Clinical trial results:
Efficacy and long-term safety of oral semaglutide versus sitagliptin in subjects with type 2 diabetes

Summary

EudraCT number	2015-001351-71
Trial protocol	DE GB
Global end of trial date	28 March 2018

Results information

Result version number	v1 (current)
This version publication date	12 April 2019
First version publication date	12 April 2019

Trial information

Trial identification

Sponsor protocol code	NN9924-4222

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02607865
WHO universal trial number (UTN)	U1111-1168-4339
Other trial identifiers	JapicCTI: 163174

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 February 2017
Global end of trial reached?	Yes
Global end of trial date	28 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the effect of once-daily dosing of three dose levels (3 mg, 7 mg and 14 mg) of oral semaglutide versus sitagliptin 100 mg once-daily, both in combination with metformin with or without sulfonylurea (SU), on glycaemic control in subjects with type 2 diabetes mellitus (T2DM).

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013), ICH Good Clinical Practice, including archiving of essential documents (1996), and 21 CFR 312.120.

Background therapy:

Subjects were to continue their pre-trial metformin (≥1500 mg or maximum tolerated dose) alone or in combination with sulphonylurea (SU) (≥half of the maximum approved dose according to local label or maximum tolerated dose) throughout the trial.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	15 February 2016
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	Argentina: 104
Country: Number of subjects enrolled	Brazil: 23
Country: Number of subjects enrolled	Germany: 105
Country: Number of subjects enrolled	France: 36
Country: Number of subjects enrolled	United Kingdom: 118
Country: Number of subjects enrolled	Israel: 65
Country: Number of subjects enrolled	Japan: 207
Country: Number of subjects enrolled	Mexico: 109
Country: Number of subjects enrolled	Romania: 142
Country: Number of subjects enrolled	Russian Federation: 106
Country: Number of subjects enrolled	Turkey: 66
Country: Number of subjects enrolled	Ukraine: 100
Country: Number of subjects enrolled	United States: 538
Country: Number of subjects enrolled	South Africa: 144
Worldwide total number of subjects	1863
EEA total number of subjects	401

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)	1362
From 65 to 84 years	501
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 200 sites in 14 countries: Argentina-5, Brazil-1, France-10, Germany-12, Israel-8, Japan-16, Mexico-5, Romania-12, Russian Federation-8, South Africa-11, Turkey-7, Ukraine-8, United Kingdom (UK)-14, United States (US)-83. In addition, 6 sites screened, but didn't randomise any subjects: France-1, Turkey-1, UK-1 and US-3.

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:

The trial was double-blinded and the clinical study group and the investigator remained blinded throughout the trial. The blinding was to be maintained until the database had been released for statistical analysis after database lock. For both semaglutide and sitagliptin, respectively, the active trial product and the corresponding placebo tablets were visually identical.

Arms

Are arms mutually exclusive?	Yes
Arm title	Oral semaglutide 3 mg

Arm description:

Subjects were to take oral semaglutide 3 mg tablets once daily from weeks 1 - 78. In addition, subjects were to take sitagliptin placebo tablets once daily from weeks 1 - 78.

Arm type	Experimental
Investigational medicinal product name	Semaglutide 3 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Semaglutide tablets were to be taken once daily in the morning in a fasting state and at least 30 minutes before the first meal of the day. The trial product could be taken with up to half a glass of water (approximately 120 mL/4 fluid oz) and was to be swallowed whole and not broken or chewed. Oral medication other than trial product could only be taken 30 minutes after administration of trial product.

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 tablets were to be taken once daily throughout the trial. The sitagliptin tablet was to be swallowed whole and not broken or chewed and could be taken with or without food.

Arm title	Oral semaglutide 7 mg

Arm description:

Subjects were to take oral semaglutide tablets once daily in a dose escalation manner from weeks 1 - 78: 3 mg from weeks 1 - 4 and 7 mg from weeks 5 - 78. In addition, subjects were to take sitagliptin placebo tablets once daily from weeks 1 - 78.

Arm type	Experimental
Investigational medicinal product name	Semaglutide 7 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Semaglutide tablets were to be taken once daily in the morning in a fasting state and at least 30 minutes before the first meal of the day. The trial product could be taken with up to half a glass of water (approximately 120 mL/4 fluid oz) and was to be swallowed whole and not broken or chewed. Oral medication other than trial product could only be taken 30 minutes after administration of trial product.

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 tablets were to be taken once daily throughout the trial. The sitagliptin tablet was to be swallowed whole and not broken or chewed and could be taken with or without food.

Arm title	Oral semaglutide 14 mg

Arm description:

Subjects were to take oral semaglutide tablets once daily in a dose escalation manner from weeks 1 - 78: 3 mg from weeks 1 - 4, 7 mg from weeks 5 - 8 and 14 mg from weeks 9 - 78. In addition, subjects were to take sitagliptin placebo tablets once daily from weeks 1 - 78.

Arm type	Experimental
Investigational medicinal product name	Semaglutide 14 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Semaglutide tablets were to be taken once daily in the morning in a fasting state and at least 30 minutes before the first meal of the day. The trial product could be taken with up to half a glass of water (approximately 120 mL/4 fluid oz) and was to be swallowed whole and not broken or chewed. Oral medication other than trial product could only be taken 30 minutes after administration of trial product.

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 tablets were to be taken once daily throughout the trial. The sitagliptin tablet was to be swallowed whole and not broken or chewed and could be taken with or without food.

Arm title	Sitagliptin 100 mg

Arm description:

Subjects were to take sitagliptin 100 mg tablets once daily from weeks 1 - 78. In addition, subjects were to take semaglutide placebo tablets once daily from weeks 1 - 78.

Arm type	Active comparator
Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	Januvia®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Sitagliptin 100 mg tablets were to be taken once daily throughout the trial without any dose escalation or dose adjustment. The sitagliptin tablet was to be swallowed whole and not broken or chewed and could be taken with or without food.

Investigational medicinal product name	Semaglutide placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Semaglutide placebo tablets were to be taken once daily in the morning in a fasting state and at least 30 minutes before the first meal of the day. The trial product could be taken with up to half a glass of water (approximately 120 mL/4 fluid oz) and was to be swallowed whole and not broken or chewed. Oral medication other than trial product could only be taken 30 minutes after administration of trial product.

Number of subjects in period 1	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg
Started	466	465	465
Completed	433	436	438
Not completed	33	29	27
Adverse event, serious fatal	5	4	1
Consent withdrawn by subject	18	18	17
Unclassified	1	-	2
Lost to follow-up	9	7	7

Number of subjects in period 1	Sitagliptin 100 mg
Started	467
Completed	451
Not completed	16
Adverse event, serious fatal	3
Consent withdrawn by subject	8
Unclassified	-
Lost to follow-up	5

Baseline characteristics

Reporting groups	
Reporting group title	Oral semaglutide 3 mg
Reporting group description:	
Subjects were to take oral semaglutide 3 mg tablets once daily from weeks 1 - 78. In addition, subjects were to take sitagliptin placebo tablets once daily from weeks 1 - 78.	
Reporting group title	Oral semaglutide 7 mg
Reporting group description:	
Subjects were to take oral semaglutide tablets once daily in a dose escalation manner from weeks 1 - 78: 3 mg from weeks 1 - 4 and 7 mg from weeks 5 - 78. In addition, subjects were to take sitagliptin placebo tablets once daily from weeks 1 - 78.	
Reporting group title	Oral semaglutide 14 mg
Reporting group description:	
Subjects were to take oral semaglutide tablets once daily in a dose escalation manner from weeks 1 - 78: 3 mg from weeks 1 - 4, 7 mg from weeks 5 - 8 and 14 mg from weeks 9 - 78. In addition, subjects were to take sitagliptin placebo tablets once daily from weeks 1 - 78.	
Reporting group title	Sitagliptin 100 mg
Reporting group description:	
Subjects were to take sitagliptin 100 mg tablets once daily from weeks 1 - 78. In addition, subjects were to take semaglutide placebo tablets once daily from weeks 1 - 78.	

Reporting group values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg
Number of subjects	466	465	465
Age Categorical			
Units: Subjects			
Adults (18-64 years)	339	335	342
From 65-84 years	127	130	123
Age Continuous			
Units: years			
arithmetic mean	58	58	57
standard deviation	± 10	± 10	± 10
Gender Categorical			
Units: Subjects			
Female	212	220	218
Male	254	245	247
Glycosylated haemoglobin (HbA1c)			
Units: Percentage of HbA1c			
arithmetic mean	8.3	8.4	8.3
standard deviation	± 1.0	± 1.0	± 0.9
Body weight			
Units: Kg			
arithmetic mean	91.6	91.3	91.2
standard deviation	± 22.0	± 20.8	± 21.7

Reporting group values	Sitagliptin 100 mg	Total	
Number of subjects	467	1863	
Age Categorical			
Units: Subjects			
Adults (18-64 years)	346	1362	

From 65-84 years	121	501	

Age Continuous Units: years			
arithmetic mean	58		
standard deviation	± 10	-	
Gender Categorical Units: Subjects			
Female	229	879	
Male	238	984	
Glycosylated haemoglobin (HbA1c) Units: Percentage of HbA1c			
arithmetic mean	8.3		
standard deviation	± 0.9	-	
Body weight Units: Kg			
arithmetic mean	90.9		
standard deviation	± 21.0	-	

End points

End points reporting groups

Reporting group title	Oral semaglutide 3 mg
Reporting group description:	
Subjects were to take oral semaglutide 3 mg tablets once daily from weeks 1 - 78. In addition, subjects were to take sitagliptin placebo tablets once daily from weeks 1 - 78.	
Reporting group title	Oral semaglutide 7 mg
Reporting group description:	
Subjects were to take oral semaglutide tablets once daily in a dose escalation manner from weeks 1 - 78: 3 mg from weeks 1 - 4 and 7 mg from weeks 5 - 78. In addition, subjects were to take sitagliptin placebo tablets once daily from weeks 1 - 78.	
Reporting group title	Oral semaglutide 14 mg
Reporting group description:	
Subjects were to take oral semaglutide tablets once daily in a dose escalation manner from weeks 1 - 78: 3 mg from weeks 1 - 4, 7 mg from weeks 5 - 8 and 14 mg from weeks 9 - 78. In addition, subjects were to take sitagliptin placebo tablets once daily from weeks 1 - 78.	
Reporting group title	Sitagliptin 100 mg
Reporting group description:	
Subjects were to take sitagliptin 100 mg tablets once daily from weeks 1 - 78. In addition, subjects were to take semaglutide placebo tablets once daily from weeks 1 - 78.	

Primary: Change in HbA1c (in-trial observation period): Week 26

End point title	Change in HbA1c (in-trial observation period): Week 26
End point description:	
Change from baseline (week 0) in glycosylated haemoglobin (HbA1c) was evaluated at week 26. Results are based on the in-trial observation period, which was the time period from when a subject was randomised until the final scheduled visit, including any period after initiation of rescue medication and/or premature discontinuation of trial product. Population analysed: The full analysis set (FAS), which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.	
End point type	Primary
End point timeframe:	
From baseline to week 26.	

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	435	438	436	446
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-0.6 (± 1.0)	-1.1 (± 1.1)	-1.3 (± 1.0)	-0.8 (± 0.9)

Statistical analyses

Statistical analysis title	Oral semaglutide 14 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a pattern mixture model that used multiple imputation to impute missing week-26 data, assuming that such data were missing at random. The imputed data sets were analysed using an analysis of covariance (ANCOVA) model with trial product, region and stratification factor as fixed effects and the baseline HbA1c value as the covariate.

Comparison groups	Oral semaglutide 14 mg v Sitagliptin 100 mg
Number of subjects included in analysis	882
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.0001 [2]
Method	Pattern mixture model
Parameter estimate	Mean treatment difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	-0.4

Notes:

[1] - This hypothesis was controlled for multiplicity. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand). A value of 0.3% (the non-inferiority margin) was added to imputed values at week 26 for the oral semaglutide treatment arm only.
[2] - Unadjusted two-sided p-value for test of no difference from the non-inferiority margin (non-inferiority).

Statistical analysis title	Oral semaglutide 14 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a pattern mixture model that used multiple imputation to impute missing week-26 data, assuming that such data were missing at random. The imputed data sets were analysed using an ANCOVA model with trial product, region and stratification factor as fixed effects and the baseline HbA1c value as the covariate.

Comparison groups	Oral semaglutide 14 mg v Sitagliptin 100 mg
Number of subjects included in analysis	882
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001 [4]
Method	Pattern mixture model
Parameter estimate	Mean treatment difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	-0.4

Notes:

[3] - This hypothesis was controlled for multiplicity. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand).
[4] - Unadjusted two-sided p-value for test of no difference from 0 (superiority).

Statistical analysis title	Oral semaglutide 7 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a pattern mixture model that used multiple imputation to impute missing week-26 data, assuming that such data were missing at random. The imputed data sets were analysed using an ANCOVA model with trial product, region and stratification factor as fixed effects and the baseline HbA1c value as the covariate.

Comparison groups	Oral semaglutide 7 mg v Sitagliptin 100 mg
Number of subjects included in analysis	884
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	< 0.0001 [6]
Method	Pattern mixture model
Parameter estimate	Mean treatment difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.1

Notes:

[5] - This hypothesis was controlled for multiplicity. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand). A value of 0.3% (the non-inferiority margin) was added to imputed values at week 26 for the oral semaglutide treatment arm only.
[6] - Unadjusted two-sided p-value for test of no difference from the non-inferiority margin (non-inferiority).

Statistical analysis title	Oral semaglutide 7 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a pattern mixture model that used multiple imputation to impute missing week-26 data, assuming that such data were missing at random. The imputed data sets were analysed using an ANCOVA model with trial product, region and stratification factor as fixed effects and the baseline HbA1c value as the covariate.

Comparison groups	Oral semaglutide 7 mg v Sitagliptin 100 mg
Number of subjects included in analysis	884
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.0001 [8]
Method	Pattern mixture model
Parameter estimate	Mean treatment difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.1

Notes:

[7] - This hypothesis was controlled for multiplicity. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand).
[8] - Unadjusted two-sided p-value for test of no difference from 0 (superiority).

Statistical analysis title	Oral semaglutide 3 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a pattern mixture model that used multiple imputation to impute missing week-26 data, assuming that such data were missing at random. The imputed data sets were analysed using an ANCOVA model with trial product, region and stratification factor as fixed effects and the baseline HbA1c value as the covariate.

Comparison groups	Oral semaglutide 3 mg v Sitagliptin 100 mg

Number of subjects included in analysis	881
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
P-value	= 0.0856 [10]
Method	Pattern mixture model
Parameter estimate	Mean treatment difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.3

Notes:

[9] - This hypothesis was controlled for multiplicity, but could not be confirmed. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand). A value of 0.3% (the non-inferiority margin) was added to imputed values at week 26 for the oral semaglutide treatment arm only.
[10] - Unadjusted two-sided p-value for test of no difference from the non-inferiority margin (non-inferiority).

Statistical analysis title	Oral semaglutide 3 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a pattern mixture model that used multiple imputation to impute missing week-26 data, assuming that such data were missing at random. The imputed data sets were analysed using an ANCOVA model with trial product, region and stratification factor as fixed effects and the baseline HbA1c value as the covariate.

Comparison groups	Oral semaglutide 3 mg v Sitagliptin 100 mg
Number of subjects included in analysis	881
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.008 [12]
Method	Pattern mixture model
Parameter estimate	Mean treatment difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.3

Notes:

[11] - This hypothesis was not controlled for multiplicity, since the non-inferiority test of change in HbA1c for oral semaglutide 3 mg versus sitagliptin 100 mg could not be confirmed. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand).
[12] - Unadjusted two-sided p-value for test of no difference from 0 (superiority).

Primary: Change in HbA1c (on treatment without rescue medication observation period): Week 26

End point title	Change in HbA1c (on treatment without rescue medication observation period): Week 26

End point description:

Change from baseline (week 0) in HbA1c was evaluated at week 26. Results are based on the on treatment without rescue medication observation period, which was the time period when a subject was on treatment with trial product, excluding any period after initiation of rescue medication and/or premature trial product discontinuation. Population analysed: The FAS. Number of subjects analysed = number of subjects with available data.

End point type	Primary

End point timeframe:

From baseline to week 26

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	391	409	398	419
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-0.6 (± 1.0)	-1.2 (± 1.1)	-1.4 (± 1.0)	-0.8 (± 0.9)

Statistical analyses

Statistical analysis title	Oral semaglutide 14 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a mixed model for repeated measurements (MMRM) that assumed data to be missing at random. As dependent variables, the MMRM model included all post-baseline values collected at scheduled visits up to and including week 26. The independent effects were trial product, region and stratification factor as categorical fixed effects and the baseline HbA1c value as a covariate, all nested within visit.

Comparison groups	Oral semaglutide 14 mg v Sitagliptin 100 mg
Number of subjects included in analysis	817
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
P-value	= 0.0001 [14]
Method	MMRM
Parameter estimate	Mean treatment difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.5

Notes:

[13] - This hypothesis was not controlled for multiplicity. The estimated treatment effect excludes the effect of any rescue medication and any effect after premature trial product discontinuation (hypothetical estimand). Non-inferiority margin = 0.3%.

[14] - Unadjusted two-sided p-value for test of no difference from the non-inferiority margin (non-inferiority).

Statistical analysis title	Oral semaglutide 14 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a mixed MMRM that assumed data to be missing at random. As dependent variables, the MMRM model included all post-baseline values collected at scheduled visits up to and including week 26. The independent effects were trial product, region and stratification factor as categorical fixed effects and the baseline HbA1c value as a covariate, all nested within visit.

Comparison groups	Oral semaglutide 14 mg v Sitagliptin 100 mg

Number of subjects included in analysis	817
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	< 0.0001 [16]
Method	MMRM
Parameter estimate	Mean treatment difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.5

Notes:

[15] - This hypothesis was not controlled for multiplicity. The estimated treatment effect excludes the effect of any rescue medication and any effect after premature trial product discontinuation (hypothetical estimand).
[16] - Unadjusted two-sided p-value for test of no difference from 0 (superiority).

Statistical analysis title	Oral semaglutide 7 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a mixed MMRM that assumed data to be missing at random. As dependent variables, the MMRM model included all post-baseline values collected at scheduled visits up to and including week 26. The independent effects were trial product, region and stratification factor as categorical fixed effects and the baseline HbA1c value as a covariate, all nested within visit.

Comparison groups	Oral semaglutide 7 mg v Sitagliptin 100 mg
Number of subjects included in analysis	828
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
P-value	< 0.0001 [18]
Method	MMRM
Parameter estimate	Mean treatment difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.2

Notes:

[17] - This hypothesis was not controlled for multiplicity. The estimated treatment effect excludes the effect of any rescue medication and any effect after premature trial product discontinuation (hypothetical estimand). Non-inferiority margin = 0.3%.
[18] - Unadjusted two-sided p-value for test of no difference from the non-inferiority margin (non-inferiority).

Statistical analysis title	Oral semaglutide 7 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a mixed MMRM that assumed data to be missing at random. As dependent variables, the MMRM model included all post-baseline values collected at scheduled visits up to and including week 26. The independent effects were trial product, region and stratification factor as categorical fixed effects and the baseline HbA1c value as a covariate, all nested within visit.

Comparison groups	Oral semaglutide 7 mg v Sitagliptin 100 mg

Number of subjects included in analysis	828
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	< 0.0001 [20]
Method	MMRM
Parameter estimate	Mean treatment difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.2

Notes:

[19] - This hypothesis was not controlled for multiplicity. The estimated treatment effect excludes the effect of any rescue medication and any effect after premature trial product discontinuation (hypothetical estimand).
[20] - Unadjusted two-sided p-value for test of no difference from 0 (superiority).

Statistical analysis title	Oral semaglutide 3 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a mixed MMRM that assumed data to be missing at random. As dependent variables, the MMRM model included all post-baseline values collected at scheduled visits up to and including week 26. The independent effects were trial product, region and stratification factor as categorical fixed effects and the baseline HbA1c value as a covariate, all nested within visit.

Comparison groups	Oral semaglutide 3 mg v Sitagliptin 100 mg
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
P-value	= 0.3851 [22]
Method	MMRM
Parameter estimate	Mean treatment difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.4

Notes:

[21] - This hypothesis was not controlled for multiplicity. The estimated treatment effect excludes the effect of any rescue medication and any effect after premature trial product discontinuation (hypothetical estimand). Non-inferiority margin = 0.3%.
[22] - Unadjusted two-sided p-value for test of no difference from the non-inferiority margin (non-inferiority).

Statistical analysis title	Oral semaglutide 3 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a mixed MMRM that assumed data to be missing at random. As dependent variables, the MMRM model included all post-baseline values collected at scheduled visits up to and including week 26. The independent effects were trial product, region and stratification factor as categorical fixed effects and the baseline HbA1c value as a covariate, all nested within visit.

Comparison groups	Oral semaglutide 3 mg v Sitagliptin 100 mg

Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	= 0.0001 [24]
Method	MMRM
Parameter estimate	Mean treatment difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.4

Notes:

[23] - This hypothesis was not controlled for multiplicity. The estimated treatment effect excludes the effect of any rescue medication and any effect after premature trial product discontinuation (hypothetical estimand).

[24] - Unadjusted two-sided p-value for test of no difference from 0 (superiority).

Secondary: Change in body weight (in-trial observation period): Week 26

End point title	Change in body weight (in-trial observation period): Week 26

End point description:

Change from baseline (week 0) in body weight was evaluated at week 26. Results are based on the in-trial observation period. Population analysed: The FAS. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline to week 26

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	438	440	439	447
Units: Kg				
arithmetic mean (standard deviation)	-1.2 (± 3.2)	-2.2 (± 3.9)	-3.1 (± 3.8)	-0.6 (± 3.2)

Statistical analyses

Statistical analysis title	Oral semaglutide 14 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a pattern mixture model that used multiple imputation to impute missing week-26 data, assuming that such data were missing at random. The imputed data sets were analysed using an ANCOVA model with trial product, region and stratification factor as fixed effects and the baseline body weight value as the covariate.

Comparison groups	Oral semaglutide 14 mg v Sitagliptin 100 mg

Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	< 0.0001 [26]
Method	Pattern mixture model
Parameter estimate	Mean treatment difference
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-2

Notes:

[25] - This hypothesis was controlled for multiplicity. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand).
[26] - Unadjusted two-sided p-value for test of no difference from 0 (superiority).

Statistical analysis title	Oral semaglutide 7 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a pattern mixture model that used multiple imputation to impute missing week-26 data, assuming that such data were missing at random. The imputed data sets were analysed using an ANCOVA model with trial product, region and stratification factor as fixed effects and the baseline body weight value as the covariate.

Comparison groups	Oral semaglutide 7 mg v Sitagliptin 100 mg
Number of subjects included in analysis	887
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	< 0.0001 [28]
Method	Pattern mixture model
Parameter estimate	Mean treatment difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1.1

Notes:

[27] - This hypothesis was controlled for multiplicity. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand).
[28] - Unadjusted two-sided p-value for test of no difference from 0 (superiority).

Statistical analysis title	Oral semaglutide 3 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a pattern mixture model that used multiple imputation to impute missing week-26 data, assuming that such data were missing at random. The imputed data sets were analysed using an ANCOVA model with trial product, region and stratification factor as fixed effects and the baseline body weight value as the covariate.

Comparison groups	Oral semaglutide 3 mg v Sitagliptin 100 mg

Number of subjects included in analysis	885
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	= 0.0185 [30]
Method	Pattern mixture model
Parameter estimate	Mean treatment difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.1

Notes:

[29] - This hypothesis was not controlled for multiplicity, since the non-inferiority test of change in HbA1c for oral semaglutide 3 mg versus sitagliptin 100 mg could not be confirmed. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand).

[30] - Unadjusted two-sided p-value for test of no difference from 0 (superiority).

Secondary: Change in body weight (on treatment without rescue medication observation period): Week 26

End point title	Change in body weight (on treatment without rescue medication observation period): Week 26

End point description:

Change from baseline (week 0) in body weight was evaluated at week 26. Results are based on the on treatment without rescue medication observation period. Population analysed: The FAS. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline to week 26

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	394	411	401	420
Units: Kg				
arithmetic mean (standard deviation)	-1.2 (± 3.3)	-2.2 (± 4.0)	-3.2 (± 3.8)	-0.6 (± 3.2)

Statistical analyses

Statistical analysis title	Oral semaglutide 14 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a MMRM that assumed data to be missing at random. As dependent variables, the MMRM model included all post-baseline values collected at scheduled visits up to and including week 26. The independent effects were trial product, region and stratification factor as categorical fixed effects and the baseline body weight value as a covariate, all nested within visit.

Comparison groups	Oral semaglutide 14 mg v Sitagliptin 100 mg

Number of subjects included in analysis	821
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	< 0.0001 [32]
Method	MMRM
Parameter estimate	Mean treatment difference
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	-2.1

Notes:

[31] - This hypothesis was not controlled for multiplicity. The estimated treatment effect excludes the effect of any rescue medication and any effect after premature trial product discontinuation (hypothetical estimand).
[32] - Unadjusted two-sided p-value for test of no difference from 0 (superiority).

Statistical analysis title	Oral semaglutide 7 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a MMRM that assumed data to be missing at random. As dependent variables, the MMRM model included all post-baseline values collected at scheduled visits up to and including week 26. The independent effects were trial product, region and stratification factor as categorical fixed effects and the baseline body weight value as a covariate, all nested within visit.

Comparison groups	Oral semaglutide 7 mg v Sitagliptin 100 mg
Number of subjects included in analysis	831
Analysis specification	Pre-specified
Analysis type	superiority[33]
P-value	< 0.0001 [34]
Method	MMRM
Parameter estimate	Mean treatment difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1.1

Notes:

[33] - This hypothesis was not controlled for multiplicity. The estimated treatment effect excludes the effect of any rescue medication and any effect after premature trial product discontinuation (hypothetical estimand).
[34] - Unadjusted two-sided p-value for test of no difference from 0 (superiority).

Statistical analysis title	Oral semaglutide 3 mg versus sitagliptin 100 mg

Statistical analysis description:

The analysis was based on a MMRM that assumed data to be missing at random. As dependent variables, the MMRM model included all post-baseline values collected at scheduled visits up to and including week 26. The independent effects were trial product, region and stratification factor as categorical fixed effects and the baseline body weight value as a covariate, all nested within visit.

Comparison groups	Oral semaglutide 3 mg v Sitagliptin 100 mg

Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	superiority[35]
P-value	= 0.0257 [36]
Method	MMRM
Parameter estimate	Mean treatment difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.1

Notes:

[35] - This hypothesis was not controlled for multiplicity. The estimated treatment effect excludes the effect of any rescue medication and any effect after premature trial product discontinuation (hypothetical estimand).

[36] - Unadjusted two-sided p-value for test of no difference from 0 (superiority).

Secondary: Change in FPG: Week 26

End point title	Change in FPG: Week 26

End point description:

Change from baseline (week 0) in fasting plasma glucose (FPG) was evaluated at week 26. Results are based on the in-trial observation period. Population analysed: The FAS. Number of subjects analysed (n) = number of subjects with available data at specified time points.

End point type	Secondary

End point timeframe:

From baseline to week 26

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	466	465	465	467
Units: mmol/L				
arithmetic mean (standard deviation)				
Baseline (n=464, 463, 462, 464)	9.67 (± 2.80)	9.45 (± 2.38)	9.32 (± 2.50)	9.53 (± 2.33)
Change from baseline (n=433, 436, 433, 443)	-0.83 (± 2.69)	-1.17 (± 2.54)	-1.67 (± 2.60)	-0.90 (± 2.32)

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects who achieve (yes/no) HbA1c <7.0% (53 mmol/mol), ADA target: Week 26

End point title	Subjects who achieve (yes/no) HbA1c <7.0% (53 mmol/mol), ADA target: Week 26

End point description:

Subjects who achieved (yes/no) HbA1c <7.0% (American Diabetes Association (ADA) target), was

evaluated at week 26. Results are based on the in-trial observation period. Population analysed: The FAS. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

After 26 weeks of treatment

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	435	438	436	446
Units: Subjects				
Yes	116	192	246	144
No	319	246	190	302

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects who achieve (yes/no) HbA1c <7.0% (53 mmol/mol), ADA target: Week 52

End point title	Subjects who achieve (yes/no) HbA1c <7.0% (53 mmol/mol), ADA target: Week 52

End point description:

Subjects who achieved (yes/no) HbA1c <7.0% ADA target, was evaluated at week 52. Results are based on the in-trial observation period. Population analysed: The FAS. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

After 52 weeks of treatment

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	427	431	434	436
Units: Subjects				
Yes	113	168	238	138
No	314	263	196	298

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects who achieve (yes/no) HbA1c <7.0% (53 mmol/mol), ADA target: Week 78

End point title	Subjects who achieve (yes/no) HbA1c <7.0% (53 mmol/mol), ADA target: Week 78

End point description:

Subjects who achieved (yes/no) HbA1c <7.0% ADA target, was evaluated at week 78. Results are based on the in-trial observation period. Population analysed: The FAS. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

After 78 weeks of treatment

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	421	424	425	439
Units: Subjects				
Yes	113	165	191	129
No	308	259	234	310

Statistical analyses

No statistical analyses for this end point

Secondary: Change in HbA1c: Week 52

End point title	Change in HbA1c: Week 52

End point description:

Change from baseline (week 0) in HbA1c was evaluated at week 52. Results are based on the in-trial observation period. Population analysed: The FAS. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline to week 52

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	427	431	434	436
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-0.6 (± 1.1)	-1.0 (± 1.2)	-1.2 (± 1.1)	-0.7 (± 1.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in HbA1c: Week 78

End point title	Change in HbA1c: Week 78

End point description:

Change from baseline (week 0) in HbA1c was evaluated at week 52. Results are based on the in-trial observation period. Population analysed: The FAS. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline to week 78

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	421	424	425	439
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-0.6 (± 1.1)	-0.9 (± 1.3)	-1.1 (± 1.1)	-0.7 (± 1.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body weight: Week 52

End point title	Change in body weight: Week 52

End point description:

Change from baseline (week 0) in body weight was evaluated at week 52. Results are based on the in-trial observation period. Population analysed: The FAS. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline to week 52

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	428	433	435	437
Units: Kg				
arithmetic mean (standard deviation)	-1.6 (± 4.1)	-2.5 (± 4.9)	-3.5 (± 4.7)	-0.7 (± 3.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body weight: Week 78

End point title	Change in body weight: Week 78

End point description:

Change from baseline (week 0) in body weight was evaluated at week 78. Results are based on the in-trial observation period. Population analysed: The FAS. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline to week 78

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	425	425	428	443
Units: Kg				
arithmetic mean (standard deviation)	-1.8 (± 4.9)	-2.8 (± 5.4)	-3.2 (± 4.9)	-1.0 (± 4.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in FPG: Week 52

End point title	Change in FPG: Week 52

End point description:

Change from baseline (week 0) in FPG was evaluated at week 52. Results are based on the in-trial observation period. Population analysed: The FAS. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline to week 52

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	419	429	432	433
Units: mmol/L				
arithmetic mean (standard deviation)	-0.98 (± 2.78)	-1.28 (± 2.62)	-1.75 (± 2.57)	-1.03 (± 2.60)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in FPG: Week 78

End point title	Change in FPG: Week 78

End point description:

Change from baseline (week 0) in FPG was evaluated at week 78. Results are based on the in-trial observation period. Population analysed: The FAS. Number of subjects analysed = number of subjects with available data.

End point type	Secondary

End point timeframe:

From baseline to week 78

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	418	419	419	434
Units: mmol/L				
arithmetic mean (standard deviation)	-1.07 (± 3.21)	-1.11 (± 2.92)	-1.65 (± 2.71)	-0.91 (± 2.59)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment emergent adverse events (TEAEs) during exposure to trial product

End point title	Number of treatment emergent adverse events (TEAEs) during exposure to trial product

End point description:

TEAEs were recorded during the exposure to trial products. Adverse events (AEs) with onset during the on-treatment observation period were considered treatment-emergent. On-treatment observation period: Time period when a subject was on treatment with trial product, including any period after initiation of rescue medication. Results are based on the safety analysis set, which included all randomised subjects who received at least one dose of trial product.

End point type	Secondary

End point timeframe:

Assessed up to approximately 83 weeks

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	466	464	465	466
Units: Events	1774	1686	1824	1852

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment emergent severe or blood glucose (BG) confirmed symptomatic hypoglycaemic episodes during exposure to trial product

End point title	Number of treatment emergent severe or blood glucose (BG) confirmed symptomatic hypoglycaemic episodes during exposure to trial product

End point description:

Treatment emergent severe or BG confirmed symptomatic hypoglycaemic episodes were recorded during exposure to trial products. Hypoglycaemic episodes with onset during the on-treatment observation period were considered treatment-emergent. Severe hypoglycaemia was defined as an episode requiring assistance of another person to actively administer carbohydrate or glucagon, or take other corrective actions. BG-confirmed symptomatic hypoglycaemia: Confirmed by a glucose value <3.1 mmol/L (56 mg/dL) with symptoms consistent with hypoglycaemia. Results are based on the safety analysis set.

End point type	Secondary

End point timeframe:

Assessed up to approximately 83 weeks

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	466	464	465	466
Units: Episodes	56	42	60	76

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Weeks 0 – 83 (78 weeks treatment period + 5 weeks follow-up period). All presented AEs are TEAEs.	
Adverse event reporting additional description:	
Results are based on the safety analysis set.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	Oral semaglutide 3 mg
Reporting group description:	
Subjects were to take oral semaglutide 3 mg tablets once daily from weeks 1 - 78. In addition, subjects were to take sitagliptin placebo tablets once daily from weeks 1 - 78.	
Reporting group title	Oral semaglutide 7 mg
Reporting group description:	
Subjects were to take oral semaglutide tablets once daily in a dose escalation manner from weeks 1 - 78: 3 mg from weeks 1 - 4 and 7 mg from weeks 5 - 78. In addition, subjects were to take sitagliptin placebo tablets once daily from weeks 1 - 78.	
Reporting group title	Oral semaglutide 14 mg
Reporting group description:	
Subjects were to take oral semaglutide tablets once daily in a dose escalation manner from weeks 1 - 78: 3 mg from weeks 1 - 4, 7 mg from weeks 5 - 8 and 14 mg from weeks 9 - 78. In addition, subjects were to take sitagliptin placebo tablets once daily from weeks 1 - 78.	
Reporting group title	Sitagliptin 100 mg
Reporting group description:	
Subjects were to take sitagliptin 100 mg tablets once daily from weeks 1 - 78. In addition, subjects were to take semaglutide placebo tablets once daily from weeks 1 - 78.	

Serious adverse events	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	64 / 466 (13.73%)	47 / 464 (10.13%)	44 / 465 (9.46%)
number of deaths (all causes)	4	1	1
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Adenocarcinoma of colon			

subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
B-cell lymphoma			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Brain neoplasm malignant			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Breast cancer			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Breast cancer metastatic			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Colon cancer			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Nasal cavity cancer			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Ovarian cancer metastatic			

subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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 carcinoma metastatic			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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 neuroendocrine tumour			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 466 (0.21%)	1 / 464 (0.22%)	0 / 465 (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
Rectal adenocarcinoma			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell carcinoma			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Uterine leiomyoma			

subjects affected / exposed	2 / 466 (0.43%)	0 / 464 (0.00%)	0 / 465 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Essential hypertension			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Hypertension			
subjects affected / exposed	1 / 466 (0.21%)	1 / 464 (0.22%)	0 / 465 (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
Hypotension			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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 artery occlusion			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Varicose vein			

subjects affected / exposed	1 / 466 (0.21%)	1 / 464 (0.22%)	0 / 465 (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
Surgical and medical procedures			
Cataract operation			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Hospitalisation			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Laparoscopic surgery			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Umbilical hernia repair			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Complication associated with device			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Fatigue			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 466 (0.21%)	1 / 464 (0.22%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Oedema peripheral			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Polyp			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
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	2 / 466 (0.43%)	0 / 464 (0.00%)	0 / 465 (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
Immune system disorders			
Sarcoidosis			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Endometrial hyperplasia			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Prostatitis			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	1 / 466 (0.21%)	1 / 464 (0.22%)	0 / 465 (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

Uterine prolapse			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Acute respiratory failure			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Sleep apnoea syndrome			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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

Product issues			
Device dislocation			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
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			
Liver function test abnormal			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Prostatic specific antigen increased			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Cervical vertebral fracture			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Clavicle fracture			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia, obstructive			

subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scapula fracture			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fractured base			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Soft tissue injury			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 466 (0.21%)	1 / 464 (0.22%)	0 / 465 (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
Subdural haematoma			
subjects affected / exposed	0 / 466 (0.00%)	2 / 464 (0.43%)	0 / 465 (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
Ulna fracture			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Upper limb fracture			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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 pseudoaneurysm			

subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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 coronary syndrome			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Acute left ventricular failure			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 466 (0.21%)	1 / 464 (0.22%)	0 / 465 (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
Angina pectoris			
subjects affected / exposed	1 / 466 (0.21%)	1 / 464 (0.22%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	3 / 466 (0.64%)	3 / 464 (0.65%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	1 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	3 / 466 (0.64%)	2 / 464 (0.43%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial flutter			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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 arrest			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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 failure chronic			
subjects affected / exposed	2 / 466 (0.43%)	0 / 464 (0.00%)	0 / 465 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	3 / 466 (0.64%)	1 / 464 (0.22%)	2 / 465 (0.43%)
occurrences causally related to treatment / all	0 / 3	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Congestive cardiomyopathy			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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	1 / 466 (0.21%)	2 / 464 (0.43%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery insufficiency			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Coronary artery stenosis			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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 heart disease			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Myocardial fibrosis			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	2 / 466 (0.43%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Supraventricular tachycardia			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Nervous system disorders			
Brain stem stroke			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Cervicobrachial syndrome			

subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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 inflammatory demyelinating polyradiculoneuropathy			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Focal dyscognitive seizures			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Haemorrhage intracranial			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Haemorrhagic stroke			
subjects affected / exposed	2 / 466 (0.43%)	0 / 464 (0.00%)	0 / 465 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
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 stroke			

subjects affected / exposed	3 / 466 (0.64%)	0 / 464 (0.00%)	2 / 465 (0.43%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Sciatica			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thalamic infarction			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Iron deficiency anaemia			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Ear and labyrinth disorders			

Deafness neurosensory			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	2 / 465 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exostosis of external ear canal			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Vertigo			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
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			
Cataract			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Cataract diabetic			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Conjunctival irritation			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Diabetic retinopathy			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Retinal detachment			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Retinal haemorrhage			

subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Retinopathy proliferative			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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			
Abdominal pain			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	2 / 465 (0.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Barrett's oesophagus			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faeces discoloured			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Gastritis			

subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Large intestine polyp			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Nausea			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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 cyst			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	3 / 465 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			

subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Cholecystitis			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Cholecystitis acute			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Cholecystitis chronic			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	2 / 465 (0.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic hepatic failure			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Cirrhosis alcoholic			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Hepatic cirrhosis			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Hepatitis			

subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Non-alcoholic steatohepatitis			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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			
Acute kidney injury			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	3 / 465 (0.65%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
End stage renal disease			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Haematuria			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
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 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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 cyst			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Ureterolithiasis			

subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
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	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Hypopituitarism			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
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			
Arthralgia			
subjects affected / exposed	1 / 466 (0.21%)	1 / 464 (0.22%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic amyotrophy			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
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	2 / 466 (0.43%)	0 / 464 (0.00%)	0 / 465 (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
Lumbar spinal stenosis			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
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 chest pain			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Osteoarthritis			
subjects affected / exposed	3 / 466 (0.64%)	2 / 464 (0.43%)	3 / 465 (0.65%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteochondrosis			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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 osteoarthritis			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Synovitis			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
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			
Abdominal wall abscess			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Appendicitis			

subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	3 / 466 (0.64%)	0 / 464 (0.00%)	2 / 465 (0.43%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis infective			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Influenza			
subjects affected / exposed	1 / 466 (0.21%)	1 / 464 (0.22%)	0 / 465 (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
Neurosyphilis			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Osteomyelitis			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Pelvic abscess			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Peritonitis			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Peritonitis bacterial			

subjects affected / exposed	2 / 466 (0.43%)	0 / 464 (0.00%)	0 / 465 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 466 (0.64%)	1 / 464 (0.22%)	2 / 465 (0.43%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Pyelonephritis			
subjects affected / exposed	0 / 466 (0.00%)	1 / 464 (0.22%)	0 / 465 (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
Pyelonephritis acute			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Sepsis			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic phlebitis			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 466 (0.00%)	2 / 464 (0.43%)	0 / 465 (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
Testicular abscess			

subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Urinary tract infection			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Vestibular neuronitis			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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 / 466 (0.21%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection staphylococcal			
subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	0 / 465 (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
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 466 (0.21%)	1 / 464 (0.22%)	0 / 465 (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
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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
Hyperglycaemia			

subjects affected / exposed	1 / 466 (0.21%)	0 / 464 (0.00%)	1 / 465 (0.22%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 466 (0.00%)	0 / 464 (0.00%)	0 / 465 (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	Sitagliptin 100 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	58 / 466 (12.45%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Adenocarcinoma of colon			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
B-cell lymphoma			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Brain neoplasm malignant			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	2 / 466 (0.43%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Breast cancer metastatic				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colon cancer				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Invasive ductal breast carcinoma				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nasal cavity cancer				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian cancer metastatic				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatic carcinoma metastatic				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pancreatic neuroendocrine tumour				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Plasma cell myeloma				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				

subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal adenocarcinoma				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal cell carcinoma				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thyroid cancer				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine leiomyoma				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep vein thrombosis				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Essential hypertension				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				

subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral arterial occlusive disease				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral artery occlusion				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombosis				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Varicose vein				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Cataract operation				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hospitalisation				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laparoscopic surgery				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia repair				

subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Complication associated with device			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Polyp			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Sarcoidosis			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endometrial hyperplasia			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostatitis			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine polyp			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine prolapse			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			

subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sleep apnoea syndrome				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device dislocation				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Liver function test abnormal				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostatic specific antigen increased				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Injury, poisoning and procedural complications			
Cervical vertebral fracture			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clavicle fracture			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Incisional hernia			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Incisional hernia, obstructive			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Scapula fracture			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skull fractured base			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Soft tissue injury			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Subarachnoid haemorrhage				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ulna fracture				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular pseudoaneurysm				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Hydrocele				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute left ventricular failure				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Acute myocardial infarction			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	2 / 466 (0.43%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	4 / 466 (0.86%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Atrial flutter			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure acute			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure chronic			

subjects affected / exposed	2 / 466 (0.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congestive cardiomyopathy				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	2 / 466 (0.43%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Coronary artery insufficiency				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive heart disease				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial fibrosis				

subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Brain stem stroke				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cervicobrachial syndrome				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic inflammatory demyelinating polyradiculoneuropathy				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Facial paralysis				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Focal dyscognitive seizures				

subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic stroke			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thalamic infarction			

subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Iron deficiency anaemia			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Deafness neurosensory			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Exostosis of external ear canal			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vertigo			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Cataract diabetic			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Conjunctival irritation			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic retinopathy			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal detachment			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal haemorrhage			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinopathy proliferative			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Barrett's oesophagus			

subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Faeces discoloured			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine polyp			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			

subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatic cyst				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Bile duct stone				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	3 / 466 (0.64%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Cholecystitis chronic				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				

subjects affected / exposed	2 / 466 (0.43%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Chronic hepatic failure				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cirrhosis alcoholic				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hepatic cirrhosis				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatitis				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-alcoholic steatohepatitis				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Angioedema				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
End stage renal disease				

subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Haematuria				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal cyst				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ureterolithiasis				
subjects affected / exposed	0 / 466 (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 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypopituitarism				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Back pain			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic amyotrophy			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lumbar spinal stenosis			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neck pain			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	2 / 466 (0.43%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Osteochondrosis			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rotator cuff syndrome			

subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal osteoarthritis				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Synovitis				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal wall abscess				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis infective				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neurosyphilis				

subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic abscess				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis bacterial				
subjects affected / exposed	0 / 466 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	4 / 466 (0.86%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Pneumonia klebsiella				
subjects affected / exposed	1 / 466 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	2 / 466 (0.43%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				

subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic phlebitis			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Testicular abscess			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vestibular neuronitis			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			

subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound infection staphylococcal			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 466 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 466 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	222 / 466 (47.64%)	234 / 464 (50.43%)	232 / 465 (49.89%)
Vascular disorders			
Hypertension			
subjects affected / exposed	29 / 466 (6.22%)	24 / 464 (5.17%)	26 / 465 (5.59%)
occurrences (all)	32	27	26

Nervous system disorders			
Headache			
subjects affected / exposed	29 / 466 (6.22%)	30 / 464 (6.47%)	36 / 465 (7.74%)
occurrences (all)	37	40	50
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	27 / 466 (5.79%)	24 / 464 (5.17%)	16 / 465 (3.44%)
occurrences (all)	27	25	16
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	44 / 466 (9.44%)	53 / 464 (11.42%)	56 / 465 (12.04%)
occurrences (all)	62	81	74
Nausea			
subjects affected / exposed	34 / 466 (7.30%)	62 / 464 (13.36%)	70 / 465 (15.05%)
occurrences (all)	42	74	88
Vomiting			
subjects affected / exposed	13 / 466 (2.79%)	27 / 464 (5.82%)	42 / 465 (9.03%)
occurrences (all)	15	41	82
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	21 / 466 (4.51%)	13 / 464 (2.80%)	20 / 465 (4.30%)
occurrences (all)	29	17	25
Back pain			
subjects affected / exposed	24 / 466 (5.15%)	25 / 464 (5.39%)	24 / 465 (5.16%)
occurrences (all)	35	31	25
Infections and infestations			
Influenza			
subjects affected / exposed	29 / 466 (6.22%)	24 / 464 (5.17%)	18 / 465 (3.87%)
occurrences (all)	35	28	21
Nasopharyngitis			
subjects affected / exposed	53 / 466 (11.37%)	49 / 464 (10.56%)	47 / 465 (10.11%)
occurrences (all)	74	65	57
Upper respiratory tract infection			
subjects affected / exposed	36 / 466 (7.73%)	35 / 464 (7.54%)	26 / 465 (5.59%)
occurrences (all)	53	50	34
Urinary tract infection			

subjects affected / exposed	29 / 466 (6.22%)	21 / 464 (4.53%)	23 / 465 (4.95%)
occurrences (all)	32	26	30
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 466 (1.72%)	14 / 464 (3.02%)	32 / 465 (6.88%)
occurrences (all)	8	15	32

Non-serious adverse events	Sitagliptin 100 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	239 / 466 (51.29%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	29 / 466 (6.22%)		
occurrences (all)	29		
Nervous system disorders			
Headache			
subjects affected / exposed	36 / 466 (7.73%)		
occurrences (all)	57		
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	26 / 466 (5.58%)		
occurrences (all)	27		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	37 / 466 (7.94%)		
occurrences (all)	44		
Nausea			
subjects affected / exposed	31 / 466 (6.65%)		
occurrences (all)	39		
Vomiting			
subjects affected / exposed	19 / 466 (4.08%)		
occurrences (all)	26		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	29 / 466 (6.22%)		
occurrences (all)	32		
Back pain			

subjects affected / exposed occurrences (all)	29 / 466 (6.22%) 35		
Infections and infestations Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 30 / 466 (6.44%) 35 47 / 466 (10.09%) 69 32 / 466 (6.87%) 49 26 / 466 (5.58%) 32		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 14 / 466 (3.00%) 15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2015	The cut off level for repeat testing of increased levels of aminotransferases was updated from alanine aminotransferase (ALT)/aspartate aminotransferase (AST) >10x upper limit of normal (ULN) to >5x ULN. The rationale was to prompt follow-up of potential clinically significant aminotransferase levels. In addition several sections were updated to add clarity, i.e. stratification, drug accountability, electrocardiogram (ECG) reporting, antibodies and safety reporting.
23 December 2016	Eye examinations and additional data collection for diabetic retinopathy were introduced along with additional minor clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported