Clinical trial results:
Efficacy and safety of semaglutide versus dulaglutide as add-on to metformin in subjects with type 2 diabetes

Summary

EudraCT number	2014-005375-91
Trial protocol	IE FI DE GB SK LV LT GR ES PT HR
Global end of trial date	19 May 2017

Results information

Result version number	v1 (current)
This version publication date	30 May 2018
First version publication date	30 May 2018

Trial information

Trial identification

Sponsor protocol code	NN9535-4216

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02648204
WHO universal trial number (UTN)	U1111-1164-8495

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	30 November 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2017
Global end of trial reached?	Yes
Global end of trial date	19 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

o compare the effect of once-weekly dosing of two dose levels of subcutaneous semaglutide (0.5 mg and 1.0 mg) versus once-weekly dosing of two dose levels of subcutaneous dulaglutide (0.75 mg and 1.5 mg) on glycaemic control in subjects with type 2 diabetes on a background treatment with metformin.

Protection of trial subjects:

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

Background therapy:

Subjects were to continue metformin at pre-trial dose and frequency during the whole treatment period unless rescue medication was needed.

Evidence for comparator:

Not applicable

Actual start date of recruitment	06 January 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	Bulgaria: 60
Country: Number of subjects enrolled	Germany: 58
Country: Number of subjects enrolled	Spain: 63
Country: Number of subjects enrolled	Finland: 31
Country: Number of subjects enrolled	United Kingdom: 70
Country: Number of subjects enrolled	Greece: 73
Country: Number of subjects enrolled	Hong Kong: 30
Country: Number of subjects enrolled	Croatia: 27
Country: Number of subjects enrolled	India: 130
Country: Number of subjects enrolled	Ireland: 22
Country: Number of subjects enrolled	Lithuania: 40
Country: Number of subjects enrolled	Latvia: 35
Country: Number of subjects enrolled	Portugal: 14
Country: Number of subjects enrolled	Romania: 65
Country: Number of subjects enrolled	Slovakia: 40
Country: Number of subjects enrolled	United States: 441

Worldwide total number of subjects	1199
EEA total number of subjects	598

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)	939
From 65 to 84 years	260
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 210 sites were approved for recruiting subjects, of which 196 sites randomized the subjects: Bulgaria: 6; Croatia: 6; Finland: 6; Germany: 6; Greece: 8; Hong Kong: 1; India: 22; Ireland: 5; Latvia: 3; Lithuania: 5; Portugal: 4; Romania: 7; Slovakia: 6; Spain: 8; United Kingdom: 8; United States: 95.

Pre-assignment

Screening details:

A total of 1201 subjects were randomized in the trial: Semaglutide 0.5 mg-301 subjects, Semaglutide 1.0 mg-300 subjects, Dulaglutide 0.75 mg-300 subjects, Dulaglutide 1.5 mg-300 subjects. Of the 1201 subjects, 1199 were exposed to trial products and 2 randomised subjects withdrew prior to exposure (1 subject in each Dulaglutide arm).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Semaglutide 0.5 mg

Arm description:

Subjects received subcutaneous (s.c., under the skin) injections of semaglutide once weekly (OW) for treatment duration of 40 weeks. Subjects received semaglutide 0.25 mg for 4 weeks (weeks 1 to 4) followed by 0.5 mg for 36 weeks (weeks 5 to 40). Subjects were followed for 5 weeks after completion of treatment period.

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

Dosage and administration details:

Semaglutide solution for injection in pre-filled PDS290 pen-injector, was administered by s.c. injection either in the thigh, abdomen or upper arm, at any time of day irrespective of meals. The injections were to be administered on the same day of the week during the trial.

Arm title	Semaglutide 1.0 mg

Arm description:

Subjects received s.c. injections of semaglutide OW for treatment duration of 40 weeks. Subjects received semaglutide 0.25 mg for 4 weeks (weeks 1 to 4) followed by 0.5 mg for another 4 weeks (weeks 5 to 8) and then semaglutide 1.0 mg for remaining 32 weeks (weeks 9-40). Subjects were followed for 5 weeks after completion of treatment period.

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

Dosage and administration details:

Semaglutide solution for injection in pre-filled PDS290 pen-injector, was administered by s.c. injection

either in the thigh, abdomen or upper arm, at any time of day irrespective of meals. The injections were to be administered on the same day of the week during the trial.

Arm title	Dulaglutide 0.75 mg

Arm description:

Subjects received s.c. injections of dulaglutide 0.75 mg OW for treatment duration of 40 weeks. Subjects were followed for 5 weeks after completion of treatment period.

Arm type	Active comparator
Investigational medicinal product name	Dulaglutide
Investigational medicinal product code	
Other name	Trulicity®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dulaglutide solution for injection in a pre-filled pen was administered by s.c. injection either in the thigh, abdomen or upper arm, at any time of day irrespective of meals. The injections were to be administered on the same day of the
week during the trial.

Arm title	Dulaglutide 1.5 mg

Arm description:

Subjects received s.c. injections of dulaglutide 1.5 mg OW for treatment duration of 40 weeks. Subjects were followed for 5 weeks after completion of treatment period.

Arm type	Active comparator
Investigational medicinal product name	Dulaglutide
Investigational medicinal product code	
Other name	Trulicity®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dulaglutide solution for injection in a pre-filled pen was administered by s.c. injection either in the thigh, abdomen or upper arm, at any time of day irrespective of meals. The injections were to be administered on the same day of the
week during the trial.

Number of subjects in period 1	Semaglutide 0.5 mg	Semaglutide 1.0 mg	Dulaglutide 0.75 mg
Started	301	300	299
Completed	279	279	287
Not completed	22	21	12
Adverse event, serious fatal	1	1	2
Consent withdrawn by subject	12	8	1
Adverse event, non-fatal	-	-	1
Lost to follow-up	5	8	4
Missing follow-up information	4	4	4

Number of subjects in period 1	Dulaglutide 1.5 mg

Started	299
Completed	284
Not completed	15
Adverse event, serious fatal	2
Consent withdrawn by subject	5
Adverse event, non-fatal	-
Lost to follow-up	6
Missing follow-up information	2

Baseline characteristics

Reporting groups	
Reporting group title	Semaglutide 0.5 mg
Reporting group description:	
Subjects received subcutaneous (s.c., under the skin) injections of semaglutide once weekly (OW) for treatment duration of 40 weeks. Subjects received semaglutide 0.25 mg for 4 weeks (weeks 1 to 4) followed by 0.5 mg for 36 weeks (weeks 5 to 40). Subjects were followed for 5 weeks after completion of treatment period.	
Reporting group title	Semaglutide 1.0 mg
Reporting group description:	
Subjects received s.c. injections of semaglutide OW for treatment duration of 40 weeks. Subjects received semaglutide 0.25 mg for 4 weeks (weeks 1 to 4) followed by 0.5 mg for another 4 weeks (weeks 5 to 8) and then semaglutide 1.0 mg for remaining 32 weeks (weeks 9-40). Subjects were followed for 5 weeks after completion of treatment period.	
Reporting group title	Dulaglutide 0.75 mg
Reporting group description:	
Subjects received s.c. injections of dulaglutide 0.75 mg OW for treatment duration of 40 weeks. Subjects were followed for 5 weeks after completion of treatment period.	
Reporting group title	Dulaglutide 1.5 mg
Reporting group description:	
Subjects received s.c. injections of dulaglutide 1.5 mg OW for treatment duration of 40 weeks. Subjects were followed for 5 weeks after completion of treatment period.	

Reporting group values	Semaglutide 0.5 mg	Semaglutide 1.0 mg	Dulaglutide 0.75 mg
Number of subjects	301	300	299
Age Categorical Units: Subjects			
Adults (18-64 years)	222	247	238
From 65-74 years	67	45	53
75-84 years	12	8	8
Age Continuous Units: years			
arithmetic mean	56	55	55
standard deviation	± 10.9	± 10.6	± 10.4
Gender Categorical Units: Subjects			
Female	169	162	160
Male	132	138	139
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	50	38	48
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	17	18	17
White	233	243	232
More than one race	0	0	0
Unknown or Not Reported	1	1	2
Ethnicity Units: Subjects			

Hispanic or Latino	29	35	31
Not Hispanic or Latino	272	265	268

Glycosylated haemoglobin (Hb1Ac)			
Units: percentage of HbA1c			
arithmetic mean	8.3	8.2	8.2
standard deviation	± 0.96	± 0.92	± 0.91
Body weight			
Units: kg			
arithmetic mean	96.4	95.5	95.6
standard deviation	± 24.38	± 20.90	± 23.01
Fasting plasma glucose			
Number of subject analysed=298, 299, 297, 297 for semaglutide 0.5 mg, semaglutide 1.0 mg, dulaglutide 0.75 mg and dulaglutide 1.5 mg, respectively.			
Units: mmol/L			
arithmetic mean	9.8	9.8	9.7
standard deviation	± 2.54	± 2.58	± 2.65

Reporting group values	Dulaglutide 1.5 mg	Total	
Number of subjects	299	1199	
Age Categorical			
Units: Subjects			
Adults (18-64 years)	232	939	
From 65-74 years	60	225	
75-84 years	7	35	
Age Continuous			
Units: years			
arithmetic mean	56		
standard deviation	± 10.6	-	
Gender Categorical			
Units: Subjects			
Female	171	662	
Male	128	537	
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	55	191	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	18	70	
White	220	928	
More than one race	0	0	
Unknown or Not Reported	6	10	
Ethnicity			
Units: Subjects			
Hispanic or Latino	43	138	
Not Hispanic or Latino	256	1061	
Glycosylated haemoglobin (Hb1Ac)			
Units: percentage of HbA1c			
arithmetic mean	8.2		
standard deviation	± 0.89	-	
Body weight			

Units: kg			
arithmetic mean	93.4		
standard deviation	± 21.79	-	
Fasting plasma glucose			
Number of subject analysed=298, 299, 297, 297 for semaglutide 0.5 mg, semaglutide 1.0 mg, dulaglutide 0.75 mg and dulaglutide 1.5 mg, respectively.			
Units: mmol/L			
arithmetic mean	9.6		
standard deviation	± 2.29	-	

End points

End points reporting groups

Reporting group title	Semaglutide 0.5 mg

Reporting group description:

Subjects received subcutaneous (s.c., under the skin) injections of semaglutide once weekly (OW) for treatment duration of 40 weeks. Subjects received semaglutide 0.25 mg for 4 weeks (weeks 1 to 4) followed by 0.5 mg for 36 weeks (weeks 5 to 40). Subjects were followed for 5 weeks after completion of treatment period.

Reporting group title	Semaglutide 1.0 mg

Reporting group description:

Subjects received s.c. injections of semaglutide OW for treatment duration of 40 weeks. Subjects received semaglutide 0.25 mg for 4 weeks (weeks 1 to 4) followed by 0.5 mg for another 4 weeks (weeks 5 to 8) and then semaglutide 1.0 mg for remaining 32 weeks (weeks 9-40). Subjects were followed for 5 weeks after completion of treatment period.

Reporting group title	Dulaglutide 0.75 mg

Reporting group description:

Subjects received s.c. injections of dulaglutide 0.75 mg OW for treatment duration of 40 weeks. Subjects were followed for 5 weeks after completion of treatment period.

Reporting group title	Dulaglutide 1.5 mg

Reporting group description:

Subjects received s.c. injections of dulaglutide 1.5 mg OW for treatment duration of 40 weeks. Subjects were followed for 5 weeks after completion of treatment period.

Primary: Change in HbA1c

End point title	Change in HbA1c

End point description:

Results are based on HbA1c data from on-treatment without rescue medication observation period. The 'on-treatment' observation period was the period where the subject was considered to be exposed to trial product. The 'on-treatment without rescue medication' observation period was a subset of the 'on-treatment' observation period, where subjects did not receive any non-investigational antidiabetic medication (rescue medication). This period includes the observations recorded at, or after the date of first dose of trial product and not after the first occurrence of the following: the end-date of the 'on-treatment' observation period or initiation of rescue medication. The post-baseline responses are analysed using a mixed model for repeated measurements with treatment and country as fixed factors and baseline value as covariate, all nested within visit. Analysis was based on FAS (all randomised subjects exposed to at least one dose of trial product).

End point type	Primary

End point timeframe:

From baseline to week 40

End point values	Semaglutide 0.5 mg	Semaglutide 1.0 mg	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	301	300	299	299
Units: percentage of HbA1c				
least squares mean (standard error)	-1.51 (± 0.06)	-1.78 (± 0.06)	-1.11 (± 0.05)	-1.37 (± 0.06)

Statistical analyses

Statistical analysis title	Semaglutide 0.5 mg vs. Dulaglutide 0.75 mg
Comparison groups	Dulaglutide 0.75 mg v Semaglutide 0.5 mg
Number of subjects included in analysis	600
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.08

Notes:

[1] - Non-Inferiority margin: 0.4

Statistical analysis title	Semaglutide 0.5 mg vs. Dulaglutide 0.75 mg
Comparison groups	Semaglutide 0.5 mg v Dulaglutide 0.75 mg
Number of subjects included in analysis	600
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.08

Statistical analysis title	Semaglutide 1.0 mg vs. Dulaglutide 1.5 mg
Comparison groups	Semaglutide 1.0 mg v Dulaglutide 1.5 mg
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-0.41

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.08

Notes:

[2] - Non-Inferiority margin: 0.04

Statistical analysis title	Semaglutide 1.0 mg vs. Dulaglutide 1.5 mg
Comparison groups	Semaglutide 1.0 mg v Dulaglutide 1.5 mg
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.08

Secondary: Change in body weight (kg)

End point title	Change in body weight (kg)

End point description:

Results are based on body weight data from on-treatment without rescue medication observation period. The 'on-treatment' observation period was the period where the subject was considered to be exposed to trial product. The 'on-treatment without rescue medication' observation period was a subset of the 'on -treatment' observation period, where subjects did not receive any non-investigational antidiabetic medication (rescue medication). This period includes the observations recorded at, or after the date of first dose of trial product and not after the first occurrence of the following: the end-date of the 'on-treatment' observation period or initiation of rescue medication. Analysis was based on FAS. Number of subjects analysed=number of subjects with available data for body weight.

End point type	Secondary

End point timeframe:

From baseline to week 40

End point values	Semaglutide 0.5 mg	Semaglutide 1.0 mg	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	301	300	299	298
Units: kg				
least squares mean (standard error)	-4.56 (± 0.28)	-6.53 (± 0.28)	-2.30 (± 0.27)	-2.98 (± 0.27)

Statistical analyses

Statistical analysis title	Semaglutide 1.0 mg vs. Dulaglutide 1.5 mg
Comparison groups	Semaglutide 1.0 mg v Dulaglutide 1.5 mg
Number of subjects included in analysis	598
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-3.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.32
upper limit	-2.78
Variability estimate	Standard error of the mean
Dispersion value	0.39

Statistical analysis title	Semaglutide 0.5 mg vs. Dulaglutide 0.75 mg
Comparison groups	Semaglutide 0.5 mg v Dulaglutide 0.75 mg
Number of subjects included in analysis	600
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-2.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.02
upper limit	-1.51
Variability estimate	Standard error of the mean
Dispersion value	0.39

Secondary: Change in fasting plasma glucose

End point title	Change in fasting plasma glucose

End point description:

Results are based on fasting plasma glucose data from on-treatment without rescue medication observation period. The 'on-treatment' observation period was the period where the subject was considered to be exposed to trial product. The 'on-treatment without rescue medication' observation period was a subset of the 'on -treatment' observation period, where subjects did not receive any non-investigational antidiabetic medication (rescue medication). This period includes the observations recorded at, or after the date of first dose of trial product and not after the first occurrence of the following: the end-date of the 'on-treatment' observation period or initiation of rescue medication. Analysis was based on FAS. Number of participants analysed=number of participants with available data for fasting plasma glucose.

End point type	Secondary

End point timeframe:

From baseline to week 40

End point values	Semaglutide 0.5 mg	Semaglutide 1.0 mg	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	298	299	297	297
Units: mmol/L				
least squares mean (standard error)	-2.18 (± 0.12)	-2.83 (± 0.12)	-1.87 (± 0.12)	-2.25 (± 0.12)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in systolic and diastolic blood pressure

End point title	Change in systolic and diastolic blood pressure

End point description:

Results are based on systolic and diastolic blood pressure data from on-treatment without rescue medication observation period. The 'on-treatment' observation period was the period where the subject was considered to be exposed to trial product. The 'on-treatment without rescue medication' observation period was a subset of the 'on -treatment' observation period, where subjects did not receive any non-investigational antidiabetic medication (rescue medication). This period includes the observations recorded at, or after the date of first dose of trial product and not after the first occurrence of the following: the end-date of the 'on-treatment' observation period or initiation of rescue medication. Analysis was based on FAS.

End point type	Secondary

End point timeframe:

From baseline to week 40

End point values	Semaglutide 0.5 mg	Semaglutide 1.0 mg	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	301	300	299	299
Units: mmHg				
least squares mean (standard error)				
Diastolic BP	-0.57 (± 0.48)	-2.05 (± 0.49)	-0.35 (± 0.47)	-0.03 (± 0.47)

Systolic BP	-2.44 (± 0.76)	-4.88 (± 0.77)	-2.16 (± 0.75)	-2.86 (± 0.75)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall scores for patient reported outcomes: Diabetes Treatment Satisfaction Questionnaire

End point title	Overall scores for patient reported outcomes: Diabetes Treatment Satisfaction Questionnaire

End point description:

The questionnaire contains 8 items and evaluates subjects' diabetes treatment in terms of convenience, flexibility and general feelings towards treatment. The result presented is 'Treatment Satisfaction' summary score (sum of 6 of the 8 items). Response options: 6 (best case) to 0 (worst case). Total scores range: 0-36. Higher scores=higher satisfaction. Results are based on data from on-treatment without rescue medication observation period. The 'on-treatment' observation period was period where subject was considered to be exposed to trial product. The 'on-treatment without rescue medication' observation period was a subset of the 'on -treatment' observation period, where subjects did not receive any non-investigational antidiabetic medication (rescue medication). This includes observations recorded at, or after the date of first dose of trial product and not after first occurrence of following: end-date of the 'on-treatment' observation period or initiation of rescue medication

End point type	Secondary

End point timeframe:

From baseline to week 40

End point values	Semaglutide 0.5 mg	Semaglutide 1.0 mg	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	301[3]	299[4]	299[5]	298[6]
Units: units on a scale				
least squares mean (standard error)	4.60 (± 0.28)	4.55 (± 0.29)	4.52 (± 0.28)	4.65 (± 0.28)

Notes:

[3] - Number of participants with available data for diabetes treatment satisfaction questionnaire.

[4] - Number of participants with available data for diabetes treatment satisfaction questionnaire

[5] - Number of participants with available data for diabetes treatment satisfaction questionnaire

[6] - Number of participants with available data for diabetes treatment satisfaction questionnaire

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Percentage of subjects who achieved HbA1c target below or equal to 6.5% (48 mmol/mol) after 40 weeks of treatment. Results are based on data from on-treatment without rescue medication period. The 'on-treatment' observation period was the period where the subject was considered to be exposed

to trial product. The 'on-treatment without rescue medication' observation period was a subset of the 'on -treatment' observation period, where subjects did not receive any non-investigational antidiabetic medication (rescue medication). This period includes the observations recorded at, or after the date of first dose of trial product and not after the first occurrence of the following: the end-date of the 'on-treatment' observation period or initiation of rescue medication. Missing data imputed from a mixed model for repeated measurements with treatment and country as fixed factors and baseline value as covariate, all nested within visit. Results are based on the FAS.

End point type	Secondary

End point timeframe:

After 40 weeks treatment

End point values	Semaglutide 0.5 mg	Semaglutide 1.0 mg	Dulaglutide 0.75 mg	Dulaglutide 1.5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	301	300	299	299
Units: percentage of subjects				
number (not applicable)				
Yes	49.2	66.7	34.1	47.2
No	50.8	33.3	65.9	52.8

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline (week 0) to week 40 + follow up of 5 weeks (including a visit window of +7 days)

Adverse event reporting additional description:

A TEAE was defined as an AE with onset in the 'on-treatment' period (information collected while subjects were considered as exposed to trial product). This corresponded to information collected from first administration of trial product until the follow-up (5 weeks after the last treatment including a visit window of +7 days)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19

Reporting groups

Reporting group title	Semaglutide 0.5 mg

Reporting group description:

Subjects received s.c. injections of semaglutide OW for treatment duration of 40 weeks. Subjects received semaglutide 0.25 mg for 4 weeks (weeks 1 to 4) followed by 0.5 mg for 36 weeks (weeks 5 to 40).

Reporting group title	Semaglutide 1.0 mg

Reporting group description:

Subjects received s.c. injections of semaglutide OW for treatment duration of 40 weeks. Subjects received semaglutide 0.25 mg for 4 weeks (weeks 1 to 4) followed by 0.5 mg for another 4 weeks (weeks 5 to 8) and then semaglutide 1.0 mg for remaining 32 weeks (weeks 9-40). Subjects were followed for 5 weeks after completion of treatment period.

Reporting group title	Dulaglutide 0.75 mg

Reporting group description:

Subjects received s.c. injections of dulaglutide 0.75 mg OW for treatment duration of 40 weeks. Subjects were followed for 5 weeks after completion of treatment period.

Reporting group title	Dulaglutide 1.5 mg

Reporting group description:

Subjects received s.c. injections of dulaglutide 1.5 mg OW for treatment duration of 40 weeks. Subjects were followed for 5 weeks after completion of treatment period.

Serious adverse events	Semaglutide 0.5 mg	Semaglutide 1.0 mg	Dulaglutide 0.75 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 301 (5.65%)	23 / 300 (7.67%)	24 / 299 (8.03%)
number of deaths (all causes)	0	1	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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
Lipoma			

subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm of ampulla of Vater			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic squamous cell carcinoma			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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 stage IV			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Rectal adenocarcinoma			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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
Rectal cancer			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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			
Cardioversion			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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

Gastrectomy			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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
Hip arthroplasty			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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
Hospitalisation			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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
Hysterectomy			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchidectomy			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Drowning			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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
Non-cardiac chest pain			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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

Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Sarcoidosis			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cystocele			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine prolapse			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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 respiratory failure			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Epistaxis			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			

subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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
Suicide attempt			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
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			
Lipase increased			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Face injury			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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
Fall			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Femur fracture			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Meniscus injury			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Post procedural myocardial infarction			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Angina unstable			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Aortic valve stenosis			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Congestive cardiomyopathy			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
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	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Ventricular extrasystoles			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carpal tunnel syndrome			

subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	2 / 299 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
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 neuropathy			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemic unconsciousness			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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
Paraesthesia			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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
Colitis			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Crohn's disease			

subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroduodenitis			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Haemorrhoids			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Impaired gastric emptying			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Inguinal hernia			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Pancreatolithiasis			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Rectal prolapse			

subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Vomiting			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
Cholelithiasis			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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
Gallbladder pain			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 301 (0.33%)	1 / 300 (0.33%)	0 / 299 (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
Renal colic			

subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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
Ureterolithiasis			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	2 / 299 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc degeneration			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal column stenosis			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	2 / 301 (0.66%)	0 / 300 (0.00%)	0 / 299 (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

Bronchitis			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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
Cellulitis			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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
HIV infection			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	0 / 299 (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 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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 respiratory tract infection			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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
Urinary tract infection			
subjects affected / exposed	1 / 301 (0.33%)	0 / 300 (0.00%)	0 / 299 (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			
Dehydration			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
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 complication			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypercalcaemia			
subjects affected / exposed	0 / 301 (0.00%)	0 / 300 (0.00%)	1 / 299 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 301 (0.00%)	1 / 300 (0.33%)	0 / 299 (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

Serious adverse events	Dulaglutide 1.5 mg		

Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 299 (7.36%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lipoma			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm of ampulla of Vater			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic carcinoma stage IV			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal adenocarcinoma			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal cancer			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			

Hypertensive crisis			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Cardioversion			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrectomy			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip arthroplasty			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hospitalisation			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hysterectomy			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Orchidectomy			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Drowning			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Non-cardiac chest pain			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sarcoidosis			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cystocele			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Uterine prolapse			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Lipase increased			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Face injury				
subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meniscus injury				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural myocardial infarction				
subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina pectoris				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				

subjects affected / exposed	2 / 299 (0.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Aortic valve stenosis				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	2 / 299 (0.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Congestive cardiomyopathy				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				

subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular extrasystoles			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral infarction			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic neuropathy			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemic unconsciousness			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Paraesthesia			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Crohn's disease			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroduodenitis			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Impaired gastric emptying			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			

subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatolithiasis				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal prolapse				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	2 / 299 (0.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gallbladder pain				
subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic cirrhosis				

subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal colic			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ureterolithiasis			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc degeneration			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	0 / 299 (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 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Spinal column stenosis			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 299 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HIV infection			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Kidney infection			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Perirectal abscess			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Postoperative wound infection				
subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 299 (0.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Upper respiratory tract infection				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic complication				
subjects affected / exposed	0 / 299 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				

subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	0 / 299 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Semaglutide 0.5 mg	Semaglutide 1.0 mg	Dulaglutide 0.75 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	132 / 301 (43.85%)	134 / 300 (44.67%)	106 / 299 (35.45%)
Investigations			
Lipase increased			
subjects affected / exposed	19 / 301 (6.31%)	17 / 300 (5.67%)	16 / 299 (5.35%)
occurrences (all)	23	17	17
Nervous system disorders			
Headache			
subjects affected / exposed	25 / 301 (8.31%)	22 / 300 (7.33%)	12 / 299 (4.01%)
occurrences (all)	35	30	20
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	16 / 301 (5.32%)	14 / 300 (4.67%)	10 / 299 (3.34%)
occurrences (all)	18	14	10
Diarrhoea			
subjects affected / exposed	43 / 301 (14.29%)	41 / 300 (13.67%)	23 / 299 (7.69%)
occurrences (all)	79	96	42
Nausea			
subjects affected / exposed	67 / 301 (22.26%)	63 / 300 (21.00%)	39 / 299 (13.04%)
occurrences (all)	144	192	66
Vomiting			
subjects affected / exposed	30 / 301 (9.97%)	31 / 300 (10.33%)	12 / 299 (4.01%)
occurrences (all)	50	48	16
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	15 / 301 (4.98%)	14 / 300 (4.67%)	17 / 299 (5.69%)
occurrences (all)	16	16	20
Upper respiratory tract infection			
subjects affected / exposed	13 / 301 (4.32%)	10 / 300 (3.33%)	21 / 299 (7.02%)
occurrences (all)	18	11	26
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	25 / 301 (8.31%)	27 / 300 (9.00%)	9 / 299 (3.01%)
occurrences (all)	26	27	12

Non-serious adverse events	Dulaglutide 1.5 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 299 (46.49%)		
Investigations			
Lipase increased			
subjects affected / exposed	17 / 299 (5.69%)		
occurrences (all)	20		
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 299 (6.35%)		
occurrences (all)	30		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	15 / 299 (5.02%)		
occurrences (all)	18		
Diarrhoea			
subjects affected / exposed	53 / 299 (17.73%)		
occurrences (all)	75		
Nausea			
subjects affected / exposed	60 / 299 (20.07%)		
occurrences (all)	108		
Vomiting			
subjects affected / exposed	29 / 299 (9.70%)		
occurrences (all)	40		
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed occurrences (all)	20 / 299 (6.69%) 24		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	16 / 299 (5.35%) 21		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	31 / 299 (10.37%) 36		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2016	The protocol was updated to include diabetic retinopathy complications in the risk-benefit assessment of semaglutide based on clinical findings from the phase 3a programme. Other minor language corrections and updates were also included for general clarification.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported