose was 40 mg for subjects in this group. In this arm, the dose-escalation occurred every 4th week. The semaglutide 40 mg tablet contained a fixed dose of 300 mg SNAC.

Arm type	Experimental
Investigational medicinal product name	Semaglutide 40 mg
Investigational medicinal product code	
Other name	SEMAGLUTIDE
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The doses were administered according to the following rules: Fasting for at least 6 hours (e.g., in the morning following an overnight fast) before tablet ingestion. Water and oral concomitant medication was allowed up to 2 hours prior to dosing. Intake of maximum 120 mL of water was allowed when swallowing the tablet. Subjects were required to abstain from food and fluid intake for at least 30 minutes after ingestion of oral semaglutide tablet. Oral concomitant medication was allowed to be taken 2 hours post-dosing. If taken with food, concomitant medication was allowed to be administered 30 minutes after ingestion of the semaglutide tablet.

Arm title	Sema 40 mg S

Arm description:

The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 8 weeks, then 10 mg for 8 weeks, then 20 mg for 8 weeks, then 40 mg for 2 weeks. The maintenance dose was 40 mg for subjects in this group. In this arm, the dose-escalation occurred every 8th week (slow dose escalation). The semaglutide 40 mg tablet contained a fixed dose of 300 mg SNAC.

Arm type	Experimental
Investigational medicinal product name	Semaglutide 40 mg
Investigational medicinal product code	
Other name	SEMAGLUTIDE
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The doses were administered according to the following rules: Fasting for at least 6 hours (e.g., in the morning following an overnight fast) before tablet ingestion. Water and oral concomitant medication was allowed up to 2 hours prior to dosing. Intake of maximum 120 mL of water was allowed when swallowing the tablet. Subjects were required to abstain from food and fluid intake for at least 30 minutes after ingestion of oral semaglutide tablet. Oral concomitant medication was allowed to be taken 2 hours post-dosing. If taken with food, concomitant medication was allowed to be administered 30 minutes after ingestion of the semaglutide tablet.

Arm title	Sema 40 mg F

Arm description:

The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 2 weeks, then 10 mg for 2 weeks, then 20 mg for 2 weeks, then 40 mg for 20 weeks. The maintenance dose was 40 mg for subjects in this group. In this arm, the dose-escalation occurred every 2nd week

(fast dose escalation). The semaglutide 40 mg tablet contained a fixed dose of 300 mg SNAC.

Arm type	Experimental
Investigational medicinal product name	Semaglutide 40 mg
Investigational medicinal product code	
Other name	SEMAGLUTIDE
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The doses were administered according to the following rules: Fasting for at least 6 hours (e.g., in the morning following an overnight fast) before tablet ingestion. Water and oral concomitant medication was allowed up to 2 hours prior to dosing. Intake of maximum 120 mL of water was allowed when swallowing the tablet. Subjects were required to abstain from food and fluid intake for at least 30 minutes after ingestion of oral semaglutide tablet. Oral concomitant medication was allowed to be taken 2 hours post-dosing. If taken with food, concomitant medication was allowed to be administered 30 minutes after ingestion of the semaglutide tablet.

Arm title	Sema 1 mg SC

Arm description:

The subjects in this group were administered with once weekly doses of 0.25 mg of sc semaglutide for 4 weeks, then 0.50 mg for 4 weeks, then 1.0 mg for 18 weeks. The maintenance dose was 1.0 mg for subjects in this group.

Arm type	Active comparator
Investigational medicinal product name	Semaglutide B 1.34 mg/ml PDS290
Investigational medicinal product code	
Other name	SEMAGLUTIDE
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Semaglutide (sc administration) was available as 1.34 mg/mL, solution for injection, 1.5 mL pre-filled PDS290 pen-injector. The injections were administered in the thigh, abdomen or upper arm, at any time of day irrespective of meals. The injections were administered on the same day of the week during the trial.

Number of subjects in period 1	Placebo	Sema 2.5 mg	Sema 5 mg
Started	71	70	70
Exposed	71	70	70
Completed	65	61	60
Not completed	6	9	10
Consent withdrawn by subject	1	-	1
Adverse event, non-fatal	1	6	4
Other, unclassified	3	1	3
Pregnancy	-	-	-
Protocol deviation	1	2	2

Number of subjects in period 1	Sema 10 mg	Sema 20 mg	Sema 40 mg
Started	70	70	71
Exposed	69	70	71
Completed	59	48	48
Not completed	11	22	23

Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	8	19	16
Other, unclassified	2	1	4
Pregnancy	-	-	-
Protocol deviation	1	2	2

Number of subjects in period 1	Sema 40 mg S	Sema 40 mg F	Sema 1 mg SC
Started	70	70	70
Exposed	70	70	69
Completed	53	45	53
Not completed	17	25	17
Consent withdrawn by subject	1	3	1
Adverse event, non-fatal	10	18	10
Other, unclassified	4	4	3
Pregnancy	1	-	-
Protocol deviation	1	-	3

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
The subjects in this arm were administered with placebo tablets once daily orally for 26 weeks. The placebo tablets did not contain sodium N-(8-[2-hydroxybenzoyl] amino) caprylate (SNAC).	
Reporting group title	Sema 2.5 mg
Reporting group description:	
The subjects in this group were administered with 2.5 mg of oral semaglutide once daily for 26 weeks. The semaglutide 2.5 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 5 mg
Reporting group description:	
The subjects in this group were administered with once daily oral doses of 2.5 mg semaglutide for 4 weeks, then 5 mg of semaglutide for 22 weeks. The maintenance dose was 5 mg for subjects in this group. The semaglutide 5 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 10 mg
Reporting group description:	
The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 4 weeks, then 10 mg of semaglutide for 22 weeks. The maintenance dose was 10 mg for subjects in this group. The semaglutide 10 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 20 mg
Reporting group description:	
The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 4 weeks, then 10 mg for 4 weeks, then 20 mg for 18 weeks. The maintenance dose was 20 mg for subjects in this group. The semaglutide 20 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 40 mg
Reporting group description:	
The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 4 weeks, then 10 mg for 4 weeks, then 20 mg for 4 weeks, then 40 mg for 14 weeks. The maintenance dose was 40 mg for subjects in this group. In this arm, the dose-escalation occurred every 4th week. The semaglutide 40 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 40 mg S
Reporting group description:	
The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 8 weeks, then 10 mg for 8 weeks, then 20 mg for 8 weeks, then 40 mg for 2 weeks. The maintenance dose was 40 mg for subjects in this group. In this arm, the dose-escalation occurred every 8th week (slow dose escalation). The semaglutide 40 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 40 mg F
Reporting group description:	
The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 2 weeks, then 10 mg for 2 weeks, then 20 mg for 2 weeks, then 40 mg for 20 weeks. The maintenance dose was 40 mg for subjects in this group. In this arm, the dose-escalation occurred every 2nd week (fast dose escalation). The semaglutide 40 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 1 mg SC
Reporting group description:	
The subjects in this group were administered with once weekly doses of 0.25 mg of sc semaglutide for 4 weeks, then 0.50 mg for 4 weeks, then 1.0 mg for 18 weeks. The maintenance dose was 1.0 mg for subjects in this group.	

Reporting group values	Placebo	Sema 2.5 mg	Sema 5 mg
Number of subjects	71	70	70

Age categorical			
The total number of subjects include 2 subjects who were randomised but not exposed and not included in any of the analysis sets (1 subject in the Sema 10 mg arm and 1 subjects in the Sema 1 mg SC arm).			
Units: Subjects			
Adults (18-64 years)	48	55	57
From 65-84 years	23	15	12
85 years and over	0	0	1
Age continuous			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system.			
Units: years			
arithmetic mean	58.9	56.7	55.7
standard deviation	± 10.3	± 9.9	± 11
Gender categorical			
The total number of subjects include 2 subjects who were randomised but not exposed and not included in any of the analysis sets (1 subject in the Sema 10 mg arm and 1 subjects in the Sema 1 mg SC arm).			
Units: Subjects			
Female	31	25	23
Male	40	45	47
HbA1c			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system. Note: The mean and SD are reported with the precision of two decimals. However, zeros at the end of a value is deleted by the system, e.g. 8.00 is presented as 8.			
Units: percentage of haemoglobin			
arithmetic mean	8	7.99	7.8
standard deviation	± 0.8	± 0.72	± 0.62
Body weight			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system.			
Units: kg			
arithmetic mean	93.76	93.62	93.09
standard deviation	± 18.14	± 15.63	± 19.03
Waist circumference			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system. Note: The mean and SD are reported with the precision of one and two decimals, respectively. However, zeros at the end of the value is deleted by the system, e.g. 108.0 is presented as 108 and 13.30 is presented as 13.3.			
Units: centimeter			
arithmetic mean	111.1	108.5	106.1
standard deviation	± 13.56	± 11.87	± 13.73
BMI			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system.			
Units: kg/m2			
arithmetic mean	32.58	31.74	31.6
standard deviation	± 4.53	± 4.14	± 4.86

Reporting group values	Sema 10 mg	Sema 20 mg	Sema 40 mg
Number of subjects	70	70	71
Age categorical			
The total number of subjects include 2 subjects who were randomised but not exposed and not included in any of the analysis sets (1 subject in the Sema 10 mg arm and 1 subjects in the Sema 1 mg SC arm).			
Units: Subjects			
Adults (18-64 years)	57	50	52
From 65-84 years	13	20	19
85 years and over	0	0	0
Age continuous			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system.			
Units: years			
arithmetic mean	56.5	58.3	56.5
standard deviation	± 10.1	± 10.4	± 10.2
Gender categorical			
The total number of subjects include 2 subjects who were randomised but not exposed and not included in any of the analysis sets (1 subject in the Sema 10 mg arm and 1 subjects in the Sema 1 mg SC arm).			
Units: Subjects			
Female	26	26	28
Male	44	44	43
HbA1c			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system. Note: The mean and SD are reported with the precision of two decimals. However, zeros at the end of a value is deleted by the system, e.g. 8.00 is presented as 8.			
Units: percentage of haemoglobin			
arithmetic mean	7.8	7.86	8.05
standard deviation	± 0.7	± 0.69	± 0.75
Body weight			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system.			
Units: kg			
arithmetic mean	91.76	93.81	90.85
standard deviation	± 14.02	± 17.91	± 16.51
Waist circumference			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system. Note: The mean and SD are reported with the precision of one and two decimals, respectively. However, zeros at the end of the value is deleted by the system, e.g. 108.0 is presented as 108 and 13.30 is presented as 13.3.			
Units: centimeter			
arithmetic mean	107.8	108	105.4
standard deviation	± 12.28	± 13.3	± 12.78
BMI			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system.			
Units: kg/m2			
arithmetic mean	31.89	31.97	31.12

standard deviation	± 4.42	± 4.52	± 4.06

Reporting group values	Sema 40 mg S	Sema 40 mg F	Sema 1 mg SC
Number of subjects	70	70	70
Age categorical			
The total number of subjects include 2 subjects who were randomised but not exposed and not included in any of the analysis sets (1 subject in the Sema 10 mg arm and 1 subjects in the Sema 1 mg SC arm).			
Units: Subjects			
Adults (18-64 years)	55	50	55
From 65-84 years	15	20	15
85 years and over	0	0	0
Age continuous			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system.			
Units: years			
arithmetic mean	57.1	57.7	56.8
standard deviation	± 10.5	± 10.8	± 11.8
Gender categorical			
The total number of subjects include 2 subjects who were randomised but not exposed and not included in any of the analysis sets (1 subject in the Sema 10 mg arm and 1 subjects in the Sema 1 mg SC arm).			
Units: Subjects			
Female	29	26	21
Male	41	44	49
HbA1c			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system. Note: The mean and SD are reported with the precision of two decimals. However, zeros at the end of a value is deleted by the system, e.g. 8.00 is presented as 8.			
Units: percentage of haemoglobin			
arithmetic mean	7.96	7.77	7.77
standard deviation	± 0.73	± 0.75	± 0.71
Body weight			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system.			
Units: kg			
arithmetic mean	93.25	91.98	88.8
standard deviation	± 18.76	± 15.37	± 15.42
Waist circumference			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system. Note: The mean and SD are reported with the precision of one and two decimals, respectively. However, zeros at the end of the value is deleted by the system, e.g. 108.0 is presented as 108 and 13.30 is presented as 13.3.			
Units: centimeter			
arithmetic mean	107.9	106.3	105
standard deviation	± 12.46	± 11.66	± 11.27
BMI			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69			

subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system.			
Units: kg/m2			
arithmetic mean	32.26	31.66	30.72
standard deviation	± 4.46	± 3.82	± 4.03

Reporting group values	Total		
Number of subjects	632		
Age categorical			
The total number of subjects include 2 subjects who were randomised but not exposed and not included in any of the analysis sets (1 subject in the Sema 10 mg arm and 1 subjects in the Sema 1 mg SC arm).			
Units: Subjects			
Adults (18-64 years)	479		
From 65-84 years	152		
85 years and over	1		
Age continuous			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system.			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
The total number of subjects include 2 subjects who were randomised but not exposed and not included in any of the analysis sets (1 subject in the Sema 10 mg arm and 1 subjects in the Sema 1 mg SC arm).			
Units: Subjects			
Female	235		
Male	397		
HbA1c			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system. Note: The mean and SD are reported with the precision of two decimals. However, zeros at the end of a value is deleted by the system, e.g. 8.00 is presented as 8.			
Units: percentage of haemoglobin			
arithmetic mean			
standard deviation	-		
Body weight			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system.			
Units: kg			
arithmetic mean			
standard deviation	-		
Waist circumference			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system. Note: The mean and SD are reported with the precision of one and two decimals, respectively. However, zeros at the end of the value is deleted by the system, e.g. 108.0 is presented as 108 and 13.30 is presented as 13.3.			
Units: centimeter			
arithmetic mean			
standard deviation	-		

BMI			
In the treatment arms, Sema 10 mg and Sema 1 mg SC, the mean values include only the data from 69 subjects in each arm since 1 subject each in these arms were not exposed to any treatment and hence should not be counted for any data under the respective arms. The total subjects enrolled/randomised are auto calculated by the system.			
Units: kg/m2 arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
The subjects in this arm were administered with placebo tablets once daily orally for 26 weeks. The placebo tablets did not contain sodium N-(8-[2-hydroxybenzoyl] amino) caprylate (SNAC).	
Reporting group title	Sema 2.5 mg
Reporting group description:	
The subjects in this group were administered with 2.5 mg of oral semaglutide once daily for 26 weeks. The semaglutide 2.5 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 5 mg
Reporting group description:	
The subjects in this group were administered with once daily oral doses of 2.5 mg semaglutide for 4 weeks, then 5 mg of semaglutide for 22 weeks. The maintenance dose was 5 mg for subjects in this group. The semaglutide 5 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 10 mg
Reporting group description:	
The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 4 weeks, then 10 mg of semaglutide for 22 weeks. The maintenance dose was 10 mg for subjects in this group. The semaglutide 10 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 20 mg
Reporting group description:	
The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 4 weeks, then 10 mg for 4 weeks, then 20 mg for 18 weeks. The maintenance dose was 20 mg for subjects in this group. The semaglutide 20 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 40 mg
Reporting group description:	
The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 4 weeks, then 10 mg for 4 weeks, then 20 mg for 4 weeks, then 40 mg for 14 weeks. The maintenance dose was 40 mg for subjects in this group. In this arm, the dose-escalation occurred every 4th week. The semaglutide 40 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 40 mg S
Reporting group description:	
The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 8 weeks, then 10 mg for 8 weeks, then 20 mg for 8 weeks, then 40 mg for 2 weeks. The maintenance dose was 40 mg for subjects in this group. In this arm, the dose-escalation occurred every 8th week (slow dose escalation). The semaglutide 40 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 40 mg F
Reporting group description:	
The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 2 weeks, then 10 mg for 2 weeks, then 20 mg for 2 weeks, then 40 mg for 20 weeks. The maintenance dose was 40 mg for subjects in this group. In this arm, the dose-escalation occurred every 2nd week (fast dose escalation). The semaglutide 40 mg tablet contained a fixed dose of 300 mg SNAC.	
Reporting group title	Sema 1 mg SC
Reporting group description:	
The subjects in this group were administered with once weekly doses of 0.25 mg of sc semaglutide for 4 weeks, then 0.50 mg for 4 weeks, then 1.0 mg for 18 weeks. The maintenance dose was 1.0 mg for subjects in this group.	

Primary: Change in HbA1c

End point title	Change in HbA1c

End point description:

Change in HbA1c from baseline to after 26 weeks of treatment. Subjects in the full analysis set (FAS) and only measurements belonging to the on-treatment without rescue medication observation period (the primary observation period for examination of efficacy endpoints) were included in the analysis. This observation period included observations recorded at or after date of first dose of trial product and not after the first occurrence of the following: 1) The end-date of the on-treatment observation period. 2) Initiation of rescue medication. The total number of subjects included in this period were 463. FAS included subjects who had received at least 1 dose of randomised semaglutide (oral or sc) or placebo. Subjects in FAS contributed to the evaluation based on their randomised treatment. Note: The mean and SD are reported with the precision of two decimals. However, zeros at the end of a value is deleted by the system, e.g. 0.10 is presented as 0.1.

End point type	Primary

End point timeframe:

From baseline to after 26 weeks of treatment

End point values	Placebo	Sema 2.5 mg	Sema 5 mg	Sema 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	56	58	57
Units: percentage of HbA1c				
least squares mean (standard error)				
Change from baseline	-0.31 (± 0.1)	-0.71 (± 0.1)	-1.2 (± 0.1)	-1.49 (± 0.1)

End point values	Sema 20 mg	Sema 40 mg	Sema 40 mg S	Sema 40 mg F
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	46	52	44
Units: percentage of HbA1c				
least squares mean (standard error)				
Change from baseline	-1.69 (± 0.11)	-1.91 (± 0.11)	-1.74 (± 0.1)	-1.65 (± 0.11)

End point values	Sema 1 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: percentage of HbA1c				
least squares mean (standard error)				
Change from baseline	-1.87 (± 0.11)			

Statistical analyses

Statistical analysis title	Primary statistical analysis

Statistical analysis description:

The post-baseline responses were analysed using a mixed model for repeated measurements with treatment, stratum and country as fixed factors
and baseline value as covariate, all nested within visit. Group mean estimates were adjusted according to observed baseline distribution. Subjects in the FAS and only measurements belonging to the on-treatment without rescue medication observation period were included in the analysis.

Comparison groups	Placebo v Sema 2.5 mg
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.0069
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	-0.11
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[1] - The estimated treatment difference with corresponding two-sided p-value and 95% confidence interval at 26 weeks was presented, and efficacy of oral semaglutide was considered confirmed if the upper limit of the confidence interval was strictly less than zero.

Statistical analysis title	Primary statistical analysis

Statistical analysis description:

The post-baseline responses were analysed using a mixed model for repeated measurements with treatment, stratum and country as fixed factors
and baseline value as covariate, all nested within visit. Group mean estimates were adjusted according to observed baseline distribution. Subjects in the FAS and only measurements belonging to the on-treatment without rescue medication observation period were included in the analysis.

Comparison groups	Placebo v Sema 5 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.18
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[2] - The estimated treatment difference with corresponding two-sided p-value and 95% confidence interval at 26 weeks was presented, and efficacy of oral semaglutide was considered confirmed if the upper limit of the confidence interval was strictly less than zero.

Statistical analysis title	Primary statistical analysis

Statistical analysis description:

The post-baseline responses were analysed using a mixed model for repeated measurements with

treatment, stratum and country as fixed factors
and baseline value as covariate, all nested within visit. Group mean estimates were adjusted according to observed baseline distribution. Subjects in the FAS and only measurements belonging to the on-treatment without rescue medication observation period were included in the analysis.

Comparison groups	Placebo v Sema 10 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.47
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[3] - The estimated treatment difference with corresponding two-sided p-value and 95% confidence interval at 26 weeks was presented, and efficacy of oral semaglutide was considered confirmed if the upper limit of the confidence interval was strictly less than zero.

Statistical analysis title	Primary statistical analysis

Statistical analysis description:

The post-baseline responses were analysed using a mixed model for repeated measurements with treatment, stratum and country as fixed factors
and baseline value as covariate, all nested within visit. Group mean estimates were adjusted according to observed baseline distribution. Subjects in the FAS and only measurements belonging to the on-treatment without rescue medication observation period were included in the analysis.

Comparison groups	Placebo v Sema 20 mg
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	-1.09
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[4] - The estimated treatment difference with corresponding two-sided p-value and 95% confidence interval at 26 weeks was presented, and efficacy of oral semaglutide was considered confirmed if the upper limit of the confidence interval was strictly less than zero.

Statistical analysis title	Primary statistical analysis

Statistical analysis description:

The post-baseline responses were analysed using a mixed model for repeated measurements with treatment, stratum and country as fixed factors and baseline value as covariate, all nested within visit. Group mean estimates were adjusted according to observed baseline distribution. Subjects in the FAS

and only measurements belonging to the on-treatment without rescue medication observation period were included in the analysis.

Comparison groups	Placebo v Sema 40 mg
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.89
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[5] - The estimated treatment difference with corresponding two-sided p-value and 95% confidence interval at 26 weeks was presented, and efficacy of oral semaglutide was considered confirmed if the upper limit of the confidence interval was strictly less than zero.

Secondary: Subjects who achieve (yes/no) HbA1c <7% (53 mmol/mol)

End point title	Subjects who achieve (yes/no) HbA1c <7% (53 mmol/mol)

End point description:

The proportion of subjects who achieved HbA1c <7% after 26 weeks of treatment. The data presented is summary of on-treatment without rescue data with missing data imputed from a mixed model for repeated measures with treatment, country, stratum and baseline value, all nested within visit. The FAS was used in all analyses of the supportive secondary efficacy endpoints. Subjects in the FAS contributed to the evaluation based on their randomised treatment.

End point type	Secondary

End point timeframe:

After 26 weeks of treatment.

End point values	Placebo	Sema 2.5 mg	Sema 5 mg	Sema 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	71	70	70	69
Units: Percentage of subjects				
number (not applicable)				
Yes	27.54	44.12	81.16	83.58
No	72.46	55.88	18.84	16.42

End point values	Sema 20 mg	Sema 40 mg	Sema 40 mg S	Sema 40 mg F
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	71	70	70
Units: Percentage of subjects				
number (not applicable)				
Yes	85.71	89.71	86.57	87.69

No	14.29	10.29	13.43	12.31

End point values	Sema 1 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Percentage of subjects				
number (not applicable)				
Yes	92.65			
No	7.35			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body weight

End point title	Change in body weight

End point description:

Change in body weight from baseline to after 26 weeks of treatment. Analysis of observed on-treatment without rescue data. The post-baseline responses were analysed using a mixed model for repeated measurements with treatment, stratum and country as fixed factors and baseline value as covariate, all nested within visit. Group mean estimates were adjusted according to observed baseline distribution.

End point type	Secondary

End point timeframe:

From baseline to after 26 weeks of treatment

End point values	Placebo	Sema 2.5 mg	Sema 5 mg	Sema 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	56	57	57
Units: kg				
least squares mean (standard error)				
Change from baseline	-1.18 (± 0.55)	-2.06 (± 0.53)	-2.65 (± 0.53)	-4.8 (± 0.54)

End point values	Sema 20 mg	Sema 40 mg	Sema 40 mg S	Sema 40 mg F
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	46	51	44
Units: kg				
least squares mean (standard error)				
Change from baseline	-6.14 (± 0.57)	-6.89 (± 0.56)	-6.05 (± 0.54)	-8.16 (± 0.58)

End point values	Sema 1 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	46			
Units: kg				
least squares mean (standard error)				
Change from baseline	-6.43 (± 0.55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in waist circumference

End point title	Change in waist circumference

End point description:

Change in waist circumference from baseline to after 26 weeks of treatment. Analysis of observed on-treatment without rescue data. The post-baseline responses were analysed using a mixed model for repeated measurements with treatment, stratum and country as fixed factors and baseline value as covariate, all nested within visit. Group mean estimates were adjusted according to observed baseline distribution.

End point type	Secondary

End point timeframe:

From baseline to after 26 weeks of treatment

End point values	Placebo	Sema 2.5 mg	Sema 5 mg	Sema 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	56	56	57
Units: centimeter				
least squares mean (standard error)				
Change from baseline	-1.66 (± 0.62)	-1.84 (± 0.6)	-2.21 (± 0.61)	-4.48 (± 0.6)

End point values	Sema 20 mg	Sema 40 mg	Sema 40 mg S	Sema 40 mg F
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	46	51	44
Units: centimeter				
least squares mean (standard error)				
Change from baseline	-4.47 (± 0.63)	-5.78 (± 0.63)	-5.06 (± 0.61)	-6.27 (± 0.65)

End point values	Sema 1 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	46			
Units: centimeter				
least squares mean (standard error)				
Change from baseline	-6.21 (± 0.63)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body mass index (BMI)

End point title	Change in body mass index (BMI)

End point description:

Change in BMI from baseline to after 26 weeks of treatment. Analysis of observed on-treatment without rescue data. The post-baseline responses were analysed using a mixed model for repeated measurements with treatment, stratum and country as fixed factors and baseline value as covariate, all nested within visit. Group mean estimates were adjusted according to observed baseline distribution.

End point type	Secondary

End point timeframe:

From baseline to after 26 weeks of treatment

End point values	Placebo	Sema 2.5 mg	Sema 5 mg	Sema 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	56	57	57
Units: kg/m2				
least squares mean (standard error)				
Change from baseline	-0.41 (± 0.19)	-0.7 (± 0.18)	-0.91 (± 0.18)	-1.69 (± 0.19)

End point values	Sema 20 mg	Sema 40 mg	Sema 40 mg S	Sema 40 mg F
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	46	51	44
Units: kg/m2				
least squares mean (standard error)				
Change from baseline	-2.11 (± 0.2)	-2.38 (± 0.19)	-2.1 (± 0.19)	-2.86 (± 0.2)

End point values	Sema 1 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	46			
Units: kg/m2				
least squares mean (standard error)				

Change from baseline	-2.25 (± 0.19)			

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:

The on-treatment summary of adverse events included treatment emergent events with onset on or after the day of first randomised dose and not after the follow-up visit scheduled 5 weeks after end of treatment. This endpoint was summarised and analysed using the safety analysis set. The on-treatment observation period was the primary observation period for examination of all safety endpoints. Subjects in the safety analysis set contributed to the evaluation 'as treated'.

End point type	Secondary

End point timeframe:

Recorded from baseline until week 31

End point values	Placebo	Sema 2.5 mg	Sema 5 mg	Sema 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	71	70	70	69
Units: Number of events				
Number of events	127	142	169	233

End point values	Sema 20 mg	Sema 40 mg	Sema 40 mg S	Sema 40 mg F
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	71	70	70
Units: Number of events				
Number of events	289	230	233	245

End point values	Sema 1 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Number of events				
Number of events	218			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of confirmed hypoglycaemic episodes

End point title	Number of confirmed hypoglycaemic episodes

End point description:

Confirmed hypoglycaemic episodes were defined as episode that is severe according to the American Diabetes Association (ADA) classification (an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or take other corrective actions) or blood glucose confirmed by a plasma glucose value <3.1 mmol/L (56 mg/dL) with or without symptoms consistent with hypoglycaemia.

End point type	Secondary

End point timeframe:

Recorded from baseline until week 31

End point values	Placebo	Sema 2.5 mg	Sema 5 mg	Sema 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	71	70	70	69
Units: Number of episodes				
Number of episodes	5	4	4	6

End point values	Sema 20 mg	Sema 40 mg	Sema 40 mg S	Sema 40 mg F
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	71	70	70
Units: Number of episodes				
Number of episodes	1	1	3	1

End point values	Sema 1 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Number of episodes				
Number of episodes	6			

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs) either observed by the investigator or reported spontaneously by the subjects were recorded. This included events from when the subject had signed the informed consent until the end of the post-treatment follow-up period.

Adverse event reporting additional description:

Safety analysis set was used for the assessment of safety including AEs. Safety analysis set included 630 subjects who had been exposed to at least 1 dose of semaglutide (oral or sc) or placebo and excluded 2 subjects who were randomised but not exposed to treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

The subjects in this arm were administered with placebo tablets once daily orally for 26 weeks. The placebo tablets did not contain sodium N-(8-[2-hydroxybenzoyl] amino) caprylate (SNAC).

Reporting group title	Sema 2.5 mg

Reporting group description:

The subjects in this group were administered with 2.5 mg of oral semaglutide once daily for 26 weeks. The semaglutide 2.5 mg tablet contained a fixed dose of 300 mg SNAC.

Reporting group title	Sema 5 mg

Reporting group description:

The subjects in this group were administered with once daily oral doses of 2.5 mg semaglutide for 4 weeks, then 5 mg of semaglutide for 22 weeks. The maintenance dose was 5 mg for subjects in this group. The semaglutide 5 mg tablet contained a fixed dose of 300 mg SNAC.

Reporting group title	Sema 10 mg

Reporting group description:

The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 4 weeks, then 10 mg of semaglutide for 22 weeks. The maintenance dose was 10 mg for subjects in this group. The semaglutide 10 mg tablet contained a fixed dose of 300 mg SNAC.

Reporting group title	Sema 20 mg

Reporting group description:

The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 4 weeks, then 10 mg for 4 weeks, then 20 mg for 18 weeks. The maintenance dose was 20 mg for subjects in this group. The semaglutide 20 mg tablet contained a fixed dose of 300 mg SNAC.

Reporting group title	Sema 40 mg

Reporting group description:

The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 4 weeks, then 10 mg for 4 weeks, then 20 mg for 4 weeks, then 40 mg for 14 weeks. The maintenance dose was 40 mg for subjects in this group. In this arm, the dose-escalation occurred every 4th week. The semaglutide 40 mg tablet contained a fixed dose of 300 mg SNAC.

Reporting group title	Sema 40 mg S

Reporting group description:

The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 8 weeks, then 10 mg for 8 weeks, then 20 mg for 8 weeks, then 40 mg for 2 weeks.The maintenance dose was 40 mg for subjects in this group. In this arm, the dose-escalation occurred every 8th week (slow dose escalation). The semaglutide 40 mg tablet contained a fixed dose of 300 mg SNAC.

Reporting group title	Sema 40 mg F

Reporting group description:

The subjects in this group were administered with once daily oral doses of 5 mg semaglutide for 2 weeks, then 10 mg for 2 weeks, then 20 mg for 2 weeks, then 40 mg for 20 weeks. The maintenance dose was 40 mg for subjects in this group. In this arm, the dose-escalation occurred every 2nd week

(fast dose escalation). The semaglutide 40 mg tablet contained a fixed dose of 300 mg SNAC.

Reporting group title	Sema 1 mg SC

Reporting group description:

The subjects in this group were administered with once weekly doses of 0.25 mg of subcutaneous (sc) semaglutide for 4 weeks, then 0.50 mg for 4 weeks, then 1.0 mg for 18 weeks. The maintenance dose was 1.0 mg for subjects in this group.

Serious adverse events	Placebo	Sema 2.5 mg	Sema 5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 71 (7.04%)	1 / 70 (1.43%)	2 / 70 (2.86%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal neoplasm			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Investigations			
Pancreatic enzymes increased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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
Postoperative adhesion			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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

Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Eye disorders			
Pterygium			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Diverticulum intestinal			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Nausea			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Vomiting			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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
Renal failure acute			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Infections and infestations			
Appendicitis			

subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Gastroenteritis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Groin abscess			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint abscess			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Pneumonia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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
Hypoglycaemia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (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

Serious adverse events	Sema 10 mg	Sema 20 mg	Sema 40 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 69 (2.90%)	0 / 70 (0.00%)	1 / 71 (1.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal neoplasm			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Investigations			
Pancreatic enzymes increased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Postoperative adhesion			
subjects affected / exposed	1 / 69 (1.45%)	0 / 70 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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

Transient ischaemic attack			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Eye disorders			
Pterygium			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Diverticulum intestinal			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Nausea			
subjects affected / exposed	1 / 69 (1.45%)	0 / 70 (0.00%)	0 / 71 (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
Vomiting			
subjects affected / exposed	1 / 69 (1.45%)	0 / 70 (0.00%)	0 / 71 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Skin and subcutaneous tissue disorders			
Diabetic foot			

subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Renal failure acute			
subjects affected / exposed	1 / 69 (1.45%)	0 / 70 (0.00%)	0 / 71 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	1 / 71 (1.41%)
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	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Groin abscess			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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

Joint abscess			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Pneumonia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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
Hypoglycaemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 70 (0.00%)	0 / 71 (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

Serious adverse events	Sema 40 mg S	Sema 40 mg F	Sema 1 mg SC
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 70 (4.29%)	5 / 70 (7.14%)	2 / 69 (2.90%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal neoplasm			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 69 (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
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	0 / 69 (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
Investigations			
Pancreatic enzymes increased			

subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 69 (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
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 69 (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
Postoperative adhesion			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 69 (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
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 69 (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
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 69 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	0 / 69 (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
Eye disorders			
Pterygium			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 69 (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			
Diarrhoea			

subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 69 (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
Diverticulum intestinal			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 69 (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
Vomiting			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 69 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 69 (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
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 69 (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
Renal failure acute			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 69 (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

Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 69 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 69 (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 / 70 (0.00%)	0 / 70 (0.00%)	0 / 69 (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
Gastroenteritis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 69 (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
Groin abscess			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 69 (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
Joint abscess			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	0 / 69 (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
Pneumonia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	0 / 69 (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
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 69 (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
Hypoglycaemia			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	0 / 69 (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

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

Non-serious adverse events	Placebo	Sema 2.5 mg	Sema 5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 71 (47.89%)	35 / 70 (50.00%)	32 / 70 (45.71%)
Investigations			
Lipase increased			
subjects affected / exposed	2 / 71 (2.82%)	2 / 70 (2.86%)	1 / 70 (1.43%)
occurrences (all)	2	2	1
Weight decreased			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 71 (1.41%)	4 / 70 (5.71%)	3 / 70 (4.29%)
occurrences (all)	1	4	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 71 (0.00%)	5 / 70 (7.14%)	3 / 70 (4.29%)
occurrences (all)	0	5	3
Headache			
subjects affected / exposed	4 / 71 (5.63%)	4 / 70 (5.71%)	9 / 70 (12.86%)
occurrences (all)	4	6	9
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 71 (2.82%)	3 / 70 (4.29%)	3 / 70 (4.29%)
occurrences (all)	2	3	3
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	5 / 71 (7.04%)	0 / 70 (0.00%)	3 / 70 (4.29%)
occurrences (all)	5	0	3
Abdominal pain			
subjects affected / exposed	0 / 71 (0.00%)	3 / 70 (4.29%)	1 / 70 (1.43%)
occurrences (all)	0	3	1
Abdominal pain upper			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Constipation			
subjects affected / exposed	4 / 71 (5.63%)	4 / 70 (5.71%)	4 / 70 (5.71%)
occurrences (all)	5	4	4
Diarrhoea			
subjects affected / exposed	7 / 71 (9.86%)	5 / 70 (7.14%)	7 / 70 (10.00%)
occurrences (all)	10	6	7
Dyspepsia			
subjects affected / exposed	3 / 71 (4.23%)	2 / 70 (2.86%)	5 / 70 (7.14%)
occurrences (all)	3	6	7
Eructation			
subjects affected / exposed	0 / 71 (0.00%)	0 / 70 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 71 (1.41%)	2 / 70 (2.86%)	2 / 70 (2.86%)
occurrences (all)	1	2	2
Nausea			
subjects affected / exposed	1 / 71 (1.41%)	9 / 70 (12.86%)	10 / 70 (14.29%)
occurrences (all)	1	12	13
Vomiting			
subjects affected / exposed	3 / 71 (4.23%)	4 / 70 (5.71%)	4 / 70 (5.71%)
occurrences (all)	3	8	5
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	1 / 71 (1.41%)	2 / 70 (2.86%)	2 / 70 (2.86%)
occurrences (all)	1	2	2
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	5 / 71 (7.04%)	2 / 70 (2.86%)	0 / 70 (0.00%)
occurrences (all)	7	2	0
Nasopharyngitis			
subjects affected / exposed	9 / 71 (12.68%)	6 / 70 (8.57%)	3 / 70 (4.29%)
occurrences (all)	9	7	4
Upper respiratory tract infection			
subjects affected / exposed	1 / 71 (1.41%)	3 / 70 (4.29%)	4 / 70 (5.71%)
occurrences (all)	1	3	5
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 71 (1.41%)	3 / 70 (4.29%)	2 / 70 (2.86%)
occurrences (all)	1	4	2

Non-serious adverse events	Sema 10 mg	Sema 20 mg	Sema 40 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 69 (53.62%)	49 / 70 (70.00%)	49 / 71 (69.01%)
Investigations			
Lipase increased			
subjects affected / exposed	1 / 69 (1.45%)	3 / 70 (4.29%)	3 / 71 (4.23%)
occurrences (all)	1	3	3
Weight decreased			
subjects affected / exposed	0 / 69 (0.00%)	2 / 70 (2.86%)	4 / 71 (5.63%)
occurrences (all)	0	2	4
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 69 (2.90%)	6 / 70 (8.57%)	1 / 71 (1.41%)
occurrences (all)	2	6	1
Nervous system disorders			
Dizziness			

subjects affected / exposed	3 / 69 (4.35%)	3 / 70 (4.29%)	4 / 71 (5.63%)
occurrences (all)	3	3	4
Headache			
subjects affected / exposed	8 / 69 (11.59%)	10 / 70 (14.29%)	4 / 71 (5.63%)
occurrences (all)	10	18	7
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 69 (4.35%)	5 / 70 (7.14%)	1 / 71 (1.41%)
occurrences (all)	3	6	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 69 (2.90%)	3 / 70 (4.29%)	2 / 71 (2.82%)
occurrences (all)	2	3	2
Abdominal distension			
subjects affected / exposed	1 / 69 (1.45%)	2 / 70 (2.86%)	6 / 71 (8.45%)
occurrences (all)	1	2	6
Abdominal pain			
subjects affected / exposed	1 / 69 (1.45%)	4 / 70 (5.71%)	3 / 71 (4.23%)
occurrences (all)	1	7	3
Abdominal pain upper			
subjects affected / exposed	1 / 69 (1.45%)	6 / 70 (8.57%)	2 / 71 (2.82%)
occurrences (all)	1	8	2
Constipation			
subjects affected / exposed	6 / 69 (8.70%)	5 / 70 (7.14%)	9 / 71 (12.68%)
occurrences (all)	8	8	11
Diarrhoea			
subjects affected / exposed	16 / 69 (23.19%)	14 / 70 (20.00%)	10 / 71 (14.08%)
occurrences (all)	20	18	15
Dyspepsia			
subjects affected / exposed	6 / 69 (8.70%)	8 / 70 (11.43%)	6 / 71 (8.45%)
occurrences (all)	6	8	8
Eructation			
subjects affected / exposed	1 / 69 (1.45%)	2 / 70 (2.86%)	5 / 71 (7.04%)
occurrences (all)	1	2	5
Gastrooesophageal reflux disease			

subjects affected / exposed	4 / 69 (5.80%)	5 / 70 (7.14%)	4 / 71 (5.63%)
occurrences (all)	4	7	4
Nausea			
subjects affected / exposed	23 / 69 (33.33%)	24 / 70 (34.29%)	24 / 71 (33.80%)
occurrences (all)	27	36	37
Vomiting			
subjects affected / exposed	14 / 69 (20.29%)	11 / 70 (15.71%)	14 / 71 (19.72%)
occurrences (all)	18	14	25
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 69 (5.80%)	1 / 70 (1.43%)	0 / 71 (0.00%)
occurrences (all)	4	1	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 69 (2.90%)	2 / 70 (2.86%)	2 / 71 (2.82%)
occurrences (all)	3	2	2
Influenza			
subjects affected / exposed	3 / 69 (4.35%)	3 / 70 (4.29%)	2 / 71 (2.82%)
occurrences (all)	5	4	2
Nasopharyngitis			
subjects affected / exposed	3 / 69 (4.35%)	5 / 70 (7.14%)	5 / 71 (7.04%)
occurrences (all)	3	6	5
Upper respiratory tract infection			
subjects affected / exposed	1 / 69 (1.45%)	6 / 70 (8.57%)	1 / 71 (1.41%)
occurrences (all)	1	7	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 69 (14.49%)	8 / 70 (11.43%)	10 / 71 (14.08%)
occurrences (all)	10	8	11

Non-serious adverse events	Sema 40 mg S	Sema 40 mg F	Sema 1 mg SC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 70 (60.00%)	55 / 70 (78.57%)	44 / 69 (63.77%)
Investigations			
Lipase increased			
subjects affected / exposed	4 / 70 (5.71%)	4 / 70 (5.71%)	2 / 69 (2.90%)
occurrences (all)	4	4	2

Weight decreased			
subjects affected / exposed	0 / 70 (0.00%)	3 / 70 (4.29%)	1 / 69 (1.45%)
occurrences (all)	0	3	1
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 70 (2.86%)	2 / 70 (2.86%)	3 / 69 (4.35%)
occurrences (all)	2	2	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 70 (0.00%)	5 / 70 (7.14%)	2 / 69 (2.90%)
occurrences (all)	0	5	2
Headache			
subjects affected / exposed	8 / 70 (11.43%)	7 / 70 (10.00%)	10 / 69 (14.49%)
occurrences (all)	10	7	21
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 70 (1.43%)	3 / 70 (4.29%)	2 / 69 (2.90%)
occurrences (all)	1	3	3
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 70 (1.43%)	4 / 70 (5.71%)	5 / 69 (7.25%)
occurrences (all)	1	5	7
Abdominal distension			
subjects affected / exposed	1 / 70 (1.43%)	3 / 70 (4.29%)	3 / 69 (4.35%)
occurrences (all)	1	3	4
Abdominal pain			
subjects affected / exposed	4 / 70 (5.71%)	3 / 70 (4.29%)	4 / 69 (5.80%)
occurrences (all)	4	3	4
Abdominal pain upper			
subjects affected / exposed	4 / 70 (5.71%)	1 / 70 (1.43%)	0 / 69 (0.00%)
occurrences (all)	6	1	0
Constipation			
subjects affected / exposed	7 / 70 (10.00%)	8 / 70 (11.43%)	7 / 69 (10.14%)
occurrences (all)	7	9	7
Diarrhoea			

subjects affected / exposed	14 / 70 (20.00%)	12 / 70 (17.14%)	10 / 69 (14.49%)
occurrences (all)	27	15	14
Dyspepsia			
subjects affected / exposed	6 / 70 (8.57%)	5 / 70 (7.14%)	10 / 69 (14.49%)
occurrences (all)	8	5	11
Eructation			
subjects affected / exposed	1 / 70 (1.43%)	2 / 70 (2.86%)	2 / 69 (2.90%)
occurrences (all)	1	2	2
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 70 (5.71%)	4 / 70 (5.71%)	1 / 69 (1.45%)
occurrences (all)	4	4	1
Nausea			
subjects affected / exposed	23 / 70 (32.86%)	25 / 70 (35.71%)	22 / 69 (31.88%)
occurrences (all)	29	27	23
Vomiting			
subjects affected / exposed	11 / 70 (15.71%)	16 / 70 (22.86%)	6 / 69 (8.70%)
occurrences (all)	22	20	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	3 / 69 (4.35%)
occurrences (all)	0	2	3
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 70 (2.86%)	4 / 70 (5.71%)	2 / 69 (2.90%)
occurrences (all)	2	6	2
Influenza			
subjects affected / exposed	1 / 70 (1.43%)	1 / 70 (1.43%)	1 / 69 (1.45%)
occurrences (all)	1	1	1
Nasopharyngitis			
subjects affected / exposed	3 / 70 (4.29%)	4 / 70 (5.71%)	2 / 69 (2.90%)
occurrences (all)	4	5	3
Upper respiratory tract infection			
subjects affected / exposed	2 / 70 (2.86%)	0 / 70 (0.00%)	4 / 69 (5.80%)
occurrences (all)	2	0	4
Metabolism and nutrition disorders			

Decreased appetite subjects affected / exposed occurrences (all)	3 / 70 (4.29%) 4	10 / 70 (14.29%) 10	9 / 69 (13.04%) 9

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 February 2014	The HbA1c criterion was removed as part of the rescue criteria during the treatment period. The process of reporting central electrocardiogram (ECG) evaluation back to investigator was changed. The ADA classification of hypoglycaemia was recently been updated. The definition of thyroid events for adjudication was updated. Minor inconsistencies were updated and amendment number 1 (local amendment for Sweden) was included.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported