Clinical trial results:
Efficacy and safety of semaglutide once-weekly versus sitagliptin once daily as add-on to metformin and/or thiazolidinedione (TZD) in subjects with type 2 diabetes

Summary

EudraCT number	2012-004827-19
Trial protocol	SE BG PT ES HU CZ NO
Global end of trial date	12 October 2015

Results information

Result version number	v1 (current)
This version publication date	05 November 2016
First version publication date	05 November 2016

Trial information

Trial identification

Sponsor protocol code	NN9535-3626

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01930188
WHO universal trial number (UTN)	U1111-1135-8730

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Vandtaarnsvej 114, VTB, Soeborg, Denmark, DK2860
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	20 July 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 October 2015
Global end of trial reached?	Yes
Global end of trial date	12 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the effect of once-weekly dosing of two dose levels of semaglutide versus sitagliptin 100 mg once-daily on glycaemic control after 56 weeks of treatment.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki, ICH Good Clinical Practice and FDA 21 CFR 312.50 and 56.

Background therapy:

The following compounds were considered as background medication:
• Metformin
• Thiazolidinedione (TZD) (pioglitazone and rosiglitazone)

Subjects were on stable treatment for at least 90 days prior to screening with either metformin ≥ 1500 mg (or maximum tolerated dose), pioglitazone ≥ 30 mg (or maximum tolerated dose), rosiglitazone ≥ 4 mg (or maximum tolerated dose) or a combination of either metformin/pioglitazone or metformin/rosiglitazone (doses as for individual therapies).

Subjects upon inclusion continued pre-trial background medication throughout the entire trial. The background medication were maintained at the stable, pre-trial dose and frequency during the whole treatment period unless rescue medication was needed.

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?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 65
Country: Number of subjects enrolled	Bulgaria: 99
Country: Number of subjects enrolled	Czech Republic: 49
Country: Number of subjects enrolled	Spain: 69
Country: Number of subjects enrolled	Hong Kong: 18
Country: Number of subjects enrolled	Hungary: 46
Country: Number of subjects enrolled	India: 93
Country: Number of subjects enrolled	Japan: 140
Country: Number of subjects enrolled	Mexico: 63
Country: Number of subjects enrolled	Norway: 32
Country: Number of subjects enrolled	Portugal: 15

Country: Number of subjects enrolled	Romania: 60
Country: Number of subjects enrolled	Russian Federation: 133
Country: Number of subjects enrolled	Sweden: 58
Country: Number of subjects enrolled	Thailand: 39
Country: Number of subjects enrolled	Turkey: 87
Country: Number of subjects enrolled	Ukraine: 81
Country: Number of subjects enrolled	South Africa: 78
Worldwide total number of subjects	1225
EEA total number of subjects	428

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)	993
From 65 to 84 years	232
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 124 sites in 18 countries: Argentina: 4; Bulgaria: 10; Czech Republic: 5; Hong Kong: 1; Hungary: 4; India: 11; Japan: 14; Mexico: 5 Norway: 5; Portugal: 6; Romania: 5; Russian Federation: 17; South Africa: 7; Spain: 7: Sweden: 4; Thailand: 4; Turkey: 9; and Ukraine: 6 sites.

Pre-assignment

Screening details:

Not applicable

Period 1

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

Blinding implementation details:

Semaglutide and semaglutide placebo were supplied in similar 1.5 mL pre-filled PDS290 pen-injectors which were visually identical, and were packaged and labelled to fulfil the requirements for double-blind procedures. Equal volumes of semaglutide and semaglutide placebo were administered during treatment, further ensuring blinding during the trial. Sitagliptin and sitagliptin placebo were identical in appearance and were packaged and labelled as per requirements for double-blind procedures.

Arms

Are arms mutually exclusive?	Yes
Arm title	Semaglutide 0.5 mg + Sitagliptin placebo

Arm description:

Semaglutide 0.5 mg administered subcutaneously (s.c., under the skin) once weekly, in the thigh, abdomen, or upper arm, at any time of day irrespective of meals. Sitagliptin placebo (0 mg) administered orally once daily.

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

Dosage and administration details:

Semaglutide (0.5 mg) was administered in the thigh, abdomen, or upper arm, at any time of the day irrespective of meals. The maintenance dose of 0.5 mg was reached after four doses (4 weeks) of 0.25 mg. The maintenance dose of 1.0 mg was reached after four doses (4 weeks) of 0.25 mg, followed by four doses (4 weeks) of 0.5 mg. After the maintenance dose was reached, the dose was not to be changed during the remainder of the trial.

Investigational medicinal product name	Sitagliptin placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Sitagliptin placebo was provided as 100 mg tablets and administered orally once daily at any time of the day irrespective of meals.

Arm title	Semaglutide 1.0 mg + Sitagliptin placebo

Arm description:

Semaglutide 1.0 mg administered subcutaneously (s.c., under the skin) once weekly, in the thigh,

abdomen, or upper arm, at any time of day irrespective of meals. Sitagliptin placebo (0 mg) administered orally once daily.

Arm type	Experimental
Investigational medicinal product name	Sitagliptin placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Sitagliptin placebo was provided as tablets and administered orally once daily at any time of the day

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

Dosage and administration details:

Semaglutide 1.0 mg was administered in the thigh, abdomen, or upper arm, at any time of the day irrespective of meals. The maintenance dose of 1.0 mg was reached after four doses (4 weeks) of 0.25 mg, followed by four doses (4 weeks) of 0.5 mg. After the maintenance dose was reached, the dose was not to be changed during the remainder of the trial.

Arm title	Sitagliptin + Semaglutide placebo

Arm description:

Subjects were randomised to 2 different sitagliptin arms (sitagliptin + semaglutide placebo 0.5 mg and sitagliptin + semaglutide placebo 1.0 mg). Both arms were pooled together for data analysis. Semaglutide placebo administered subcutaneously (s.c., under the skin) once weekly, in the thigh, abdomen, or upper arm, at any time of day irrespective of meals. Sitagliptin (100 mg) administered orally once daily.

Arm type	Active comparator
Investigational medicinal product name	Semaglutide placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Semaglutide placebo was administered in the thigh, abdomen, or upper arm, at any time of the day

Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	Januvia
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Sitagliptin was provided as 100 mg tablets and administered orally once daily at any time of the day irrespective of meals.

Number of subjects in period 1	Semaglutide 0.5 mg + Sitagliptin placebo	Semaglutide 1.0 mg + Sitagliptin placebo	Sitagliptin + Semaglutide placebo
Started	409	409	407
Premature discontinuation of treatment	53 [1]	61 [2]	32 [3]
Completed	387	388	388
Not completed	22	21	19
Not completed	22	21	19

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This number represents only those participants who prematurely discontinued the treatment. However, subjects who prematurely discontinued treatment were allowed to continue participation in the trial.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This number represents only those participants who prematurely discontinued the treatment. However, subjects who prematurely discontinued treatment were allowed to continue participation in the trial.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This number represents only those participants who prematurely discontinued the treatment. However, subjects who prematurely discontinued treatment were allowed to continue participation in the trial.

Baseline characteristics

Reporting groups	
Reporting group title	Semaglutide 0.5 mg + Sitagliptin placebo
Reporting group description:	
Semaglutide 0.5 mg administered subcutaneously (s.c., under the skin) once weekly, in the thigh, abdomen, or upper arm, at any time of day irrespective of meals. Sitagliptin placebo (0 mg) administered orally once daily.	
Reporting group title	Semaglutide 1.0 mg + Sitagliptin placebo
Reporting group description:	
Semaglutide 1.0 mg administered subcutaneously (s.c., under the skin) once weekly, in the thigh, abdomen, or upper arm, at any time of day irrespective of meals. Sitagliptin placebo (0 mg) administered orally once daily.	
Reporting group title	Sitagliptin + Semaglutide placebo
Reporting group description:	
Subjects were randomised to 2 different sitagliptin arms (sitagliptin + semaglutide placebo 0.5 mg and sitagliptin + semaglutide placebo 1.0 mg). Both arms were pooled together for data analysis. Semaglutide placebo administered subcutaneously (s.c., under the skin) once weekly, in the thigh, abdomen, or upper arm, at any time of day irrespective of meals. Sitagliptin (100 mg) administered orally once daily.	

Reporting group values	Semaglutide 0.5 mg + Sitagliptin placebo	Semaglutide 1.0 mg + Sitagliptin placebo	Sitagliptin + Semaglutide placebo
Number of subjects	409	409	407
Age Categorical			
Units: Subjects			
Adults (18-64 years)	333	332	328
Elderly (From 65-84 years)	76	77	79
Age Continuous			
Units: years			
arithmetic mean	54.8	56	54.6
standard deviation	± 10.2	± 9.4	± 10.4
Gender Categorical			
Units: Subjects			
Female	202	204	199
Male	207	205	208
HbA1c			
Units: percentage			
arithmetic mean	8.01	8.04	8.17
standard deviation	± 0.92	± 0.93	± 0.92
Body Weight			
Units: kilograms			
arithmetic mean	89.93	89.21	89.29
standard deviation	± 20.39	± 20.74	± 19.67
Fasting Plasma Glucose			
Units: mmol/L			
arithmetic mean	9.33	9.29	9.6
standard deviation	± 2.38	± 2.22	± 2.16
Diastolic Blood Pressure			
Units: mmHg			
arithmetic mean	80.63	80.87	80.48
standard deviation	± 9.76	± 9.08	± 8.7

Systolic Blood Pressure			
Units: mmHg			
arithmetic mean	132.73	132.56	132.66
standard deviation	± 16.09	± 13.93	± 14.58

Reporting group values	Total		
Number of subjects	1225		
Age Categorical			
Units: Subjects			
Adults (18-64 years)	993		
Elderly (From 65-84 years)	232		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Units: Subjects			
Female	605		
Male	620		
HbA1c			
Units: percentage			
arithmetic mean			
standard deviation	-		
Body Weight			
Units: kilograms			
arithmetic mean			
standard deviation	-		
Fasting Plasma Glucose			
Units: mmol/L			
arithmetic mean			
standard deviation	-		
Diastolic Blood Pressure			
Units: mmHg			
arithmetic mean			
standard deviation	-		
Systolic Blood Pressure			
Units: mmHg			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Semaglutide 0.5 mg + Sitagliptin placebo
Reporting group description:	
Semaglutide 0.5 mg administered subcutaneously (s.c., under the skin) once weekly, in the thigh, abdomen, or upper arm, at any time of day irrespective of meals. Sitagliptin placebo (0 mg) administered orally once daily.	
Reporting group title	Semaglutide 1.0 mg + Sitagliptin placebo
Reporting group description:	
Semaglutide 1.0 mg administered subcutaneously (s.c., under the skin) once weekly, in the thigh, abdomen, or upper arm, at any time of day irrespective of meals. Sitagliptin placebo (0 mg) administered orally once daily.	
Reporting group title	Sitagliptin + Semaglutide placebo
Reporting group description:	
Subjects were randomised to 2 different sitagliptin arms (sitagliptin + semaglutide placebo 0.5 mg and sitagliptin + semaglutide placebo 1.0 mg). Both arms were pooled together for data analysis. Semaglutide placebo administered subcutaneously (s.c., under the skin) once weekly, in the thigh, abdomen, or upper arm, at any time of day irrespective of meals. Sitagliptin (100 mg) administered orally once daily.	

Primary: Change in HbA1c

End point title	Change in HbA1c
End point description:	
Change in glycosylated haemoglobin (HbA1c) from baseline to week 56. Full analysis set (FAS=1225) included all randomised subjects who had received at least one dose of semaglutide or sitagliptin. Missing data imputed from a mixed model for repeated measurements for treatment and country as fixed factors and baseline value as covariate, all nested within visit.	
End point type	Primary
End point timeframe:	
From Baseline to week 56	

End point values	Semaglutide 0.5 mg + Sitagliptin placebo	Semaglutide 1.0 mg + Sitagliptin placebo	Sitagliptin + Semaglutide placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	409	409	407	
Units: Percentage				
least squares mean (standard error)	-1.32 (± 0.05)	-1.61 (± 0.05)	-0.55 (± 0.05)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The post-baseline responses are analysed using a mixed model for repeated measurements with treatment and country as fixed factors and baseline value as covariate, all nested within visit

Comparison groups	Semaglutide 1.0 mg + Sitagliptin placebo v Sitagliptin + Semaglutide placebo
Number of subjects included in analysis	816
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.21
upper limit	-0.91

Notes:

[1] - Non-inferiority was concluded if the upper limit of the two-sided 95% confidence interval for the estimated treatment difference between semaglutide 1.0 mg and sitagliptin was below the pre-specified non-inferiority margin (0.3 %)

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The post-baseline responses are analysed using a mixed model for repeated measurements with treatment and country as fixed factors and baseline value as covariate, all nested within visit

Comparison groups	Semaglutide 0.5 mg + Sitagliptin placebo v Sitagliptin + Semaglutide placebo
Number of subjects included in analysis	816
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	-0.62

Notes:

[2] - Non-inferiority was concluded if the upper limit of the two-sided 95% confidence interval for the estimated treatment difference between semaglutide 0.5 mg and sitagliptin was below the pre-specified non-inferiority margin (0.3 %)

Secondary: Change in Body Weight

End point title	Change in Body Weight

End point description:

Change in body weight from baseline to week 56. Full analysis set (FAS=1225) included all randomised subjects who had received at least one dose of semaglutide or sitagliptin. Missing data imputed from a mixed model for repeated measurements for treatment and country as fixed factors and baseline value as covariate, all nested within visit.

End point type	Secondary

End point timeframe:

From baseline to week 56

End point values	Semaglutide 0.5 mg + Sitagliptin placebo	Semaglutide 1.0 mg + Sitagliptin placebo	Sitagliptin + Semaglutide placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	409	409	407	
Units: kilogram(s)				
least squares mean (standard error)	-4.28 (± 0.25)	-6.13 (± 0.25)	-1.93 (± 0.26)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Fasting Plasma Glucose

End point title	Change in Fasting Plasma Glucose

End point description:

Change in fasting plasma glucose from baseline to week 56. Full analysis set (FAS=1225) included all randomised subjects who had received at least one dose of semaglutide or sitagliptin. Missing data imputed from a mixed model for repeated measurements for treatment and country as fixed factors and baseline value as covariate, all nested within visit.

End point type	Secondary

End point timeframe:

From baseline to week 56

End point values	Semaglutide 0.5 mg + Sitagliptin placebo	Semaglutide 1.0 mg + Sitagliptin placebo	Sitagliptin + Semaglutide placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	409	409	407	
Units: mg/dL				
least squares mean (standard error)	-37.38 (± 1.79)	-46.72 (± 1.78)	-19.85 (± 1.88)	

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:

Change in diastolic and systolic blood pressure from baseline to week 56. Full analysis set (FAS=1225) included all randomised subjects who had received at least one dose of semaglutide or sitagliptin.

Missing data imputed from a mixed model for repeated measurements for treatment and country as fixed factors and baseline value as covariate, all nested within visit.

End point type	Secondary

End point timeframe:

From baseline to week 56

End point values	Semaglutide 0.5 mg + Sitagliptin placebo	Semaglutide 1.0 mg + Sitagliptin placebo	Sitagliptin + Semaglutide placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	409	409	407	
Units: mmHg				
least squares mean (standard error)				
Systolic blood presuure	-5.07 (± 0.64)	-5.61 (± 0.63)	-2.29 (± 0.67)	
Diastolic blood pressure	-2.01 (± 0.42)	-1.91 (± 0.42)	-1.11 (± 0.44)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Patient Reported Outcome (PRO) questionnaire Diabetes Treatment Satisfaction Questionnaire status (DTSQs)

End point title	Change in Patient Reported Outcome (PRO) questionnaire Diabetes Treatment Satisfaction Questionnaire status (DTSQs)

End point description:

Full analysis set (FAS=1225) included all randomised subjects who had received at least one dose of semaglutide or sitagliptin. Of the 1225 subjects in FAS, 76 in semaglutide 0.5 mg arm, 76 in semaglutide 1.0 mg arm, and 113 in placebo arm had missing data for the endpoint. Missing data imputed from a mixed model for repeated measurements for treatment and country as fixed factors and baseline value as covariate, all nested within visit. The DTSQs questionnaire was used to assess subjects' treatment satisfaction and contained 8 components and evaluates the diabetes treatment (including insulin, tablets and/or diet) in terms of convenience, flexibility and general feelings towards the treatment. The result presented is the 'Treatment Satisfaction' summary score, which is the sum of 6 of the 8 items of the DTSQs questionnaire. Response options range from 6 (best case) to 0 (worst case). Total scores for treatment satisfaction range from 0-36. Higher scores indicate higher satisfaction.

End point type	Secondary

End point timeframe:

From baseline to week 56

End point values	Semaglutide 0.5 mg + Sitagliptin placebo	Semaglutide 1.0 mg + Sitagliptin placebo	Sitagliptin + Semaglutide placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	333	333	294	
Units: Units on a scale				
least squares mean (standard error)	5.28 (± 0.23)	5.91 (± 0.23)	4.45 (± 0.24)	

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects who achieve HbA1c ≤6.5% (48 mmol/mol) American Association of Clinical Endocrinologists (AACE) target (yes/no)

End point title	Subjects who achieve HbA1c ≤6.5% (48 mmol/mol) American Association of Clinical Endocrinologists (AACE) target (yes/no)

End point description:

Subjects who achieved HbA1c ≤6.5% (48 mmol/mol) American Association of Clinical Endocrinologists (AACE) target (yes/no) after week 56 weeks of treatment. Full analysis set (FAS=1225) included all randomised subjects who had received at least one dose of semaglutide or sitagliptin. All 1225 subjects included in the FAS contributed to this analysis.

End point type	Secondary

End point timeframe:

After 56 weeks of treatment

End point values	Semaglutide 0.5 mg + Sitagliptin placebo	Semaglutide 1.0 mg + Sitagliptin placebo	Sitagliptin + Semaglutide placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	409	409	407	
Units: Subjects				
Yes	215	270	83	
No	194	139	324	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For AEs on-treatment period - From date of first trial product (visit 2) until date of the end of treatment follow-up visit (visit 14) or date of the last trial product dose plus 42 days (5 weeks plus the 7 days visit window), whichever comes first.

Adverse event reporting additional description:

Safety analysis set included all subjects randomised to at least one dose of semaglutide or sitagliptin. Number of deaths causally related to treatment is the data considered to present under 'total number of deaths resulting from adverse events'.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Semaglutide 0.5 mg + Sitagliptin placebo

Reporting group description:

Semaglutide 0.5 mg administered subcutaneously (s.c., under the skin) once weekly, in the thigh, abdomen, or upper arm, at any time of day irrespective of meals. Sitagliptin placebo (0 mg) administered orally once daily.

Reporting group title	Semaglutide 1.0 mg + Sitagliptin placebo

Reporting group description:

Semaglutide 1.0 mg administered subcutaneously (s.c., under the skin) once weekly, in the thigh, abdomen, or upper arm, at any time of day irrespective of meals. Sitagliptin placebo (0 mg) administered orally once daily.

Reporting group title	Sitagliptin + Semaglutide placebo

Reporting group description:

Subjects were randomised to 2 different placebo arms (sitagliptin + semaglutide placebo 0.5 mg and sitagliptin + semaglutide placebo 1.0 mg). Both arms were pooled together for data analysis. Semaglutide placebo administered subcutaneously (s.c., under the skin) once weekly, in the thigh, abdomen, or upper arm, at any time of day irrespective of meals. Sitagliptin (100 mg) administered orally once daily.

Serious adverse events	Semaglutide 0.5 mg + Sitagliptin placebo	Semaglutide 1.0 mg + Sitagliptin placebo	Sitagliptin + Semaglutide placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 409 (7.33%)	30 / 409 (7.33%)	29 / 407 (7.13%)
number of deaths (all causes)	2	1	3
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of eyelid			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Bladder cancer			

subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Metastatic neoplasm			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine carcinoma metastatic			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Thyroid adenoma			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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 leiomyoma			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Hypertensive emergency			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Hypovolaemic shock			

subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Peripheral venous disease			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Surgical and medical procedures			
Haemorrhoid operation			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Meniscus operation			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fatigue			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Granuloma			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Ovarian cyst			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchiectasis			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Dyspnoea			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Epistaxis			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Pharyngeal oedema			

subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Troponin I increased			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Gas poisoning			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Road traffic accident			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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 second degree			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 409 (0.24%)	1 / 409 (0.24%)	0 / 407 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiovascular disorder			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Congestive cardiomyopathy			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Coronary artery disease			

subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cardiomyopathy			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Hypoglycaemic unconsciousness			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	3 / 407 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Syncope			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Blood and lymphatic system disorders			

Abdominal lymphadenopathy			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Anaemia			
subjects affected / exposed	1 / 409 (0.24%)	1 / 409 (0.24%)	0 / 407 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic lesion			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Eye disorders			
Cataract			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Abdominal pain upper			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Chronic gastritis			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colitis			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Diarrhoea			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Enteritis			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Gastritis erosive			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	2 / 409 (0.49%)	0 / 409 (0.00%)	0 / 407 (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
Inguinal hernia			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Intestinal obstruction			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Large intestine polyp			

subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Mallory-Weiss syndrome			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Pancreatic disorder			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Pancreatitis			
subjects affected / exposed	2 / 409 (0.49%)	0 / 409 (0.00%)	0 / 407 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Pancreatitis necrotising			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Papilla of Vater stenosis			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Swollen tongue			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			

subjects affected / exposed	2 / 409 (0.49%)	1 / 409 (0.24%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Cholecystitis acute			
subjects affected / exposed	0 / 409 (0.00%)	2 / 409 (0.49%)	0 / 407 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 409 (0.24%)	2 / 409 (0.49%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Dermatitis			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Xanthelasma			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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 and urinary disorders			

Calculus bladder			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Glycosuria			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ketonuria			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intervertebral disc protrusion			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligamentitis			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Lumbar spinal stenosis			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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 chest pain			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Osteitis			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 409 (0.24%)	1 / 409 (0.24%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiglottitis			

subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Lower respiratory tract infection			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Perineal abscess			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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
Peritonitis			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 409 (0.49%)	0 / 409 (0.00%)	0 / 407 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis chronic			
subjects affected / exposed	0 / 409 (0.00%)	0 / 409 (0.00%)	1 / 407 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			

subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Urosepsis			
subjects affected / exposed	0 / 409 (0.00%)	1 / 409 (0.24%)	0 / 407 (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			
Decreased appetite			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	0 / 407 (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
Hyperglycaemia			
subjects affected / exposed	1 / 409 (0.24%)	0 / 409 (0.00%)	2 / 407 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Semaglutide 0.5 mg + Sitagliptin placebo	Semaglutide 1.0 mg + Sitagliptin placebo	Sitagliptin + Semaglutide placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	204 / 409 (49.88%)	194 / 409 (47.43%)	151 / 407 (37.10%)
Investigations			
Lipase increased			
subjects affected / exposed	33 / 409 (8.07%)	32 / 409 (7.82%)	29 / 407 (7.13%)
occurrences (all)	41	38	33
Nervous system disorders			
Headache			
subjects affected / exposed	26 / 409 (6.36%)	29 / 409 (7.09%)	17 / 407 (4.18%)
occurrences (all)	81	42	29
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	18 / 409 (4.40%)	23 / 409 (5.62%)	8 / 407 (1.97%)
occurrences (all)	20	29	9
Diarrhoea			

subjects affected / exposed	53 / 409 (12.96%)	53 / 409 (12.96%)	29 / 407 (7.13%)
occurrences (all)	91	85	35
Dyspepsia			
subjects affected / exposed	26 / 409 (6.36%)	20 / 409 (4.89%)	9 / 407 (2.21%)
occurrences (all)	28	27	11
Nausea			
subjects affected / exposed	73 / 409 (17.85%)	72 / 409 (17.60%)	30 / 407 (7.37%)
occurrences (all)	110	140	38
Vomiting			
subjects affected / exposed	33 / 409 (8.07%)	41 / 409 (10.02%)	11 / 407 (2.70%)
occurrences (all)	49	119	16
Infections and infestations			
Influenza			
subjects affected / exposed	18 / 409 (4.40%)	22 / 409 (5.38%)	27 / 407 (6.63%)
occurrences (all)	23	25	30
Nasopharyngitis			
subjects affected / exposed	50 / 409 (12.22%)	29 / 409 (7.09%)	42 / 407 (10.32%)
occurrences (all)	63	33	51
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	26 / 409 (6.36%)	27 / 409 (6.60%)	11 / 407 (2.70%)
occurrences (all)	28	29	11

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 November 2013	Storage condition description for sitagliptin 100 mg and sitagliptin 100 mg placebo was amended to reflect current storage conditions. Dosage of placebo was changed to 0 mg in the treatment of subjects table (5.1) to ensure alignment within the table and for further clarity.
10 April 2014	Definition of hypoglycaemia including an additional hypoglycaemia endpoint was amended to include ''severe or BG confirmed systemic hypoglycaemia". Accordingly, associated statistical analysis, trial design and population, laboratory assessments, and minor updates for general clarification were amended.

Notes:

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.

None reported

Notes: