Clinical trial results:
Dose-finding of semaglutide administered subcutaneously once daily versus placebo and liraglutide in subjects with type 2 diabetes

Summary

EudraCT number	2014-003196-39
Trial protocol	GB DE CZ AT
Global end of trial date	13 October 2016

Results information

Result version number	v1 (current)
This version publication date	27 October 2017
First version publication date	27 October 2017

Trial information

Trial identification

Sponsor protocol code	NN9535-4191

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02461589
WHO universal trial number (UTN)	U1111-1159-4923

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	16 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 October 2016
Global end of trial reached?	Yes
Global end of trial date	13 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of four dose-levels of semaglutide administered subcutaneously (s.c.) once daily (OD) versus placebo on glycaemic control after 26 weeks of treatment

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki, ICH Good Clinical Practice and EN ISO 14155 Part 1 and 2, and 21 CFR 312.120.

Background therapy:

Subjects continued the pre-trial stable diabetes treatment consisting of diet and exercise with or without metformin (≥ 1500 mg daily or maximum tolerated dose) during the trial.

Evidence for comparator:

Not applicable

Actual start date of recruitment	21 September 2015
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	Austria: 31
Country: Number of subjects enrolled	Canada: 39
Country: Number of subjects enrolled	Czech Republic: 53
Country: Number of subjects enrolled	Germany: 42
Country: Number of subjects enrolled	United Kingdom: 76
Country: Number of subjects enrolled	Malaysia: 31
Country: Number of subjects enrolled	Russian Federation: 50
Country: Number of subjects enrolled	Serbia: 84
Country: Number of subjects enrolled	United States: 239
Country: Number of subjects enrolled	South Africa: 60
Worldwide total number of subjects	705
EEA total number of subjects	202

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)	550
From 65 to 84 years	155
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 139 sites in 10 countries as follows:
Austria: 3 sites; Canada: 8 sites; Czech Republic: 9 sites; Germany: 7 sites; Malaysia: 5 sites; Russian Federation: 7 sites; Serbia: 9 sites; South Africa: 7 sites; United Kingdom: 13 sites; United States: 71 sites.

Pre-assignment

Screening details:

Not applicable

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:

A portion of this trial was double-blinded (sponsor, investigators, and subjects) within dose level in order to minimise bias during trial conduct. Semaglutide, liraglutide, and placebo were visually identical to fulfil the requirements for double-blind procedures. Furthermore, equal volumes of semaglutide, liraglutide, and placebo were administered during treatment ensuring blinding within dose-level. An open-label design was chosen for the semaglutide flexible dose arm of the trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Semaglutide 0.05 mg

Arm description:

Participants received semaglutide 0.05 mg sc injection once daily for 26 weeks.

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

Dosage and administration details:

Participants were administered with semaglutide sc injection in the thigh, abdomen, or upper arm, using a durable pen injector (NovoPen® 4) preferably around the same time of the day irrespective of meals.

Arm title	Semaglutide 0.1 mg

Arm description:

Participants received semaglutide 0.05 mg sc injection once daily for 4 weeks followed by semaglutide 0.1 mg once daily upto week 26.

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

Dosage and administration details:

Participants were administered with semaglutide sc injection in the thigh, abdomen, or upper arm, using a durable pen injector (NovoPen® 4) preferably around the same time of the day irrespective of meals.

Arm title	Semaglutide 0.2 mg

Arm description:

Participants received semaglutide 0.05 mg sc injection once daily for 4 weeks followed by semaglutide 0.1 mg once daily for next 4 weeks and then semaglutide 0.2 mg once daily upto week 26.

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

Dosage and administration details:

Participants were administered with semaglutide sc injection in the thigh, abdomen, or upper arm, using a durable pen injector (NovoPen® 4) preferably around the same time of the day irrespective of meals.

Arm title	Semaglutide 0.3 mg

Arm description:

Participants received semaglutide 0.05 mg sc injection once daily for 4 weeks followed by semaglutide 0.1 mg once daily for next 4 weeks sequentially followed by 0.2 mg once daily for next 4 weeks and then semaglutide 0.3 mg once daily upto week 26.

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

Dosage and administration details:

Participants were administered with semaglutide sc injection in the thigh, abdomen, or upper arm, using a durable pen injector (NovoPen® 4) preferably around the same time of the day irrespective of meals.

Arm title	Liraglutide 0.3 mg

Arm description:

Participants received liraglutide 0.3 mg sc injection once daily for 26 weeks.

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

Dosage and administration details:

Participants were administered with liraglutide sc injection in the thigh, abdomen, or upper arm, using a durable pen injector (NovoPen® 4) preferably around the same time of the day irrespective of meals.

Arm title	Liraglutide 0.6 mg

Arm description:

Participants received liraglutide 0.3 mg sc injection once daily for 4 weeks followed by liraglutide 0.6 mg once daily upto week 26.

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

Dosage and administration details:

Participants were administered with liraglutide sc injection in the thigh, abdomen, or upper arm, using a durable pen injector (NovoPen® 4) preferably around the same time of the day irrespective of meals.

Arm title	Liraglutide 1.2 mg

Arm description:

Participants received liraglutide 0.3 mg sc injection once daily for 4 weeks followed by liraglutide 0.6 mg once daily for next 4 weeks and then liraglutide 1.2 mg once daily upto week 26.

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

Dosage and administration details:

Participants were administered with liraglutide sc injection in the thigh, abdomen, or upper arm, using a durable pen injector (NovoPen® 4) preferably around the same time of the day irrespective of meals.

Arm title	Liraglutide 1.8 mg

Arm description:

Participants received liraglutide 0.3 mg sc injection once daily for 4 weeks followed by liraglutide 0.6 mg once daily for next 4 weeks sequentially followed by liraglutide 1.2 mg once daily for next 4 weeks and then liraglutide 1.8 mg once daily upto week 26.

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

Dosage and administration details:

Participants were administered with liraglutide sc injection in the thigh, abdomen, or upper arm, using a durable pen injector (NovoPen® 4) preferably around the same time of the day irrespective of meals.

Arm title	Placebo

Arm description:

Participants received placebo (equal volumes as semaglutide or liraglutide) sc injection once daily upto 26 weeks.

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

Dosage and administration details:

Participants were administered with placebo sc injection in the thigh, abdomen, or upper arm, using a durable pen injector (NovoPen® 4) preferably around the same time of the day irrespective of meals.

Arm title	Semaglutide flexible

Arm description:

Participants received semaglutide 0.05 mg sc injection once daily for 4 weeks followed by semaglutide 0.1 mg once daily for next 4 weeks sequentially followed by 0.2 mg once daily for next 4 weeks and then semaglutide 0.3 mg once daily upto week 26. Participants were allowed to follow a more flexible dose-escalation regimen. Semaglutide dose levels could be temporarily reduced in participants with poor gastrointestinal tolerability depending on investigator’s assessment.

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

Dosage and administration details:

Participants were administered with semaglutide sc injection in the thigh, abdomen, or upper arm, using

a durable pen injector (NovoPen® 4) preferably around the same time of the day irrespective of meals.

Number of subjects in period 1	Semaglutide 0.05 mg	Semaglutide 0.1 mg	Semaglutide 0.2 mg
Started	64	63	65
Completed	58	61	60
Not completed	6	2	5
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	5	1	3
Unclassified	-	-	-
Lost to follow-up	-	-	2
Missing follow-up information	1	1	-

Number of subjects in period 1	Semaglutide 0.3 mg	Liraglutide 0.3 mg	Liraglutide 0.6 mg
Started	63	64	64
Completed	58	62	61
Not completed	5	2	3
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	2	1	2
Unclassified	-	-	-
Lost to follow-up	3	1	1
Missing follow-up information	-	-	-

Number of subjects in period 1	Liraglutide 1.2 mg	Liraglutide 1.8 mg	Placebo
Started	64	65	129
Completed	58	60	123
Not completed	6	5	6
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	1	3	3
Unclassified	1	-	-
Lost to follow-up	3	1	3
Missing follow-up information	1	-	-

Number of subjects in period 1	Semaglutide flexible
Started	64
Completed	60
Not completed	4

Adverse event, serious fatal	-
Consent withdrawn by subject	1
Unclassified	2
Lost to follow-up	1
Missing follow-up information	-

Baseline characteristics

Reporting groups	
Reporting group title	Semaglutide 0.05 mg
Reporting group description:	
Participants received semaglutide 0.05 mg sc injection once daily for 26 weeks.	
Reporting group title	Semaglutide 0.1 mg
Reporting group description:	
Participants received semaglutide 0.05 mg sc injection once daily for 4 weeks followed by semaglutide 0.1 mg once daily upto week 26.	
Reporting group title	Semaglutide 0.2 mg
Reporting group description:	
Participants received semaglutide 0.05 mg sc injection once daily for 4 weeks followed by semaglutide 0.1 mg once daily for next 4 weeks and then semaglutide 0.2 mg once daily upto week 26.	
Reporting group title	Semaglutide 0.3 mg
Reporting group description:	
Participants received semaglutide 0.05 mg sc injection once daily for 4 weeks followed by semaglutide 0.1 mg once daily for next 4 weeks sequentially followed by 0.2 mg once daily for next 4 weeks and then semaglutide 0.3 mg once daily upto week 26.	
Reporting group title	Liraglutide 0.3 mg
Reporting group description:	
Participants received liraglutide 0.3 mg sc injection once daily for 26 weeks.	
Reporting group title	Liraglutide 0.6 mg
Reporting group description:	
Participants received liraglutide 0.3 mg sc injection once daily for 4 weeks followed by liraglutide 0.6 mg once daily upto week 26.	
Reporting group title	Liraglutide 1.2 mg
Reporting group description:	
Participants received liraglutide 0.3 mg sc injection once daily for 4 weeks followed by liraglutide 0.6 mg once daily for next 4 weeks and then liraglutide 1.2 mg once daily upto week 26.	
Reporting group title	Liraglutide 1.8 mg
Reporting group description:	
Participants received liraglutide 0.3 mg sc injection once daily for 4 weeks followed by liraglutide 0.6 mg once daily for next 4 weeks sequentially followed by liraglutide 1.2 mg once daily for next 4 weeks and then liraglutide 1.8 mg once daily upto week 26.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo (equal volumes as semaglutide or liraglutide) sc injection once daily upto 26 weeks.	
Reporting group title	Semaglutide flexible
Reporting group description:	
Participants received semaglutide 0.05 mg sc injection once daily for 4 weeks followed by semaglutide 0.1 mg once daily for next 4 weeks sequentially followed by 0.2 mg once daily for next 4 weeks and then semaglutide 0.3 mg once daily upto week 26. Participants were allowed to follow a more flexible dose-escalation regimen. Semaglutide dose levels could be temporarily reduced in participants with poor gastrointestinal tolerability depending on investigator’s assessment.	

Reporting group values	Semaglutide 0.05 mg	Semaglutide 0.1 mg	Semaglutide 0.2 mg
Number of subjects	64	63	65
Age categorical Units: Subjects			
Adults (18-64 years)	49	45	44
From 65-84 years	15	18	21

Age Continuous			
Units: years			
arithmetic mean	57.53	57.51	58.37
standard deviation	± 9.8	± 10.0	± 9.58
Gender, Male/Female			
Units: Subjects			
Female	31	28	22
Male	33	35	43
Study Specific Characteristic | glycosylated haemoglobin (HbA1c)			
Units: percentage of HbA1c			
arithmetic mean	7.87	7.91	7.96
standard deviation	± 0.71	± 0.83	± 0.82
Study Specific Characteristic | Fasting plasma glucose			
Units: mmol/L			
arithmetic mean	9.26	8.97	9.20
standard deviation	± 2.60	± 2.22	± 2.28
Study Specific Characteristic | Body weight			
Units: kg			
arithmetic mean	93.44	92.40	98.07
standard deviation	± 18.27	± 17.20	± 17.92
Study Specific Characteristic | Systolic blood pressure			
Units: mmHg			
arithmetic mean	133.70	130.97	131.34
standard deviation	± 15.14	± 14.92	± 12.55
Study Specific Characteristic | Diastolic blood pressure			
Units: mmHg			
arithmetic mean	80.06	79.71	80.48
standard deviation	± 8.90	± 8.56	± 8.87

Reporting group values	Semaglutide 0.3 mg	Liraglutide 0.3 mg	Liraglutide 0.6 mg
Number of subjects	63	64	64
Age categorical			
Units: Subjects			
Adults (18-64 years)	54	47	46
From 65-84 years	9	17	18
Age Continuous			
Units: years			
arithmetic mean	54.76	57.20	59.45
standard deviation	± 9.66	± 10.78	± 9.77
Gender, Male/Female			
Units: Subjects			
Female	31	35	32
Male	32	29	32
Study Specific Characteristic | glycosylated haemoglobin (HbA1c)			
Units: percentage of HbA1c			
arithmetic mean	8.23	8.06	8.12
standard deviation	± 0.80	± 0.86	± 0.81

Study Specific Characteristic | Fasting plasma glucose			
Units: mmol/L			
arithmetic mean	9.67	9.32	9.34
standard deviation	± 2.56	± 2.54	± 2.33
Study Specific Characteristic | Body weight			
Units: kg			
arithmetic mean	94.82	92.25	92.68
standard deviation	± 17.84	± 17.48	± 16.46
Study Specific Characteristic | Systolic blood pressure			
Units: mmHg			
arithmetic mean	132.08	134.02	132.41
standard deviation	± 11.69	± 11.30	± 12.37
Study Specific Characteristic | Diastolic blood pressure			
Units: mmHg			
arithmetic mean	81.41	81.83	81.28
standard deviation	± 8.05	± 6.98	± 6.90

Reporting group values	Liraglutide 1.2 mg	Liraglutide 1.8 mg	Placebo
Number of subjects	64	65	129
Age categorical			
Units: Subjects			
Adults (18-64 years)	54	51	105
From 65-84 years	10	14	24
Age Continuous			
Units: years			
arithmetic mean	53.73	55.82	57.08
standard deviation	± 11.35	± 9.19	± 9.25
Gender, Male/Female			
Units: Subjects			
Female	30	32	57
Male	34	33	72
Study Specific Characteristic | glycosylated haemoglobin (HbA1c)			
Units: percentage of HbA1c			
arithmetic mean	8.14	8.07	8.12
standard deviation	± 0.87	± 0.85	± 0.87
Study Specific Characteristic | Fasting plasma glucose			
Units: mmol/L			
arithmetic mean	9.91	9.18	9.67
standard deviation	± 2.70	± 2.45	± 2.98
Study Specific Characteristic | Body weight			
Units: kg			
arithmetic mean	96.67	93.40	93.98
standard deviation	± 18.28	± 19.34	± 17.75
Study Specific Characteristic | Systolic blood pressure			
Units: mmHg			
arithmetic mean	134.20	131.02	132.17

standard deviation	± 12.73	± 11.86	± 14.26
Study Specific Characteristic | Diastolic blood pressure			
Units: mmHg			
arithmetic mean	82.98	80.66	80.98
standard deviation	± 6.94	± 7.62	± 8.00

Reporting group values	Semaglutide flexible	Total	
Number of subjects	64	705	
Age categorical			
Units: Subjects			
Adults (18-64 years)	55	550	
From 65-84 years	9	155	
Age Continuous			
Units: years			
arithmetic mean	54.81		
standard deviation	± 9.70	-	
Gender, Male/Female			
Units: Subjects			
Female	28	326	
Male	36	379	
Study Specific Characteristic | glycosylated haemoglobin (HbA1c)			
Units: percentage of HbA1c			
arithmetic mean	8.10		
standard deviation	± 0.91	-	
Study Specific Characteristic | Fasting plasma glucose			
Units: mmol/L			
arithmetic mean	9.82		
standard deviation	± 2.66	-	
Study Specific Characteristic | Body weight			
Units: kg			
arithmetic mean	95.29		
standard deviation	± 15.43	-	
Study Specific Characteristic | Systolic blood pressure			
Units: mmHg			
arithmetic mean	132.70		
standard deviation	± 12.74	-	
Study Specific Characteristic | Diastolic blood pressure			
Units: mmHg			
arithmetic mean	81.89		
standard deviation	± 8.40	-	

End points

End points reporting groups

Reporting group title	Semaglutide 0.05 mg
Reporting group description:	
Participants received semaglutide 0.05 mg sc injection once daily for 26 weeks.	
Reporting group title	Semaglutide 0.1 mg
Reporting group description:	
Participants received semaglutide 0.05 mg sc injection once daily for 4 weeks followed by semaglutide 0.1 mg once daily upto week 26.	
Reporting group title	Semaglutide 0.2 mg
Reporting group description:	
Participants received semaglutide 0.05 mg sc injection once daily for 4 weeks followed by semaglutide 0.1 mg once daily for next 4 weeks and then semaglutide 0.2 mg once daily upto week 26.	
Reporting group title	Semaglutide 0.3 mg
Reporting group description:	
Participants received semaglutide 0.05 mg sc injection once daily for 4 weeks followed by semaglutide 0.1 mg once daily for next 4 weeks sequentially followed by 0.2 mg once daily for next 4 weeks and then semaglutide 0.3 mg once daily upto week 26.	
Reporting group title	Liraglutide 0.3 mg
Reporting group description:	
Participants received liraglutide 0.3 mg sc injection once daily for 26 weeks.	
Reporting group title	Liraglutide 0.6 mg
Reporting group description:	
Participants received liraglutide 0.3 mg sc injection once daily for 4 weeks followed by liraglutide 0.6 mg once daily upto week 26.	
Reporting group title	Liraglutide 1.2 mg
Reporting group description:	
Participants received liraglutide 0.3 mg sc injection once daily for 4 weeks followed by liraglutide 0.6 mg once daily for next 4 weeks and then liraglutide 1.2 mg once daily upto week 26.	
Reporting group title	Liraglutide 1.8 mg
Reporting group description:	
Participants received liraglutide 0.3 mg sc injection once daily for 4 weeks followed by liraglutide 0.6 mg once daily for next 4 weeks sequentially followed by liraglutide 1.2 mg once daily for next 4 weeks and then liraglutide 1.8 mg once daily upto week 26.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo (equal volumes as semaglutide or liraglutide) sc injection once daily upto 26 weeks.	
Reporting group title	Semaglutide flexible
Reporting group description:	
Participants received semaglutide 0.05 mg sc injection once daily for 4 weeks followed by semaglutide 0.1 mg once daily for next 4 weeks sequentially followed by 0.2 mg once daily for next 4 weeks and then semaglutide 0.3 mg once daily upto week 26. Participants were allowed to follow a more flexible dose-escalation regimen. Semaglutide dose levels could be temporarily reduced in participants with poor gastrointestinal tolerability depending on investigator’s assessment.	

Primary: Change in HbA1c (Glycosylated haemoglobin)

End point title	Change in HbA1c (Glycosylated haemoglobin)

End point description:

Mean change from baseline in HbA1c at week 26.
The full analysis set (FAS) included all randomised subjects exposed to at least one dose of trial product. Subjects in the FAS would contribute to the evaluation “as randomised”.

Analysis was performed using a mixed model for repeated measurements with treatment, region and stratum as fixed factors and baseline value as covariate, all nested within visit.

End point type	Primary

End point timeframe:

Week 0, week 26

End point values	Semaglutide 0.05 mg	Semaglutide 0.1 mg	Semaglutide 0.2 mg	Semaglutide 0.3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	63	65	63
Units: percentage of HbA1c				
arithmetic mean (standard deviation)	-0.97 (± 0.85)	-1.30 (± 1.03)	-1.65 (± 0.79)	-1.96 (± 0.95)

End point values	Liraglutide 0.3 mg	Liraglutide 0.6 mg	Liraglutide 1.2 mg	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	64	64	65
Units: percentage of HbA1c				
arithmetic mean (standard deviation)	-0.50 (± 0.93)	-0.88 (± 0.90)	-0.86 (± 0.92)	-1.32 (± 0.78)

End point values	Placebo	Semaglutide flexible		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	64		
Units: percentage of HbA1c				
arithmetic mean (standard deviation)	-0.05 (± 0.90)	-1.72 (± 0.97)		

Statistical analyses

Statistical analysis title	Semaglutide 0.05 vs placebo

Statistical analysis description:

Analysis was performed using a mixed model for repeated measurements with treatment, region and stratum as fixed factors and baseline value as covariate, all nested within visit.

Comparison groups	Semaglutide 0.05 mg v Placebo
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-1.04

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.77

Statistical analysis title	Semaglutide 0.1 vs placebo

Statistical analysis description:

Analysis was performed using a mixed model for repeated measurements with treatment, region and stratum as fixed factors and baseline value as covariate, all nested within visit.

Comparison groups	Semaglutide 0.1 mg v Placebo
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.61
upper limit	-1.08

Statistical analysis title	Semaglutide 0.2 vs placebo

Statistical analysis description:

Analysis was performed using a mixed model for repeated measurements with treatment, region and stratum as fixed factors and baseline value as covariate, all nested within visit.

Comparison groups	Semaglutide 0.2 mg v Placebo
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.95
upper limit	-1.42

Statistical analysis title	Semaglutide 0.3 vs placebo

Statistical analysis description:

Analysis was performed using a mixed model for repeated measurements with treatment, region and stratum as fixed factors and baseline value as covariate, all nested within visit.

Comparison groups	Semaglutide 0.3 mg v Placebo
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.12
upper limit	-1.6

Secondary: Change in Fasting plasma glucose (FPG)

End point title	Change in Fasting plasma glucose (FPG)

End point description:

Mean change from baseline in FPG at week 26.
The FAS included all randomised subjects exposed to at least one dose of trial product. Subjects in the FAS would contribute to the evaluation "as randomised".
Analysis was performed using a mixed model for repeated measurements with treatment, region and stratum as fixed factors and baseline value as covariate, all nested within visit.

End point type	Secondary

End point timeframe:

Week 0, Week 26

End point values	Semaglutide 0.05 mg	Semaglutide 0.1 mg	Semaglutide 0.2 mg	Semaglutide 0.3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	63	65	63
Units: mmol/L				
arithmetic mean (standard deviation)	-2.09 (± 1.96)	-2.08 (± 2.23)	-2.64 (± 2.07)	-3.53 (± 2.20)

End point values	Liraglutide 0.3 mg	Liraglutide 0.6 mg	Liraglutide 1.2 mg	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	64	64	65
Units: mmol/L				
arithmetic mean (standard deviation)	-1.33 (± 2.06)	-1.56 (± 1.74)	-1.51 (± 2.41)	-1.92 (± 2.34)

End point values	Placebo	Semaglutide flexible		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	63		
Units: mmol/L				
arithmetic mean (standard deviation)	-0.54 (± 2.45)	-3.40 (± 2.84)		

Statistical analyses

No statistical analyses for this end point

Secondary: Body weight change

End point title	Body weight change

End point description:

Mean change from baseline in body weight at week 26.
The FAS included all randomised subjects exposed to at least one dose of trial product. Subjects in the FAS would contribute to the evaluation "as randomised". Missing data imputed from a mixed model for repeated measures with treatment, region and stratum as fixed factors and baseline value as covariate, all nested within visit.

End point type	Secondary

End point timeframe:

Week 0, Week 26

End point values	Semaglutide 0.05 mg	Semaglutide 0.1 mg	Semaglutide 0.2 mg	Semaglutide 0.3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	63	65	63
Units: kg				
arithmetic mean (standard deviation)	-2.75 (± 2.82)	-4.36 (± 4.24)	-6.70 (± 4.57)	-8.23 (± 5.34)

End point values	Liraglutide 0.3 mg	Liraglutide 0.6 mg	Liraglutide 1.2 mg	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	64	64	65
Units: kg				
arithmetic mean (standard deviation)	-1.48 (± 3.06)	-1.81 (± 3.06)	-1.78 (± 3.41)	-3.68 (± 4.26)

End point values	Placebo	Semaglutide flexible		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	64		
Units: kg				
arithmetic mean (standard deviation)	-1.22 (± 3.42)	-6.60 (± 4.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Systolic and diastolic blood pressure

End point title	Change in Systolic and diastolic blood pressure

End point description:

Mean change from baseline in blood pressure (systolic and diastolic) at week 26.
The FAS included all randomised subjects exposed to at least one dose of trial product. Subjects in the FAS would contribute to the evaluation "as randomised". Missing data imputed from a mixed model for repeated measures with treatment, region and stratum as fixed factors and baseline value as covariate, all nested within visit.

End point type	Secondary

End point timeframe:

Week 0, Week 26

End point values	Semaglutide 0.05 mg	Semaglutide 0.1 mg	Semaglutide 0.2 mg	Semaglutide 0.3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	63	65	63
Units: mmHg				
arithmetic mean (standard deviation)				
Systolicblood pressure	-5.74 (± 12.30)	-2.77 (± 13.21)	-4.25 (± 12.24)	-9.85 (± 11.58)
Diastolic blood pressure	-0.60 (± 8.78)	0.66 (± 8.26)	-1.62 (± 9.38)	-4.02 (± 8.56)

End point values	Liraglutide 0.3 mg	Liraglutide 0.6 mg	Liraglutide 1.2 mg	Liraglutide 1.8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	64	64	65
Units: mmHg				
arithmetic mean (standard deviation)				
Systolicblood pressure	-3.77 (± 9.79)	-3.20 (± 10.89)	-4.69 (± 12.73)	-2.99 (± 11.94)
Diastolic blood pressure	-1.77 (± 7.37)	-1.89 (± 8.20)	-0.60 (± 6.78)	0.63 (± 8.13)

End point values	Placebo	Semaglutide flexible		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	64		

Units: mmHg				
arithmetic mean (standard deviation)				
Systolicblood pressure	-2.34 (± 11.40)	-6.62 (± 14.02)		
Diastolic blood pressure	-0.61 (± 8.50)	-1.69 (± 8.25)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline up to week 33.

Adverse event reporting additional description:

Safety analysis set (SAS) included all randomised subjects exposed to at least one dose of trial product. Subjects in the SAS would contribute to the evaluation "as treated". Treatment-emergent adverse events (TEAEs) were defined as events recorded from baseline and until completion of the post-treatment follow-up visit (7 weeks).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19

Reporting groups

Reporting group title	Sema 0.05 mg
Reporting group description: -	
Reporting group title	Sema 0.10 mg
Reporting group description: -	
Reporting group title	Sema 0.20 mg
Reporting group description: -	
Reporting group title	Sema 0.30 mg
Reporting group description: -	
Reporting group title	Lira 0.30 mg
Reporting group description: -	
Reporting group title	Lira 0.60 mg
Reporting group description: -	
Reporting group title	Lira 1.20 mg
Reporting group description: -	
Reporting group title	Lira 1.80 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Sema flexible

Reporting group description: -

Serious adverse events	Sema 0.05 mg	Sema 0.10 mg	Sema 0.20 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 64 (10.94%)	3 / 63 (4.76%)	2 / 65 (3.08%)
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)			
Adenocarcinoma of colon			

subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Pancreatic carcinoma			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Spinal meningioma benign			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 65 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Surgical and medical procedures			
Coronary revascularisation			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 65 (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
Endarterectomy			

subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 65 (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
Percutaneous coronary intervention			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 65 (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
Stent placement			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Vascular graft			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Uterine polyp			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			

subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Pulmonary oedema			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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			
Catheterisation cardiac			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystoscopy			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 65 (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
Atrioventricular block complete			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Bundle branch block left			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Myocardial infarction			

subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Ventricular fibrillation			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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			
Carotid artery stenosis			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 65 (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
Ischaemic stroke			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Seizure			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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			
Retinal detachment			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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			
Anal fistula			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	0 / 65 (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

Epiploic appendagitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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			
Back pain			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Dupuytren's contracture			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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			
Diverticulitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Escherichia pyelonephritis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	0 / 65 (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
Gastroenteritis viral			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Pharyngitis			

subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	0 / 65 (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
Sepsis			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 65 (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
Viral infection			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	0 / 65 (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

Serious adverse events	Sema 0.30 mg	Lira 0.30 mg	Lira 0.60 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 63 (3.17%)	1 / 64 (1.56%)	2 / 64 (3.13%)
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)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Pancreatic carcinoma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Prostate cancer			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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

Spinal meningioma benign			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Surgical and medical procedures			
Coronary revascularisation			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Endarterectomy			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Percutaneous coronary intervention			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Stent placement			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Vascular graft			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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

Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 64 (1.56%)	0 / 64 (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
Uterine polyp			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Pulmonary oedema			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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			
Catheterisation cardiac			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Cystoscopy			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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			

Acute myocardial infarction			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Atrioventricular block complete			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	0 / 64 (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
Bundle branch block left			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Coronary artery disease			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Myocardial infarction			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Ventricular fibrillation			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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			
Carotid artery stenosis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Ischaemic stroke			

subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Seizure			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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			
Anal fistula			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Epiploic appendagitis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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			
Back pain			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Dupuytren's contracture			

subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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			
Diverticulitis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Escherichia pyelonephritis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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 viral			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Pharyngitis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Sepsis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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
Viral infection			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	0 / 64 (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	Lira 1.20 mg	Lira 1.80 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 64 (3.13%)	7 / 65 (10.77%)	4 / 129 (3.10%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 64 (0.00%)	1 / 65 (1.54%)	0 / 129 (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
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Pancreatic carcinoma			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Prostate cancer			
subjects affected / exposed	0 / 64 (0.00%)	1 / 65 (1.54%)	0 / 129 (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
Spinal meningioma benign			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Coronary revascularisation			

subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Endarterectomy			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Percutaneous coronary intervention			
subjects affected / exposed	1 / 64 (1.56%)	0 / 65 (0.00%)	0 / 129 (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
Stent placement			
subjects affected / exposed	0 / 64 (0.00%)	1 / 65 (1.54%)	0 / 129 (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
Vascular graft			
subjects affected / exposed	0 / 64 (0.00%)	1 / 65 (1.54%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Uterine polyp			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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

Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	1 / 64 (1.56%)	0 / 65 (0.00%)	0 / 129 (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
Investigations			
Catheterisation cardiac			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Cystoscopy			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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			
Acute myocardial infarction			
subjects affected / exposed	1 / 64 (1.56%)	1 / 65 (1.54%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Bundle branch block left			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Coronary artery disease			

subjects affected / exposed	0 / 64 (0.00%)	1 / 65 (1.54%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 64 (0.00%)	1 / 65 (1.54%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	1 / 64 (1.56%)	0 / 65 (0.00%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Ischaemic stroke			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Seizure			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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			
Retinal detachment			
subjects affected / exposed	1 / 64 (1.56%)	0 / 65 (0.00%)	0 / 129 (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
Gastrointestinal disorders			

Anal fistula			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Epiploic appendagitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 64 (0.00%)	1 / 65 (1.54%)	0 / 129 (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
Dupuytren's contracture			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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			
Diverticulitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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
Escherichia pyelonephritis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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 viral			

subjects affected / exposed	0 / 64 (0.00%)	1 / 65 (1.54%)	0 / 129 (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
Pharyngitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 64 (0.00%)	0 / 65 (0.00%)	0 / 129 (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 flexible		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 64 (6.25%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatic carcinoma			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Prostate cancer			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal meningioma benign			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Coronary revascularisation			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endarterectomy			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Percutaneous coronary intervention			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stent placement			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Vascular graft			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine polyp			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Catheterisation cardiac			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cystoscopy			

subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bundle branch block left			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ventricular fibrillation			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Carotid artery stenosis				
subjects affected / exposed	0 / 64 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 64 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Retinal detachment				
subjects affected / exposed	0 / 64 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Anal fistula				
subjects affected / exposed	0 / 64 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epiploic appendagitis				
subjects affected / exposed	0 / 64 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Goitre				
subjects affected / exposed	0 / 64 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				

subjects affected / exposed	0 / 64 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dupuytren's contracture				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Diverticulitis				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia pyelonephritis				
subjects affected / exposed	0 / 64 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	0 / 64 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed	0 / 64 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 64 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	0 / 64 (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 0.05 mg	Sema 0.10 mg	Sema 0.20 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 64 (50.00%)	34 / 63 (53.97%)	39 / 65 (60.00%)
Investigations			
Lipase increased			
subjects affected / exposed	3 / 64 (4.69%)	3 / 63 (4.76%)	3 / 65 (4.62%)
occurrences (all)	3	3	3
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 64 (3.13%)	4 / 63 (6.35%)	2 / 65 (3.08%)
occurrences (all)	2	4	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 64 (3.13%)	4 / 63 (6.35%)	2 / 65 (3.08%)
occurrences (all)	4	6	2
Headache			
subjects affected / exposed	7 / 64 (10.94%)	8 / 63 (12.70%)	4 / 65 (6.15%)
occurrences (all)	17	30	13
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 64 (3.13%)	1 / 63 (1.59%)	4 / 65 (6.15%)
occurrences (all)	2	1	4
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 64 (3.13%)	3 / 63 (4.76%)	1 / 65 (1.54%)
occurrences (all)	2	4	1
Abdominal pain			
subjects affected / exposed	2 / 64 (3.13%)	2 / 63 (3.17%)	3 / 65 (4.62%)
occurrences (all)	4	4	7
Abdominal pain upper			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	4 / 65 (6.15%)
occurrences (all)	0	1	5
Constipation			

subjects affected / exposed	2 / 64 (3.13%)	4 / 63 (6.35%)	6 / 65 (9.23%)
occurrences (all)	2	4	11
Diarrhoea			
subjects affected / exposed	7 / 64 (10.94%)	10 / 63 (15.87%)	10 / 65 (15.38%)
occurrences (all)	10	13	15
Dyspepsia			
subjects affected / exposed	1 / 64 (1.56%)	5 / 63 (7.94%)	5 / 65 (7.69%)
occurrences (all)	6	7	8
Flatulence			
subjects affected / exposed	2 / 64 (3.13%)	1 / 63 (1.59%)	4 / 65 (6.15%)
occurrences (all)	2	5	6
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 64 (0.00%)	4 / 63 (6.35%)	3 / 65 (4.62%)
occurrences (all)	0	8	3
Nausea			
subjects affected / exposed	11 / 64 (17.19%)	12 / 63 (19.05%)	14 / 65 (21.54%)
occurrences (all)	16	20	22
Vomiting			
subjects affected / exposed	6 / 64 (9.38%)	4 / 63 (6.35%)	6 / 65 (9.23%)
occurrences (all)	10	13	9
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 64 (1.56%)	1 / 63 (1.59%)	0 / 65 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal pain			
subjects affected / exposed	2 / 64 (3.13%)	2 / 63 (3.17%)	0 / 65 (0.00%)
occurrences (all)	3	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 64 (4.69%)	0 / 63 (0.00%)	3 / 65 (4.62%)
occurrences (all)	3	0	3
Back pain			
subjects affected / exposed	3 / 64 (4.69%)	4 / 63 (6.35%)	2 / 65 (3.08%)
occurrences (all)	3	4	2
Muscle spasms			

subjects affected / exposed	1 / 64 (1.56%)	1 / 63 (1.59%)	0 / 65 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	7 / 64 (10.94%)	6 / 63 (9.52%)	4 / 65 (6.15%)
occurrences (all)	12	7	4
Sinusitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 63 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	7 / 64 (10.94%)	2 / 63 (3.17%)	1 / 65 (1.54%)
occurrences (all)	8	2	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 64 (4.69%)	7 / 63 (11.11%)	6 / 65 (9.23%)
occurrences (all)	3	7	6
Hyperglycaemia			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	1 / 65 (1.54%)
occurrences (all)	1	0	1

Non-serious adverse events	Sema 0.30 mg	Lira 0.30 mg	Lira 0.60 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 63 (66.67%)	35 / 64 (54.69%)	28 / 64 (43.75%)
Investigations			
Lipase increased			
subjects affected / exposed	3 / 63 (4.76%)	3 / 64 (4.69%)	3 / 64 (4.69%)
occurrences (all)	3	4	5
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 63 (0.00%)	3 / 64 (4.69%)	0 / 64 (0.00%)
occurrences (all)	0	3	0
Nervous system disorders			
Dizziness			

subjects affected / exposed	3 / 63 (4.76%)	0 / 64 (0.00%)	3 / 64 (4.69%)
occurrences (all)	4	0	4
Headache			
subjects affected / exposed	7 / 63 (11.11%)	5 / 64 (7.81%)	3 / 64 (4.69%)
occurrences (all)	11	7	11
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	4 / 64 (6.25%)
occurrences (all)	1	0	5
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 63 (3.17%)	1 / 64 (1.56%)	3 / 64 (4.69%)
occurrences (all)	3	1	5
Abdominal pain			
subjects affected / exposed	5 / 63 (7.94%)	3 / 64 (4.69%)	0 / 64 (0.00%)
occurrences (all)	6	3	0
Abdominal pain upper			
subjects affected / exposed	4 / 63 (6.35%)	1 / 64 (1.56%)	2 / 64 (3.13%)
occurrences (all)	4	2	2
Constipation			
subjects affected / exposed	5 / 63 (7.94%)	0 / 64 (0.00%)	3 / 64 (4.69%)
occurrences (all)	7	0	3
Diarrhoea			
subjects affected / exposed	16 / 63 (25.40%)	5 / 64 (7.81%)	5 / 64 (7.81%)
occurrences (all)	29	5	9
Dyspepsia			
subjects affected / exposed	6 / 63 (9.52%)	2 / 64 (3.13%)	3 / 64 (4.69%)
occurrences (all)	6	2	3
Flatulence			
subjects affected / exposed	1 / 63 (1.59%)	0 / 64 (0.00%)	2 / 64 (3.13%)
occurrences (all)	1	0	3
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 63 (4.76%)	0 / 64 (0.00%)	2 / 64 (3.13%)
occurrences (all)	3	0	2
Nausea			

subjects affected / exposed	16 / 63 (25.40%)	6 / 64 (9.38%)	7 / 64 (10.94%)
occurrences (all)	22	7	11
Vomiting			
subjects affected / exposed	6 / 63 (9.52%)	1 / 64 (1.56%)	7 / 64 (10.94%)
occurrences (all)	8	1	10
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 63 (1.59%)	3 / 64 (4.69%)	4 / 64 (6.25%)
occurrences (all)	1	4	5
Oropharyngeal pain			
subjects affected / exposed	1 / 63 (1.59%)	2 / 64 (3.13%)	4 / 64 (6.25%)
occurrences (all)	1	2	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 63 (6.35%)	1 / 64 (1.56%)	0 / 64 (0.00%)
occurrences (all)	4	1	0
Back pain			
subjects affected / exposed	2 / 63 (3.17%)	3 / 64 (4.69%)	2 / 64 (3.13%)
occurrences (all)	4	3	2
Muscle spasms			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	4 / 64 (6.25%)
occurrences (all)	0	0	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 63 (3.17%)	1 / 64 (1.56%)	1 / 64 (1.56%)
occurrences (all)	2	1	1
Nasopharyngitis			
subjects affected / exposed	5 / 63 (7.94%)	4 / 64 (6.25%)	3 / 64 (4.69%)
occurrences (all)	6	5	3
Sinusitis			
subjects affected / exposed	1 / 63 (1.59%)	5 / 64 (7.81%)	2 / 64 (3.13%)
occurrences (all)	1	5	2
Upper respiratory tract infection			
subjects affected / exposed	7 / 63 (11.11%)	6 / 64 (9.38%)	1 / 64 (1.56%)
occurrences (all)	7	6	1
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	8 / 63 (12.70%)	2 / 64 (3.13%)	1 / 64 (1.56%)
occurrences (all)	8	3	1
Hyperglycaemia			
subjects affected / exposed	0 / 63 (0.00%)	2 / 64 (3.13%)	3 / 64 (4.69%)
occurrences (all)	0	3	6

Non-serious adverse events	Lira 1.20 mg	Lira 1.80 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 64 (59.38%)	35 / 65 (53.85%)	61 / 129 (47.29%)
Investigations			
Lipase increased			
subjects affected / exposed	4 / 64 (6.25%)	7 / 65 (10.77%)	4 / 129 (3.10%)
occurrences (all)	5	7	4
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 64 (4.69%)	3 / 65 (4.62%)	3 / 129 (2.33%)
occurrences (all)	3	3	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 64 (1.56%)	4 / 65 (6.15%)	3 / 129 (2.33%)
occurrences (all)	1	5	3
Headache			
subjects affected / exposed	10 / 64 (15.63%)	4 / 65 (6.15%)	3 / 129 (2.33%)
occurrences (all)	16	8	3
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 64 (1.56%)	2 / 65 (3.08%)	3 / 129 (2.33%)
occurrences (all)	1	2	3
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 64 (3.13%)	4 / 65 (6.15%)	3 / 129 (2.33%)
occurrences (all)	2	13	4
Abdominal pain			
subjects affected / exposed	4 / 64 (6.25%)	0 / 65 (0.00%)	1 / 129 (0.78%)
occurrences (all)	4	0	1
Abdominal pain upper			

subjects affected / exposed	2 / 64 (3.13%)	3 / 65 (4.62%)	3 / 129 (2.33%)
occurrences (all)	2	4	3
Constipation			
subjects affected / exposed	1 / 64 (1.56%)	7 / 65 (10.77%)	4 / 129 (3.10%)
occurrences (all)	2	7	4
Diarrhoea			
subjects affected / exposed	5 / 64 (7.81%)	8 / 65 (12.31%)	14 / 129 (10.85%)
occurrences (all)	8	16	18
Dyspepsia			
subjects affected / exposed	1 / 64 (1.56%)	3 / 65 (4.62%)	1 / 129 (0.78%)
occurrences (all)	1	3	1
Flatulence			
subjects affected / exposed	2 / 64 (3.13%)	1 / 65 (1.54%)	1 / 129 (0.78%)
occurrences (all)	3	2	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 64 (1.56%)	1 / 65 (1.54%)	1 / 129 (0.78%)
occurrences (all)	1	1	1
Nausea			
subjects affected / exposed	7 / 64 (10.94%)	13 / 65 (20.00%)	6 / 129 (4.65%)
occurrences (all)	11	18	7
Vomiting			
subjects affected / exposed	1 / 64 (1.56%)	5 / 65 (7.69%)	3 / 129 (2.33%)
occurrences (all)	1	8	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 64 (4.69%)	1 / 65 (1.54%)	5 / 129 (3.88%)
occurrences (all)	3	2	6
Oropharyngeal pain			
subjects affected / exposed	2 / 64 (3.13%)	0 / 65 (0.00%)	2 / 129 (1.55%)
occurrences (all)	2	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 64 (3.13%)	1 / 65 (1.54%)	6 / 129 (4.65%)
occurrences (all)	2	1	7
Back pain			

subjects affected / exposed	3 / 64 (4.69%)	4 / 65 (6.15%)	3 / 129 (2.33%)
occurrences (all)	3	4	3
Muscle spasms			
subjects affected / exposed	0 / 64 (0.00%)	1 / 65 (1.54%)	2 / 129 (1.55%)
occurrences (all)	0	1	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 64 (3.13%)	4 / 65 (6.15%)	3 / 129 (2.33%)
occurrences (all)	2	4	3
Nasopharyngitis			
subjects affected / exposed	5 / 64 (7.81%)	5 / 65 (7.69%)	7 / 129 (5.43%)
occurrences (all)	7	6	9
Sinusitis			
subjects affected / exposed	2 / 64 (3.13%)	1 / 65 (1.54%)	2 / 129 (1.55%)
occurrences (all)	2	1	2
Upper respiratory tract infection			
subjects affected / exposed	2 / 64 (3.13%)	5 / 65 (7.69%)	9 / 129 (6.98%)
occurrences (all)	3	6	11
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 64 (4.69%)	3 / 65 (4.62%)	1 / 129 (0.78%)
occurrences (all)	3	3	1
Hyperglycaemia			
subjects affected / exposed	3 / 64 (4.69%)	0 / 65 (0.00%)	11 / 129 (8.53%)
occurrences (all)	3	0	11

Non-serious adverse events	Sema flexible		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 64 (68.75%)		
Investigations			
Lipase increased			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	5		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		

Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	8		
Headache			
subjects affected / exposed	7 / 64 (10.94%)		
occurrences (all)	14		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	4		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	4		
Abdominal pain			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	7		
Abdominal pain upper			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	8		
Constipation			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	6		
Diarrhoea			
subjects affected / exposed	11 / 64 (17.19%)		
occurrences (all)	22		
Dyspepsia			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	4		
Flatulence			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	9		
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	5		

Nausea			
subjects affected / exposed	25 / 64 (39.06%)		
occurrences (all)	35		
Vomiting			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	8		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences (all)	3		
Oropharyngeal pain			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	5		
Muscle spasms			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	10 / 64 (15.63%)		
occurrences (all)	11		
Sinusitis			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	6		

Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all)	 9 / 64 (14.06%) 9 0 / 64 (0.00%) 0		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Not applicable

Notes: