



Clinical trial results:

Efficacy and Safety of Oral Semaglutide Using a Flexible Dose Adjustment Based on Clinical Evaluation versus Sitagliptin in Subjects with Type 2 Diabetes Mellitus. A 52 week Randomised, Open-label, Active-controlled Trial with a 52-week Extension Phase

Summary

EudraCT number	2015-005593-38
Trial protocol	BE AT
Global end of trial date	27 March 2019

Results information

Result version number	v1 (current)
This version publication date	11 April 2020
First version publication date	11 April 2020

Trial information

Trial identification

Sponsor protocol code	NN9924-4257
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02849080
WHO universal trial number (UTN)	U1111-1177-5103

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, +1 866 8677178, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, +1 866 8677178, 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	02 October 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	27 March 2019
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 oral semaglutide using a flexible dose adjustment based on clinical evaluation versus sitagliptin once daily, both in combination with 1-2 oral antidiabetic drugs (OADs) on glycaemic control in subjects with type 2 diabetes (T2D).

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, including archiving of essential documents (2016) and 21 CFR 312.120.

Background therapy:

Subjects were to continue their anti-diabetic medication (metformin, sulphonylurea, thiazolidinedione or sodium-glucose co-transporter 2 inhibitors) throughout the trial.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	20 September 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	Austria: 32
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	Brazil: 33
Country: Number of subjects enrolled	Argentina: 41
Country: Number of subjects enrolled	Egypt: 45
Country: Number of subjects enrolled	Norway: 31
Country: Number of subjects enrolled	Korea, Republic of: 61
Country: Number of subjects enrolled	Switzerland: 21
Country: Number of subjects enrolled	Turkey: 58
Country: Number of subjects enrolled	United States: 160
Worldwide total number of subjects	504
EEA total number of subjects	85

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)	367
From 65 to 84 years	136
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The main phase of the trial was conducted at 77 sites in 10 countries, and the extension phase (Switch) at 71 sites in 9 countries, as follows (main phase/extension phase): Argentina (3/3), Austria (3/3), Belgium (7/7), Brazil (2/0), Egypt (4/4), Norway (4/4), South Korea (7/7), Switzerland (8/5), Turkey (8/8), and United States (31/30).

Pre-assignment

Screening details:

The trial consisted of two treatment periods: a 52-week main phase and a 52-week extension phase. In Switch, participants were allowed to re-randomise from sitagliptin to oral semaglutide. Sustainability included results for participants who received oral semaglutide during main + extension phase.

Period 1

Period 1 title	Main phase: 0 - 52 weeks
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Oral Semaglutide flex- Main phase

Arm description:

Subjects were to receive oral semaglutide tablets once daily from week 0 to week 52 (main phase): 3 milligrams (mg) for the first 8 weeks, 3 or 7 mg for next 8 weeks followed by 3, 7 or 14 mg for the remaining treatment period.

Arm type	Experimental
Investigational medicinal product name	Semaglutide
Investigational medicinal product code	SUB32188
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were to receive oral semaglutide 3, 7 or 14 mg. Oral semaglutide was to be administered once-daily in the morning in a fasting state and at least 30 minutes before the first meal of the day. The semaglutide tablet was to 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. The dose of oral semaglutide was adjusted every 8 weeks according to the dose adjustment criteria: HbA1c <7.0%, the current dose of oral semaglutide should be continued; HbA1c ≥7.0%, the dose of oral semaglutide should be escalated to the next dose level. In case the subject reports moderate to severe nausea or vomiting for 3 or more days in the week prior to the scheduled visit, the dose of oral semaglutide should be maintained or reduced, at the investigator's discretion, irrespective of the level of HbA1c.

Arm title	Sitagliptin 100 mg- Main phase
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Arm description:

Subjects were to receive 100 mg sitagliptin tablet once daily for 52 weeks (main phase).

Arm type	Active comparator
Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	SUB25198
Other name	Januvia
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were to receive 100 mg sitagliptin tablet once daily. The sitagliptin tablet was to be swallowed

whole and not broken or chewed and could be taken with or without food.

Number of subjects in period 1	Oral Semaglutide flex- Main phase	Sitagliptin 100 mg- Main phase
Started	253	251
Completed	241	244
Not completed	12	7
Consent withdrawn by subject	5	1
Lost to follow-up	7	4
Died	-	2

Period 2

Period 2 title	Extension phase: 53 - 104 weeks
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Oral Semaglutide flex

Arm description:

Subjects were to receive oral semaglutide tablets once daily from week 53 to week 104 (extension phase).

Arm type	Experimental
Investigational medicinal product name	Semaglutide
Investigational medicinal product code	SUB32188
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were to receive oral semaglutide 3, 7 or 14 mg. Oral semaglutide was to be administered once-daily in the morning in a fasting state and at least 30 minutes before the first meal of the day. The semaglutide tablet was to 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. The dose of oral semaglutide was adjusted every 8 weeks according to the dose adjustment criteria: HbA1c <7.0%, the current dose of oral semaglutide should be continued; HbA1c ≥7.0%, the dose of oral semaglutide should be escalated to the next dose level. In case the subject reports moderate to severe nausea or vomiting for 3 or more days in the week prior to the scheduled visit, the dose of oral semaglutide should be maintained or reduced, at the investigator's discretion, irrespective of the level of HbA1c.

Arm title	Oral Semaglutide flex- Switch
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Arm description:

Subjects who were still on sitagliptin 100 mg treatment at week 52 (end of main phase) were re-randomised to receive oral semaglutide tablets once daily from week 53 to week 104 (extension phase): 3 mg for the first 8 weeks, 3 or 7 mg for next 8 weeks followed by 3, 7 or 14 mg for the remaining treatment period.

Arm type	Experimental
Investigational medicinal product name	Semaglutide
Investigational medicinal product code	SUB32188
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were to receive oral semaglutide 3, 7 or 14 mg. Oral semaglutide was to be administered once-daily in the morning in a fasting state and at least 30 minutes before the first meal of the day. The semaglutide tablet was to 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. The dose of oral semaglutide was adjusted every 8 weeks according to the dose adjustment criteria: HbA1c <7.0%, the current dose of oral semaglutide should be continued; HbA1c ≥7.0%, the dose of oral semaglutide should be escalated to the next dose level. In case the subject reports moderate to severe nausea or vomiting for 3 or more days in the week prior to the scheduled visit, the dose of oral semaglutide should be maintained or reduced, at the investigator's discretion, irrespective of the level of HbA1c.

Arm title	Sitagliptin 100 mg- Switch
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Arm description:

Subjects who were still on sitagliptin 100 mg treatment at week 52 (end of main phase) were re-randomised to continue sitagliptin in the extension phase (week 53 to week 104).

Arm type	Active comparator
Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	SUB25198
Other name	Januvia
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were to receive 100 mg sitagliptin tablet once daily for 104 weeks. The sitagliptin tablet was to be swallowed whole and not broken or chewed and could be taken with or without food.

Number of subjects in period 2^[1]	Oral Semaglutide flex	Oral Semaglutide flex- Switch	Sitagliptin 100 mg- Switch
Started	185	100	98
Completed	182	99	98
Not completed	3	1	0
Consent withdrawn by subject	1	-	-
Unspecified	-	1	-
Lost to follow-up	2	-	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Subjects who were eligible and provided consent to continue in the extension phase.

Baseline characteristics

Reporting groups

Reporting group title	Oral Semaglutide flex- Main phase
Reporting group description: Subjects were to receive oral semaglutide tablets once daily from week 0 to week 52 (main phase): 3 milligrams (mg) for the first 8 weeks, 3 or 7 mg for next 8 weeks followed by 3, 7 or 14 mg for the remaining treatment period.	
Reporting group title	Sitagliptin 100 mg- Main phase
Reporting group description: Subjects were to receive 100 mg sitagliptin tablet once daily for 52 weeks (main phase).	

Reporting group values	Oral Semaglutide flex- Main phase	Sitagliptin 100 mg- Main phase	Total
Number of subjects	253	251	504
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	187	180	367
From 65-84 years	66	70	136
85 years and over	0	1	1
Age Continuous Units: years			
arithmetic mean	57	58	
standard deviation	± 10	± 10	-
Gender Categorical Units: Subjects			
Female	108	111	219
Male	145	140	285

End points

End points reporting groups

Reporting group title	Oral Semaglutide flex- Main phase
Reporting group description: Subjects were to receive oral semaglutide tablets once daily from week 0 to week 52 (main phase): 3 milligrams (mg) for the first 8 weeks, 3 or 7 mg for next 8 weeks followed by 3, 7 or 14 mg for the remaining treatment period.	
Reporting group title	Sitagliptin 100 mg- Main phase
Reporting group description: Subjects were to receive 100 mg sitagliptin tablet once daily for 52 weeks (main phase).	
Reporting group title	Oral Semaglutide flex
Reporting group description: Subjects were to receive oral semaglutide tablets once daily from week 53 to week 104 (extension phase).	
Reporting group title	Oral Semaglutide flex- Switch
Reporting group description: Subjects who were still on sitagliptin 100 mg treatment at week 52 (end of main phase) were re-randomised to receive oral semaglutide tablets once daily from week 53 to week 104 (extension phase): 3 mg for the first 8 weeks, 3 or 7 mg for next 8 weeks followed by 3, 7 or 14 mg for the remaining treatment period.	
Reporting group title	Sitagliptin 100 mg- Switch
Reporting group description: Subjects who were still on sitagliptin 100 mg treatment at week 52 (end of main phase) were re-randomised to continue sitagliptin in the extension phase (week 53 to week 104).	
Subject analysis set title	Oral Semaglutide flex- Sustainability
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects were to receive oral semaglutide tablets once daily for 104 weeks (week 0-52 in the main phase and week 53-104 in the extension phase): 3 mg for the first 8 weeks, 3 or 7 mg for next 8 weeks followed by 3, 7 or 14 mg for the remaining treatment period.	

Primary: Main phase: Glycosylated haemoglobin (HbA1c) < 7% (53 mmol/mol) American Diabetes Association target (yes/no)

End point title	Main phase: Glycosylated haemoglobin (HbA1c) < 7% (53 mmol/mol) American Diabetes Association target (yes/no)
End point description: Subjects who achieved HbA1c <7.0% ADA target (yes/no), was evaluated at week 52. The endpoint was evaluated based on the data from the in-trial observation period, which was the time period from when a participant was randomised until the final scheduled visit, including any period after initiation of rescue medication and/or premature discontinuation of trial product. The endpoint was also evaluated based on the data from the on-treatment without rescue medication (OWRM) observation period, which was the time period when a participant was on treatment with trial product, excluding any period after initiation of rescue medication and/or premature trial product discontinuation. Results are based on the full analysis set (FAS) which included all randomised subjects. 'n' is the number of subjects analysed for the respective reporting group.	
End point type	Primary
End point timeframe: After week 52	

End point values	Oral Semaglutide flex- Main phase	Sitagliptin 100 mg- Main phase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	238		
Units: Subjects				
In-trial: Yes (n=230,238)	134	60		
In-trial: No (n=230,238)	96	178		
OWRM: Yes (n=196,184)	123	52		
OWRM: No (n=196,184)	73	132		

Statistical analyses

Statistical analysis title	Oral Semaglutide flex Vs Sitagliptin 100 mg
Statistical analysis description:	
The analysis was based on a pattern mixture model using multiple imputation to handle missing week 52 data, assuming that data were missing at random within the groups used for imputation. The imputed data sets were analysed using a logistic regression model with treatment, strata, and region as categorical fixed effects and baseline HbA1c value as covariate for each of the 1000 imputed complete datasets, and pooled by Rubin's rule to draw inference.	
Comparison groups	Sitagliptin 100 mg- Main phase v Oral Semaglutide flex- Main phase
Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	< 0.0001 ^[2]
Method	Pattern mixture model
Parameter estimate	Odds ratio (OR)
Point estimate	4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.89
upper limit	6.7

Notes:

[1] - This hypothesis was controlled for multiplicity. Results are based on the data from the in-trial observation period. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand).

[2] - Unadjusted two-sided p-value for test of no difference from 1.

Statistical analysis title	Oral Semaglutide flex Vs Sitagliptin 100 mg
Statistical analysis description:	
The analysis was based on multiple imputation, imputing sequentially using post-baseline measurements up to and including week 52. The imputed data sets were analysed using a logistic regression model with treatment, strata, and region as categorical fixed effects and baseline HbA1c value as covariate for each of the 1000 imputed complete datasets, and pooled by Rubin's rule to draw inference.	
Comparison groups	Oral Semaglutide flex- Main phase v Sitagliptin 100 mg- Main phase

Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	< 0.0001 ^[4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.54
upper limit	8.68

Notes:

[3] - This hypothesis was not controlled for multiplicity. Results are based on the data from the on-treatment without rescue medication observation period. The estimated treatment effect excludes the effect of any rescue medication and any effect after premature trial product discontinuation (hypothetical estimand).

[4] - Unadjusted two-sided p-value for test of no difference from 1.

Secondary: Main phase: Change in body weight (kg)

End point title	Main phase: Change in body weight (kg)
End point description:	
Change from baseline (week 0) in body weight was evaluated at week 52. The endpoint was evaluated based on the data from the in-trial observation period, which was the time period from when a participant was randomised until the final scheduled visit, including any period after initiation of rescue medication and/or premature discontinuation of trial product. The endpoint was also evaluated based on the data from the on-treatment without rescue medication (OWRM) observation period, which was the time period when a participant was on treatment with trial product, excluding any period after initiation of rescue medication and/or premature trial product discontinuation. Results are based on the full analysis set (FAS) which included all randomised subjects. 'n' is the number of subjects analysed for the respective reporting group.	
End point type	Secondary
End point timeframe:	
From baseline to week 52	

End point values	Oral Semaglutide flex- Main phase	Sitagliptin 100 mg- Main phase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	253	251		
Units: Kilogram (Kg)				
arithmetic mean (standard deviation)				
In-trial (n=233,239)	-2.7 (± 3.9)	-0.7 (± 3.5)		
OWRM (n=198,188)	-2.9 (± 4.0)	-0.9 (± 3.6)		

Statistical analyses

Statistical analysis title	Oral Semaglutide flex vs Sitagliptin 100 mg
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Statistical analysis description:

This hypothesis was controlled for multiplicity. Results are based on the data from the in-trial

observation period. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand).

Comparison groups	Oral Semaglutide flex- Main phase v Sitagliptin 100 mg- Main phase
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	superiority ^[5]
P-value	< 0.0001 ^[6]
Method	Pattern mixture model
Parameter estimate	Treatment difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	-1.2

Notes:

[5] - This hypothesis was controlled for multiplicity. Results are based on the data from the in-trial observation period. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand).

[6] - Unadjusted two-sided p-value for test of no difference from 0.

Statistical analysis title	Oral Semaglutide flex, Sitagliptin 100 mg
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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 52. The independent effects were treatment, strata and region as categorical fixed effects and the baseline HbA1c value as a covariate, all nested within visit, and an unstructured residual covariance matrix.

Comparison groups	Oral Semaglutide flex- Main phase v Sitagliptin 100 mg- Main phase
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	superiority ^[7]
P-value	< 0.0001 ^[8]
Method	Mixed model for repeated measurements
Parameter estimate	Treatment difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	-1.5

Notes:

[7] - This hypothesis was not controlled for multiplicity. Results are based on the data from the on-treatment without rescue medication observation period. The estimated treatment effect excludes the effect of any rescue medication and any effect after premature trial product discontinuation (hypothetical estimand).

[8] - Unadjusted two-sided p-value for test of no difference from 0.

Secondary: Main phase: Change in HbA1c

End point title	Main phase: Change in HbA1c
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End point description:

Change from baseline (week 0) in HbA1c was evaluated at week 52. Results are based on the data from the in-trial observation period, which was the time period from when a participant was randomised until the final scheduled visit, including any period after initiation of rescue medication and/or premature

discontinuation of trial product. Results are based on the full analysis set (FAS) which included all randomised subjects. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
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End point timeframe:

From baseline to week 52

End point values	Oral Semaglutide flex- Main phase	Sitagliptin 100 mg- Main phase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	238		
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-1.3 (± 0.9)	-0.8 (± 1.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Main phase: Change in fasting plasma glucose

End point title	Main phase: Change in fasting plasma glucose
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End point description:

Change from baseline (week 0) in fasting plasma glucose (FPG) was evaluated at week 52. Results are based on the data from the in-trial observation period, which was the time period from when a participant was randomised until the final scheduled visit, including any period after initiation of rescue medication and/or premature discontinuation of trial product. Results are based on the full analysis set (FAS) which included all randomised subjects. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
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End point timeframe:

From baseline to week 52

End point values	Oral Semaglutide flex- Main phase	Sitagliptin 100 mg- Main phase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	232		
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	-2.41 (± 2.35)	-1.39 (± 3.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Main phase: Number of treatment-emergent adverse events during exposure to trial product

End point title	Main phase: Number of treatment-emergent adverse events during exposure to trial product
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End point description:

Treatment emergent adverse events (TEAEs) were recorded from week 0 to week 52. Adverse events (AEs) with onset during the on-treatment observation period were considered treatment-emergent. On-treatment observation period: Time period when a participant was on treatment with trial product, including any period after initiation of rescue medication. Results are based on the safety analysis set (SAS) which included all randomised subjects who received at least one dose of trial product.

End point type	Secondary
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End point timeframe:

Assessed up to approximately 52 weeks

End point values	Oral Semaglutide flex- Main phase	Sitagliptin 100 mg- Main phase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	253	250		
Units: Adverse events	768	519		

Statistical analyses

No statistical analyses for this end point

Secondary: Main phase: Number of treatment-emergent severe or blood glucose-confirmed symptomatic hypoglycaemic episodes during exposure to trial product

End point title	Main phase: Number of treatment-emergent severe or blood glucose-confirmed symptomatic hypoglycaemic episodes during exposure to trial product
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End point description:

Treatment emergent severe or BG confirmed symptomatic hypoglycaemic episodes were recorded during weeks 0–52. Hypoglycaemic episodes with onset during the on-treatment observation period were considered treatment-emergent. On-treatment observation period was defined as the time period when a participant was on treatment with trial product, including any period after initiation of rescue medication. 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 (SAS) which included all randomised subjects who received at least one dose of trial product. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
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End point timeframe:

Assessed up to approximately 52 weeks

End point values	Oral Semaglutide flex- Main phase	Sitagliptin 100 mg- Main phase		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	253	250		
Units: Episodes	34	22		

Statistical analyses

No statistical analyses for this end point

Secondary: Ext phase (sustainability): If a subject achieves (yes/no) HbA1c < 7% (53 mmol/mol) American Diabetes Association target

End point title	Ext phase (sustainability): If a subject achieves (yes/no) HbA1c < 7% (53 mmol/mol) American Diabetes Association target
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End point description:

Subjects who achieved HbA1c <7.0% ADA target (yes/no), was evaluated at week 104. The endpoint was evaluated based on the data from the in-trial observation period, which was the time period from when a participant was randomised until the final scheduled visit, including any period after initiation of rescue medication and/or premature discontinuation of trial product. Results are based on the full analysis set (FAS) which included all randomised subjects. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
End point timeframe:	
After week 104	

End point values	Oral Semaglutide flex- Sustainability			
Subject group type	Subject analysis set			
Number of subjects analysed	180			
Units: Subjects				
Yes	101			
No	79			

Statistical analyses

No statistical analyses for this end point

Secondary: Ext phase (sustainability): Change in body weight (kg)

End point title	Ext phase (sustainability): Change in body weight (kg)
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End point description:

Change from baseline (week 0) in body weight was evaluated at week 104. The endpoint was evaluated based on the data from the in-trial observation period, which was the time period from when a participant was randomised until the final scheduled visit, including any period after initiation of rescue

medication and/or premature discontinuation of trial product. Results are based on the full analysis set (FAS) which included all randomised subjects. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
End point timeframe:	
From baseline to week 104	

End point values	Oral Semaglutide flex-Sustainability			
Subject group type	Subject analysis set			
Number of subjects analysed	180			
Units: Kg				
arithmetic mean (standard deviation)	-3.7 (\pm 5.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ext phase (sustainability): Change in HbA1c

End point title	Ext phase (sustainability): Change in HbA1c
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End point description:

Change from baseline (week 0) in HbA1c was evaluated at week 104. The endpoint was evaluated based on the data from the in-trial observation period, which was the time period from when a participant was randomised until the final scheduled visit, including any period after initiation of rescue medication and/or premature discontinuation of trial product. Results are based on the full analysis set (FAS) which included all randomised subjects. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
End point timeframe:	
From baseline to week 104	

End point values	Oral Semaglutide flex-Sustainability			
Subject group type	Subject analysis set			
Number of subjects analysed	180			
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-1.3 (\pm 1.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ext phase (sustainability): Change in fasting plasma glucose (FPG)

End point title	Ext phase (sustainability): Change in fasting plasma glucose (FPG)
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End point description:

Change from baseline (week 0) in FPG was evaluated at week 104. The endpoint was evaluated based on the data from the in-trial observation period, which was the time period from when a participant was randomised until the final scheduled visit, including any period after initiation of rescue medication and/or premature discontinuation of trial product. Results are based on the full analysis set (FAS) which included all randomised subjects. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
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End point timeframe:

From baseline to week 104

End point values	Oral Semaglutide flex-Sustainability			
Subject group type	Subject analysis set			
Number of subjects analysed	178			
Units: mmol/L				
arithmetic mean (standard deviation)	-2.19 (± 2.84)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ext phase (sustainability): Number of treatment-emergent adverse events during exposure to trial product

End point title	Ext phase (sustainability): Number of treatment-emergent adverse events during exposure to trial product
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End point description:

Treatment emergent adverse events (TEAEs) were recorded from week 0 to week 109 ((104-week treatment period for participants who continued in the extension phase or 52-week treatment period for participants who did not continue in the extension phase) plus the 5-week follow-up period). Adverse events (AEs) with onset during the on-treatment observation period were considered treatment-emergent. On-treatment observation period: Time period when a participant was on treatment with trial product, including any period after initiation of rescue medication. Results are based on the safety analysis set (SAS) which included all randomised subjects who received at least one dose of trial product.

End point type	Secondary
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End point timeframe:

Assessed up to approximately 109 weeks

End point values	Oral Semaglutide flex- Sustainability			
Subject group type	Subject analysis set			
Number of subjects analysed	253			
Units: Adverse events	1157			

Statistical analyses

No statistical analyses for this end point

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

End point title	Ext phase (sustainability): Number of treatment-emergent severe or blood glucose-confirmed symptomatic hypoglycaemic episodes during exposure to trial product
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End point description:

Treatment emergent severe or BG confirmed symptomatic hypoglycaemic episodes were recorded during weeks 0–109. Hypoglycaemic episodes with onset during the on-treatment observation period were considered treatment-emergent. On-treatment observation period was defined as the time period when a participant was on treatment with trial product, including any period after initiation of rescue medication. 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 (SAS) which included all randomised subjects who received at least one dose of trial product. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
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End point timeframe:

Assessed up to approximately 109 weeks

End point values	Oral Semaglutide flex- Sustainability			
Subject group type	Subject analysis set			
Number of subjects analysed	253			
Units: Episodes	45			

Statistical analyses

No statistical analyses for this end point

Secondary: Ext phase (switch): If a subject achieves (yes/no) HbA1c < 7% (53 mmol/mol) American Diabetes Association target

End point title	Ext phase (switch): If a subject achieves (yes/no) HbA1c < 7% (53 mmol/mol) American Diabetes Association target
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End point description:

Subjects who achieved HbA1c <7.0% ADA target (yes/no) during switch phase was evaluated at week 104. The endpoint was evaluated based on the data from the in-trial observation period, which was the time period from when a participant was randomised until the final scheduled visit, including any period after initiation of rescue medication and/or premature discontinuation of trial product. Results are based on the full analysis set (FAS) which included all randomised subjects. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
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End point timeframe:

After week 104

End point values	Oral Semaglutide flex- Switch	Sitagliptin 100 mg- Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	96		
Units: Subjects				
Yes	44	26		
No	48	70		

Statistical analyses

No statistical analyses for this end point

Secondary: Ext phase (switch): Change in body weight (kg)

End point title	Ext phase (switch): Change in body weight (kg)
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End point description:

Change from week 52 in body weight was evaluated at week 104. The endpoint was evaluated based on the data from the in-trial observation period, which was the time period from when a participant was randomised until the final scheduled visit, including any period after initiation of rescue medication and/or premature discontinuation of trial product. Results are based on the full analysis set (FAS) which included all randomised subjects. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
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End point timeframe:

From week 52 to 104

End point values	Oral Semaglutide flex- Switch	Sitagliptin 100 mg- Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	97		
Units: kg				
arithmetic mean (standard deviation)	-2.6 (± 3.8)	-0.9 (± 5.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Ext phase (switch): Change in HbA1c

End point title	Ext phase (switch): Change in HbA1c
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End point description:

Change from week 52 in HbA1c was evaluated at week 104. The endpoint was evaluated based on the data from the in-trial observation period, which was the time period from when a participant was randomised until the final scheduled visit, including any period after initiation of rescue medication and/or premature discontinuation of trial product. Results are based on the full analysis set (FAS) which included all randomised subjects. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
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End point timeframe:

From week 52 to 104

End point values	Oral Semaglutide flex- Switch	Sitagliptin 100 mg- Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	98		
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-2 (± 13)	1 (± 11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Ext phase (switch): Change in fasting plasma glucose (FPG)

End point title	Ext phase (switch): Change in fasting plasma glucose (FPG)
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End point description:

Change from week 52 in fasting plasma glucose (FPG) was evaluated at week 104. Results are based on the data from the in-trial observation period, which was the time period from when a participant was randomised until the final scheduled visit, including any period after initiation of rescue medication and/or premature discontinuation of trial product. Results are based on the full analysis set (FAS) which included all randomised subjects. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
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End point timeframe:

From week 52 to 104

End point values	Oral Semaglutide flex- Switch	Sitagliptin 100 mg- Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	98		
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)	-0.35 (± 1.95)	0.02 (± 2.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Ext phase (switch): Number of treatment-emergent adverse events during exposure to trial product

End point title	Ext phase (switch): Number of treatment-emergent adverse events during exposure to trial product
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End point description:

Treatment emergent adverse events (TEAEs) were recorded from week 52 to week 109. Adverse events (AEs) with onset during the on-treatment observation period were considered treatment-emergent. On-treatment observation period: Time period when a participant was on treatment with trial product, including any period after initiation of rescue medication. Results are based on the safety analysis set (SAS) which included all randomised subjects who received at least one dose of trial product. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
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End point timeframe:

Assessed from week 52 up to approximately 109 weeks

End point values	Oral Semaglutide flex- Switch	Sitagliptin 100 mg- Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	97		
Units: Adverse events	75	67		

Statistical analyses

No statistical analyses for this end point

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

End point title	Ext phase (switch): Number of treatment-emergent severe or blood glucose-confirmed symptomatic hypoglycaemic episodes during exposure to trial product
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End point description:

Treatment emergent severe or BG confirmed symptomatic hypoglycaemic episodes were recorded during weeks 52 up to approximately 109 weeks. Hypoglycaemic episodes with onset during the on-treatment observation period were considered treatment-emergent. On-treatment observation period was defined as the time period when a participant was on treatment with trial product, including any

period after initiation of rescue medication. 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 (SAS) which included all randomised subjects who received at least one dose of trial product. Number of subjects analyzed is the number of subjects with available data.

End point type	Secondary
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End point timeframe:

Assessed from week 52 up to approximately 109 weeks

End point values	Oral Semaglutide flex- Switch	Sitagliptin 100 mg- Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	97		
Units: Episodes	2	12		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of first dose of trial product (week 0) to end of treatment (week 104) + 5 weeks follow-up

Results are based on the safety analysis set (SAS), which comprised all randomised participants who received at least one dose of trial product.

Adverse event reporting additional description:

Serious adverse events and other AEs were based on the on-treatment observation period. All-cause mortality were based on the in-trial observation period.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20
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Reporting groups

Reporting group title	Oral Semaglutide flex- Main phase
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Reporting group description:

Subjects were to receive oral semaglutide tablets once daily from week 0 to week 52 (main phase): 3 milligrams (mg) for the first 8 weeks, 3 or 7 mg for next 8 weeks followed by 3, 7 or 14 mg for the remaining treatment period.

Reporting group title	Sitagliptin 100 mg- Main phase
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Reporting group description:

Subjects were to receive 100 mg sitagliptin tablet once daily for 52 weeks (main phase).

Reporting group title	Oral Semaglutide flex- Sustainability
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Reporting group description:

Subjects were to receive oral semaglutide tablets once daily for 104 weeks (week 0-52 in the main phase and week 53-104 in the extension phase): 3 mg for the first 8 weeks, 3 or 7 mg for next 8 weeks followed by 3, 7 or 14 mg for the remaining treatment period.

Reporting group title	Oral Semaglutide flex- Switch
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Reporting group description:

Subjects who were still on sitagliptin 100 mg treatment at week 52 (end of main phase) were re-randomised to receive oral semaglutide tablets once daily from week 53 to week 104 (extension phase): 3 mg for the first 8 weeks, 3 or 7 mg for next 8 weeks followed by 3, 7 or 14 mg for the remaining treatment period.

Reporting group title	Sitagliptin 100 mg- Switch
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Reporting group description:

Subjects who were still on sitagliptin 100 mg treatment at week 52 (end of main phase) were re-randomised to continue sitagliptin in the extension phase (week 53 to week 104).

Serious adverse events	Oral Semaglutide flex- Main phase	Sitagliptin 100 mg- Main phase	Oral Semaglutide flex- Sustainability
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 253 (9.49%)	24 / 250 (9.60%)	36 / 253 (14.23%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			

subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of colon			
subjects affected / exposed	2 / 253 (0.79%)	0 / 250 (0.00%)	2 / 253 (0.79%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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
Choroid melanoma			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular carcinoma			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal papillary mucinous neoplasm			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			

subjects affected / exposed	1 / 253 (0.40%)	1 / 250 (0.40%)	2 / 253 (0.79%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung cancer metastatic			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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
Malignant melanoma			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian endometrioid carcinoma			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	1 / 253 (0.40%)	1 / 250 (0.40%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery stenosis			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			

Cataract operation			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric bypass			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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
Shoulder operation			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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
Pyrexia			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			

subjects affected / exposed	0 / 253 (0.00%)	2 / 250 (0.80%)	0 / 253 (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
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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
Cough			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Emphysema			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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
Pharyngeal polyp			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nightmare			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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
Investigations			
Catheterisation cardiac			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 253 (0.79%)	0 / 250 (0.00%)	2 / 253 (0.79%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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
Laceration			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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
Road traffic accident			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 253 (0.00%)	2 / 250 (0.80%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Angina unstable			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	2 / 253 (0.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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 failure congestive			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	2 / 253 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery insufficiency			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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			
Dizziness			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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
Myelopathy			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Otosclerosis			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular fibrosis			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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
Diarrhoea			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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
Gastric ulcer			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal inflammation			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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
Ileus			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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
Inguinal hernia			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal mass			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritable bowel syndrome			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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
Nausea			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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
Skin and subcutaneous tissue disorders			

Hidradenitis			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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 and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder prolapse			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	2 / 253 (0.79%)	1 / 250 (0.40%)	2 / 253 (0.79%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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
Bursitis			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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

Osteoarthritis			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	3 / 253 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia pyelonephritis			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (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
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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
Otitis media chronic			
subjects affected / exposed	0 / 253 (0.00%)	0 / 250 (0.00%)	0 / 253 (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	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis			
subjects affected / exposed	0 / 253 (0.00%)	1 / 250 (0.40%)	0 / 253 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Hyperglycaemia			
subjects affected / exposed	1 / 253 (0.40%)	0 / 250 (0.00%)	1 / 253 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Oral Semaglutide flex- Switch	Sitagliptin 100 mg- Switch	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 100 (9.00%)	7 / 97 (7.22%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Choroid melanoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 100 (1.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial adenocarcinoma			

subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal papillary mucinous neoplasm			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	1 / 100 (1.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian endometrioid carcinoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			

subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cataract operation			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric bypass			
subjects affected / exposed	0 / 100 (0.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shoulder operation			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 100 (0.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	0 / 100 (0.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal polyp			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			

subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nightmare			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Catheterisation cardiac			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 100 (1.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	1 / 100 (1.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Laceration			
subjects affected / exposed	0 / 100 (0.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 100 (1.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 100 (1.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 100 (1.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery insufficiency			

subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 100 (0.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelopathy			
subjects affected / exposed	0 / 100 (0.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Otosclerosis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 100 (0.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular fibrosis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 100 (0.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 100 (1.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal mass			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			

subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 100 (0.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder prolapse			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia pyelonephritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 100 (0.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Otitis media chronic			
subjects affected / exposed	0 / 100 (0.00%)	1 / 97 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 97 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Oral Semaglutide flex- Main phase	Sitagliptin 100 mg- Main phase	Oral Semaglutide flex- Sustainability
Total subjects affected by non-serious adverse events			
subjects affected / exposed	126 / 253 (49.80%)	70 / 250 (28.00%)	148 / 253 (58.50%)
Nervous system disorders			
Headache			
subjects affected / exposed	25 / 253 (9.88%)	15 / 250 (6.00%)	29 / 253 (11.46%)
occurrences (all)	33	15	47
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	16 / 253 (6.32%)	3 / 250 (1.20%)	20 / 253 (7.91%)
occurrences (all)	17	3	27
Constipation			
subjects affected / exposed	7 / 253 (2.77%)	7 / 250 (2.80%)	11 / 253 (4.35%)
occurrences (all)	9	8	17
Diarrhoea			

subjects affected / exposed	22 / 253 (8.70%)	8 / 250 (3.20%)	29 / 253 (11.46%)
occurrences (all)	25	11	39
Dyspepsia			
subjects affected / exposed	13 / 253 (5.14%)	2 / 250 (0.80%)	18 / 253 (7.11%)
occurrences (all)	13	4	23
Nausea			
subjects affected / exposed	53 / 253 (20.95%)	6 / 250 (2.40%)	58 / 253 (22.92%)
occurrences (all)	83	8	113
Vomiting			
subjects affected / exposed	14 / 253 (5.53%)	2 / 250 (0.80%)	18 / 253 (7.11%)
occurrences (all)	21	2	39
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 253 (3.16%)	8 / 250 (3.20%)	17 / 253 (6.72%)
occurrences (all)	12	9	34
Back pain			
subjects affected / exposed	9 / 253 (3.56%)	11 / 250 (4.40%)	17 / 253 (6.72%)
occurrences (all)	14	14	34
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	9 / 253 (3.56%)	1 / 250 (0.40%)	13 / 253 (5.14%)
occurrences (all)	9	1	19
Influenza			
subjects affected / exposed	10 / 253 (3.95%)	6 / 250 (2.40%)	15 / 253 (5.93%)
occurrences (all)	11	8	23
Nasopharyngitis			
subjects affected / exposed	26 / 253 (10.28%)	13 / 250 (5.20%)	34 / 253 (13.44%)
occurrences (all)	30	15	58
Upper respiratory tract infection			
subjects affected / exposed	9 / 253 (3.56%)	15 / 250 (6.00%)	18 / 253 (7.11%)
occurrences (all)	9	16	33

Non-serious adverse events	Oral Semaglutide flex- Switch	Sitagliptin 100 mg- Switch	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 100 (46.00%)	27 / 97 (27.84%)	

Nervous system disorders			
Headache			
subjects affected / exposed	4 / 100 (4.00%)	3 / 97 (3.09%)	
occurrences (all)	4	3	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	6 / 100 (6.00%)	1 / 97 (1.03%)	
occurrences (all)	6	2	
Constipation			
subjects affected / exposed	5 / 100 (5.00%)	1 / 97 (1.03%)	
occurrences (all)	5	1	
Diarrhoea			
subjects affected / exposed	10 / 100 (10.00%)	3 / 97 (3.09%)	
occurrences (all)	11	5	
Dyspepsia			
subjects affected / exposed	4 / 100 (4.00%)	2 / 97 (2.06%)	
occurrences (all)	4	2	
Nausea			
subjects affected / exposed	17 / 100 (17.00%)	3 / 97 (3.09%)	
occurrences (all)	19	3	
Vomiting			
subjects affected / exposed	7 / 100 (7.00%)	2 / 97 (2.06%)	
occurrences (all)	8	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 100 (3.00%)	4 / 97 (4.12%)	
occurrences (all)	5	4	
Back pain			
subjects affected / exposed	3 / 100 (3.00%)	5 / 97 (5.15%)	
occurrences (all)	3	5	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	3 / 100 (3.00%)	0 / 97 (0.00%)	
occurrences (all)	3	0	
Influenza			

subjects affected / exposed	6 / 100 (6.00%)	4 / 97 (4.12%)	
occurrences (all)	6	5	
Nasopharyngitis			
subjects affected / exposed	7 / 100 (7.00%)	10 / 97 (10.31%)	
occurrences (all)	8	11	
Upper respiratory tract infection			
subjects affected / exposed	1 / 100 (1.00%)	4 / 97 (4.12%)	
occurrences (all)	2	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 November 2016	Introduction of additional eye examinations and additional data collection on diabetic retinopathy; addition of bicarbonate as part of the biochemistry laboratory assessment; investigator's responsibility in ensuring evaluation and management of certain risk factors and complications; clarification of the criteria for completion, withdrawal and lost to follow-up and other minor adjustments.
14 March 2017	Created to add a 52-week extension period to the trial in order to assess: (1) sustainability of glycaemic control and long-term safety in subjects exposed to oral semaglutide using flexible dose adjustment for a period of up to 104 weeks and (2) effect of switching from sitagliptin to oral semaglutide on glycaemic control and safety for a period of up to 52 weeks.
24 July 2018	Only relevant for extension phase. Created to include blood samples in the extension phase of the trial at week 100 (visit 18) and week 104 (visit 19) for assessments of semaglutide plasma concentrations (long-term exposure and population PK analysis).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported