Clinical trial results:
A Randomized, Double-Blind Study with an Open-Label Extension Comparing the Effect of Once-Weekly Dulaglutide with Placebo in Pediatric Patients with Type 2 Diabetes Mellitus

Summary

EudraCT number	2016-000361-22
Trial protocol	DE GB FR HU
Global end of trial date	12 January 2022

Results information

Result version number	v1 (current)
This version publication date	23 June 2022
First version publication date	23 June 2022

Trial information

Trial identification

Sponsor protocol code	H9X-MC-GBGC

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02963766
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 14171

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000783-PIP01-09
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	12 January 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the safety, efficacy, pharmacokinetics and pharmacodynamics of the study drug dulaglutide compared to placebo in pediatric participants with type 2 diabetes. The study duration is approximately 60 weeks.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy:

Background therapy included diet and exercise with or without metformin and/or basal insulin.

Evidence for comparator: -

Actual start date of recruitment	29 December 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 16
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	India: 11
Country: Number of subjects enrolled	Mexico: 36
Country: Number of subjects enrolled	Puerto Rico: 2
Country: Number of subjects enrolled	Saudi Arabia: 3
Country: Number of subjects enrolled	Turkey: 3
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 71
Worldwide total number of subjects	154
EEA total number of subjects	7

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)	15
Adolescents (12-17 years)	139
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were randomized at 46 centers in 9 countries.

Pre-assignment

Screening details:

Not Applicable.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo administered subcutaneously (SC) for 26 weeks during the double-blind period.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo administered SC for 26 weeks during the double-blind period.

Arm title	0.75 milligram (mg) Dulaglutide

Arm description:

Participants received 0.75 mg/week dulaglutide administered SC for 26 weeks during the double-blind period.

Arm type	Experimental
Investigational medicinal product name	Dulaglutide
Investigational medicinal product code	LY2189265
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

0.75 mg/week dulaglutide administered SC for 26 weeks during the double-blind period.

Arm title	1.5 mg Dulaglutide

Arm description:

Participants received 1.5 mg/week dulaglutide administered SC for 26 weeks during the double-blind period.

Arm type	Experimental

Investigational medicinal product name	Dulaglutide
Investigational medicinal product code	LY2189265
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants assigned to the dulaglutide 1.5-mg group were administered the 0.75-mg/week dose for the first 4 weeks and were then escalated to the 1.5-mg/week dose if they tolerated the 0.75-mg dose based on investigator assessment

Number of subjects in period 1	Placebo	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide
Started	51	51	52
Received at Least 1 Dose of Study Drug	51	51	52
Completed	47	49	50
Not completed	4	2	2
Physician decision	1	-	-
Consent withdrawn by subject	1	1	-
Adverse event, non-fatal	1	-	1
Withdrawal by Parent or Guardian	-	-	1
Lost to follow-up	-	1	-
Protocol deviation	1	-	-

Period 2

Period 2 title	Open Label Extension (OLE)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/0.75 milligram (mg) Dulaglutide

Arm description:

Participants received placebo administered subcutaneously (SC) for 26 weeks during the double-blind period and open-label 0.75 mg/week dulaglutide for 26 weeks during the Open Label Extension (OLE).

Arm type	Experimental
Investigational medicinal product name	Dulaglutide
Investigational medicinal product code	LY2189265
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

0.75 mg/week dulaglutide administered SC for 26 weeks during the OLE.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo administered SC for 26 weeks during the double-blind period.

Arm title	0.75 mg Dulaglutide

Arm description:

Participants received 0.75 mg/week dulaglutide administered SC for 26 weeks during the double-blind period and open-label 0.75 mg/week for 26 weeks during the OLE.

Arm type	Experimental
Investigational medicinal product name	Dulaglutide
Investigational medicinal product code	LY2189265
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

0.75 mg/week dulaglutide administered SC for 26 weeks during the double-blind period and open-label 0.75 mg/week for 26 weeks during the OLE.

Arm title	1.5 mg Dulaglutide

Arm description:

Participants received 1.5 mg/week dulaglutide administered SC for 26 weeks during the double-blind period and open-label 1.5 mg/week for 26 weeks during the OLE.

Arm type	Experimental
Investigational medicinal product name	Dulaglutide
Investigational medicinal product code	LY2189265
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

1.5 mg/week dulaglutide administered SC for 26 weeks during the double-blind period and open-label 1.5 mg/week for 26 weeks during the OLE.

Number of subjects in period 2	Placebo/0.75 milligram (mg) Dulaglutide	0.75 mg Dulaglutide	1.5 mg Dulaglutide
Started	47	49	50
Completed	45	46	48
Not completed	2	3	2
Physician decision	1	2	2
Consent withdrawn by subject	1	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered subcutaneously (SC) for 26 weeks during the double-blind period.	
Reporting group title	0.75 milligram (mg) Dulaglutide
Reporting group description:	
Participants received 0.75 mg/week dulaglutide administered SC for 26 weeks during the double-blind period.	
Reporting group title	1.5 mg Dulaglutide
Reporting group description:	
Participants received 1.5 mg/week dulaglutide administered SC for 26 weeks during the double-blind period.	

Reporting group values	Placebo	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide
Number of subjects	51	51	52
Age categorical			
Units: Subjects			
Age continuous			
All randomized participants.			
Units: years			
arithmetic mean	14.20	14.70	14.70
standard deviation	± 2.08	± 2.21	± 1.81
Gender categorical			
All randomized participants.			
Units: Subjects			
Female	41	35	34
Male	10	16	18
Ethnicity (NIH/OMB)			
All randomized participants.			
Units: Subjects			
Hispanic or Latino	26	31	28
Not Hispanic or Latino	25	18	22
Unknown or Not Reported	0	2	2
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	6	6	4
Asian	11	4	4
Native Hawaiian or Other Pacific Islander	1	0	0
Black or African American	5	9	9
White	25	29	30
More than one race	3	1	3
Unknown or Not Reported	0	2	2
Region of Enrollment			
All randomized participants.			
Units: Subjects			

Brazil	4	7	5
France	0	2	2
Germany	2	1	0
India	3	4	4
Mexico	14	12	10
Puerto Rico	0	1	1
Saudi Arabia	2	0	1
Turkey	1	1	1
United Kingdom	3	2	0
United States	22	21	28
Percentage of Hemoglobin A1c (HbA1c) at Baseline			
All randomized participants.			
Units: Percentage of HbA1c			
arithmetic mean	8.14	7.92	8.16
standard deviation	± 1.12	± 1.27	± 1.39

Reporting group values	Total		
Number of subjects	154		
Age categorical			
Units: Subjects			
Age continuous			
All randomized participants.			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
All randomized participants.			
Units: Subjects			
Female	110		
Male	44		
Ethnicity (NIH/OMB)			
All randomized participants.			
Units: Subjects			
Hispanic or Latino	85		
Not Hispanic or Latino	65		
Unknown or Not Reported	4		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	16		
Asian	19		
Native Hawaiian or Other Pacific Islander	1		
Black or African American	23		
White	84		
More than one race	7		
Unknown or Not Reported	4		
Region of Enrollment			
All randomized participants.			
Units: Subjects			
Brazil	16		

France	4		
Germany	3		
India	11		
Mexico	36		
Puerto Rico	2		
Saudi Arabia	3		
Turkey	3		
United Kingdom	5		
United States	71		
Percentage of Hemoglobin A1c (HbA1c) at Baseline			
All randomized participants.			
Units: Percentage of HbA1c			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered subcutaneously (SC) for 26 weeks during the double-blind period.	
Reporting group title	0.75 milligram (mg) Dulaglutide
Reporting group description:	
Participants received 0.75 mg/week dulaglutide administered SC for 26 weeks during the double-blind period.	
Reporting group title	1.5 mg Dulaglutide
Reporting group description:	
Participants received 1.5 mg/week dulaglutide administered SC for 26 weeks during the double-blind period.	
Reporting group title	Placebo/0.75 milligram (mg) Dulaglutide
Reporting group description:	
Participants received placebo administered subcutaneously (SC) for 26 weeks during the double-blind period and open-label 0.75 mg/week dulaglutide for 26 weeks during the Open Label Extension (OLE).	
Reporting group title	0.75 mg Dulaglutide
Reporting group description:	
Participants received 0.75 mg/week dulaglutide administered SC for 26 weeks during the double-blind period and open-label 0.75 mg/week for 26 weeks during the OLE.	
Reporting group title	1.5 mg Dulaglutide
Reporting group description:	
Participants received 1.5 mg/week dulaglutide administered SC for 26 weeks during the double-blind period and open-label 1.5 mg/week for 26 weeks during the OLE.	
Subject analysis set title	Placebo/0.75 mg Dulaglutide
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants received placebo administered SC for 26 weeks during the double-blind period and open-label 0.75 mg/week dulaglutide for 26 weeks during the OLE.	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants received placebo administered SC for 26 weeks.	
Subject analysis set title	Pooled Dulaglutide
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants received pooled: 0.75 mg/week dulaglutide and 1.5 mg/week dulaglutide administered SC for 26 weeks.	

Primary: Change from Baseline in Hemoglobin A1c (HbA1c) (Pooled Doses) at Week 26

End point title	Change from Baseline in Hemoglobin A1c (HbA1c) (Pooled Doses) at Week 26
End point description:	
HbA1c is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. Least square (LS) mean in HbA1c was calculated using a restricted maximum likelihood (REML) based mixed-effects model for repeated measures (MMRM) and adjusted by, baseline + insulin Use + metformin Use + treatment + time + treatment*time (Type III sum of squares). Variance-covariance structure = unstructured (for actual value) / unstructured (for change from baseline). Analysis population description (APD) included all randomized participants who received at least one dose of study drug and had evaluable baseline and post-baseline HbA1c. APD is	
End point type	Primary

End point timeframe:

Baseline, Week 26

End point values	Placebo	Pooled Dulaglutide		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	45	100		
Units: percentage of HbA1C				
least squares mean (standard error)	0.5 (± 0.24)	-0.7 (± 0.16)		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Placebo v Pooled Dulaglutide
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-0.7

Secondary: Change from Baseline in HbA1c (Individual Doses) at Week 26

End point title	Change from Baseline in HbA1c (Individual Doses) at Week

End point description:

HbA1c is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. LS mean in HbA1c was calculated using a REML based MMRM and adjusted by, baseline + insulin use + metformin use + treatment + time + treatment*time (Type III sum of squares). Variance-covariance structure = unstructured (for actual value) / unstructured (for change from baseline). APD included all randomized participants who received at least one dose of study drug and had evaluable baseline and post-baseline HbA1c.

End point type	Secondary

End point timeframe:

Baseline, Week 26

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	50	50	45	
Units: percentage of HbA1c				
least squares mean (standard error)	-0.5 (± 0.22)	-1.0 (± 0.22)	0.5 (± 0.24)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	0.75 milligram (mg) Dulaglutide v Placebo
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	-0.4

Statistical analysis title	Statistical analysis 2
Comparison groups	1.5 mg Dulaglutide v Placebo
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.9

Secondary: Change from Baseline in Fasting Blood Glucose (FBG) at Week 26

End point title	Change from Baseline in Fasting Blood Glucose (FBG) at Week 26[2]

End point description:

Fasting blood glucose is a test to determine how much glucose (sugar) is in a blood sample after an

overnight fast. Least squares (LS) means were calculated using a mixed-effects model for repeated measures (MMRM) analysis and adjusted by baseline, strata, treatment, time, treatment*time, (Type III sum of squares). Variance-Covariance structure = Unstructured (for actual value) / Unstructured (for change from baseline). Strata refer to: insulin use + metformin use + baseline HbA1c group [less than (<) 8%, greater than or equal to (>=) 8%). APD included all randomized participants who received at least one dose of study drug and had evaluable fasting blood glucose data. Only pre-rescue measurements were used.

End point type	Secondary

End point timeframe:

Baseline, Week 26

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo	Pooled Dulaglutide
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	49	50	43	99
Units: millimoles per liter (mmol/L)				
least squares mean (standard error)	-0.47 (± 0.41)	-1.54 (± 0.41)	0.96 (± 0.45)	-1.03 (± 0.29)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	0.75 milligram (mg) Dulaglutide v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.65
upper limit	-0.22

Statistical analysis title	Statistical analysis 2
Comparison groups	1.5 mg Dulaglutide v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-2.51

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.72
upper limit	-1.29

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo v Pooled Dulaglutide
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-1.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.03
upper limit	-0.91

Secondary: Percentage of Participants with HbA1c ≤7.0%

End point title	Percentage of Participants with HbA1c ≤7.0%[3]

End point description:

The percentage of participants was calculated by dividing the number of participants reaching target HbA1c by the total number of participants analyzed, multiplied by 100. APD included all randomized participants who received at least 1 dose of study drug and had evaluable baseline and post-baseline HbA1c.

End point type	Secondary

End point timeframe:

Week 26

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo	Pooled Dulaglutide
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	45	100
Units: percentage of participants				
number (not applicable)	60.00	53.19	18.42	56.52

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	0.75 milligram (mg) Dulaglutide v Placebo
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11.038
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.491
upper limit	34.902

Statistical analysis title	Statistical analysis 2
Comparison groups	1.5 mg Dulaglutide v Placebo
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11.666
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.653
upper limit	37.253

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo v Pooled Dulaglutide
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11.348
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.163
upper limit	30.932

Secondary: Change from Baseline in Body Mass Index (BMI) at Week 26

End point title	Change from Baseline in Body Mass Index (BMI) at Week 26[4]

End point description:

BMI is an estimate of body fat based on body weight divided by height squared. LS mean were calculated using a MMRM analysis and adjusted by baseline, strata, treatment, time, treatment*time, (Type III sum of squares). Variance-Covariance structure = Unstructured (for actual value) / Unstructured (for change from baseline). Strata refer to: insulin use + metformin use + baseline HbA1c group (< 8%, >= 8%). APD included all randomized participants who received at least one dose of study drug and had evaluable BMI data.

End point type	Secondary

End point timeframe:

Baseline, Week 26

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo	Pooled Dulaglutide
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	51	52	50	103
Units: kilograms/square meter (kg/m^2)				
least squares mean (standard error)	-0.2 (± 0.20)	-0.1 (± 0.19)	-0.0 (± 0.21)	-0.1 (± 0.14)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	0.75 milligram (mg) Dulaglutide v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.689
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.5

Statistical analysis title	Statistical analysis 2
Comparison groups	1.5 mg Dulaglutide v Placebo

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.924
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.5

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo v Pooled Dulaglutide
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.776
Method	Mixed models analysis
Parameter estimate	LS Mean difference (Final Values)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.4

Secondary: Percentage of Participants with Self-Reported Events of Hypoglycemia

End point title	Percentage of Participants with Self-Reported Events of Hypoglycemia[5]

End point description:

Summary and analysis of Incidence of all hypoglycemia with Plasma Glucose <54mg/dL. APD included all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 26

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	51	52	51	
Units: percentage of participants				
number (not applicable)	3.92	3.85	1.96	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Requiring Rescue for Severe, Persistent Hyperglycemia

End point title	Percentage of Participants Requiring Rescue for Severe, Persistent Hyperglycemia[6]

End point description:

Percentage of Participants Requiring Rescue for Severe, Persistent Hyperglycemia was summarized. APD included all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 26

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo	Pooled Dulaglutide
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	51	52	51	103
Units: percentage of participants				
number (not applicable)	3.9	1.9	17.6	2.9

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adjudicated Pancreatitis

End point title	Number of Participants with Adjudicated Pancreatitis[7]

End point description:

The number of participants with pancreatitis confirmed by adjudication is summarized cumulatively at 26 weeks. A summary of serious and other non-serious adverse events regardless of causality is located in the Reported Adverse Events module. APD included all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 26

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo	Pooled Dulaglutide
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	51	52	51	103
Units: participants				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pancreatic Enzymes at Week 26

End point title	Change from Baseline in Pancreatic Enzymes at Week 26[8]

End point description:

Serum Amylase (total and pancreas-derived) and lipase concentrations were measured. APD included all randomized participants who received at least one dose of study drug and had evaluable pancreatic enzymes data.

End point type	Secondary

End point timeframe:

Baseline, Week 26

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo	Pooled Dulaglutide
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	51	52	47	103
Units: Units/Liter (U/L)				
arithmetic mean (standard deviation)				
Serum Amylase	4.80 (± 9.39)	6.50 (± 8.91)	0.09 (± 17.36)	5.64 (± 9.15)
Serum Amylase, Pancreatic	1.77 (± 4.72)	2.90 (± 6.10)	0.60 (± 9.94)	2.32 (± 5.45)
Serum Lipase	4.37 (± 8.28)	3.88 (± 6.63)	2.23 (± 31.99)	4.12 (± 7.47)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Thyroid Treatment-Emergent Adverse Events

End point title	Number of Participants with Thyroid Treatment-Emergent Adverse Events[9]

End point description:

Number of Participants with Thyroid Treatment-Emergent Adverse Events were summarized. APD included all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 26

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo	Pooled Dulaglutide
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	51	52	51	103
Units: participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Serum Calcitonin at Week 26

End point title	Change from Baseline in Serum Calcitonin at Week 26[10]

End point description:

Change from Baseline in Serum Calcitonin was evaluated. APD included all randomized participants who received at least one dose of study drug and had evaluable serum calcitonin data.

End point type	Secondary

End point timeframe:

Baseline, Week 26

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo	Pooled Dulaglutide
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	48	48	47	96
Units: nanograms per liter (ng/L)				
arithmetic mean (standard deviation)	0.28 (± 0.72)	0.10 (± 0.50)	0.38 (± 1.70)	0.19 (± 0.62)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Allergic, Hypersensitivity Reactions

End point title	Percentage of Participants with Allergic, Hypersensitivity Reactions[11]

End point description:

The percentage of Participants with Allergic and hypersensitivity reactions that were considered possibly related to study drug by the investigator are presented. A summary of serious and other non-serious adverse events regardless of causality is located in the Reported Adverse Events module. APD included all randomized participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Week 26

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo	Pooled Dulaglutide
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	51	52	51	103
Units: percentage of participants				
number (not applicable)	3.9	1.9	2.0	2.9

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Injection Site Reactions

End point title	Percentage of Participants With Injection Site Reactions[12]

End point description:

The percentage of participants with at least one treatment-emergent injection site reaction is presented. A summary of serious and other non-serious adverse events regardless of causality is located in the Reported Adverse Events module. APD included all randomized participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Week 26

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo	Pooled Dulaglutide
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	51	52	51	103
Units: percentage of participants				
number (not applicable)	9.8	7.7	9.8	8.7

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-Dulaglutide Antibodies

End point title	Number of Participants with Anti-Dulaglutide Antibodies[13]

End point description:

Dulaglutide anti-drug antibodies (ADA) were assessed at baseline, Weeks 26 and 56. A participant was considered to have treatment-emergent (TE) dulaglutide ADAs if the participant had at least 1 titer that was TE relative to baseline, defined as a 4-fold or greater increase in titer from baseline measurement. APD included all randomized participants who received at least 1 dose of study drug and had at least one post-baseline Dulaglutide ADA test result.

End point type	Secondary

End point timeframe:

Baseline through Week 56

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide	Placebo/0.75 mg Dulaglutide	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	51	52	46	
Units: participants				
number (not applicable)	3	3	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Maximum Concentration of Dulaglutide at steady-state (Cmax,ss)

End point title	Pharmacokinetics (PK): Maximum Concentration of Dulaglutide at steady-state (Cmax,ss)[14]

End point description:

PK: Maximum Concentration of Dulaglutide at steady-state (Cmax,ss) was derived by a population pharmacokinetics approach. As part of addendum, additional PK samples were taken at week 9. APD included all randomized participants who received at least one dose of study drug and had evaluable PK data.

End point type	Secondary

End point timeframe:

Week 9: pre-dose,1 to 12 hours post dose and 24 to 96 hours post dose; Week 13: predose and 1 to 12 hours post dose; Week 26: predose; Week 39: up to 2 days postdose; Week 52 and Week 56: PK sample can be taken at any time during the visit

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	52		
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (confidence interval 95%)	31 (28.4 to 33.5)	62 (56.9 to 67.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Area Under the Concentration Time Curve over a 1-week interval of Dulaglutide at Steady-State [AUC(0-168)ss]

End point title	PK: Area Under the Concentration Time Curve over a 1-week interval of Dulaglutide at Steady-State [AUC(0-168)ss][15]

End point description:

PK: Area Under the Concentration Time Curve over a 1-week interval of Dulaglutide at Steady-State [AUC(0-168)ss] was derived by a population pharmacokinetics approach. As part of addendum, additional PK samples were taken at week 9. APD included all randomized participants who received at least one dose of study drug and had evaluable PK data.

End point type	Secondary

End point timeframe:

Week 9: pre-dose,1 to 12 hours post dose and 24 to 96 hours post dose; Week 13: predose and 1 to 12 hours post dose; Week 26: predose; Week 39: up to 2 days postdose; Week 52 and Week 56: PK sample can be taken at any time during the visit

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in baseline period reporting arms, subject analysis set with evaluable endpoint data.

End point values	0.75 milligram (mg) Dulaglutide	1.5 mg Dulaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	52		
Units: nanogram*hour per milliliter (ng*h/ mL)				
arithmetic mean (confidence interval 95%)	4170 (3770 to 4510)	8350 (7640 to 9070)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up To 56 Weeks	
Adverse event reporting additional description:	
All randomized participants who received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	Placebo: Double-Blind Period
Reporting group description:	
Participants received placebo administered SC for 26 weeks.	
Reporting group title	0.75 mg Dulaglutide: Double-Blind Period
Reporting group description:	
Participants received 0.75 mg/week dulaglutide administered SC for 26 weeks.	
Reporting group title	1.5 mg Dulaglutide: Double-Blind Period
Reporting group description:	
Participants received 1.5 mg/week dulaglutide administered SC for 26 weeks.	
Reporting group title	Placebo/0.75 mg Dulaglutide: OLE
Reporting group description:	
Participants who had received placebo during the double-blind period were given 0.75 mg/week dulaglutide administered SC for additional 26 weeks after the double-blind period.	
Reporting group title	0.75 mg Dulaglutide: OLE
Reporting group description:	
Participants received 0.75 mg/week dulaglutide administered SC for additional 26 weeks after the double-blind period.	
Reporting group title	1.5 mg Dulaglutide: OLE
Reporting group description:	
Participants received 1.5 mg/week dulaglutide administered SC for additional 26 weeks after the double-blind period.	

Serious adverse events	Placebo: Double-Blind Period	0.75 mg Dulaglutide: Double-Blind Period	1.5 mg Dulaglutide: Double-Blind Period
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 51 (5.88%)	1 / 51 (1.96%)	1 / 52 (1.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
carbon monoxide poisoning			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (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
stress fracture			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
right ventricular failure			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 52 (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			
nonalcoholic fatty liver disease			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	0 / 52 (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
Respiratory, thoracic and mediastinal disorders			
pulmonary embolism			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 52 (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
respiratory failure			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
suicide attempt			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 52 (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
Infections and infestations			
genital herpes			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 52 (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
pilonidal cyst			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (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			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (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
Metabolism and nutrition disorders			
diabetic ketoacidosis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo/0.75 mg Dulaglutide: OLE	0.75 mg Dulaglutide: OLE	1.5 mg Dulaglutide: OLE
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 47 (0.00%)	1 / 49 (2.04%)	2 / 50 (4.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
carbon monoxide poisoning			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
stress fracture			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (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			
right ventricular failure			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (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			
nonalcoholic fatty liver disease			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (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			
pulmonary embolism			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (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 failure			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (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
Psychiatric disorders			
suicide attempt			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (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			
genital herpes			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (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
pilonidal cyst			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 47 (0.00%)	1 / 49 (2.04%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyelonephritis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
diabetic ketoacidosis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (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

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

Non-serious adverse events	Placebo: Double-Blind Period	0.75 mg Dulaglutide: Double-Blind Period	1.5 mg Dulaglutide: Double-Blind Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 51 (50.98%)	25 / 51 (49.02%)	28 / 52 (53.85%)
Injury, poisoning and procedural complications			

accidental overdose			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 51 (0.00%)	3 / 51 (5.88%)	2 / 52 (3.85%)
occurrences (all)	0	3	2
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 51 (1.96%)	4 / 51 (7.84%)	2 / 52 (3.85%)
occurrences (all)	1	4	2
headache			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	5 / 51 (9.80%)	7 / 51 (13.73%)	8 / 52 (15.38%)
occurrences (all)	8	7	21
General disorders and administration site conditions			
pyrexia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	2 / 51 (3.92%)	2 / 51 (3.92%)	2 / 52 (3.85%)
occurrences (all)	2	3	2
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	3 / 51 (5.88%)	4 / 51 (7.84%)	1 / 52 (1.92%)
occurrences (all)	3	4	4
abdominal pain upper			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	4 / 51 (7.84%)	3 / 51 (5.88%)	5 / 52 (9.62%)
occurrences (all)	8	3	6
diarrhoea			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	7 / 51 (13.73%)	8 / 51 (15.69%)	11 / 52 (21.15%)
occurrences (all)	9	13	19
nausea			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	4 / 51 (7.84%)	7 / 51 (13.73%)	8 / 52 (15.38%)
occurrences (all)	4	16	13

vomiting			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	2 / 51 (3.92%)	9 / 51 (17.65%)	7 / 52 (13.46%)
occurrences (all)	2	10	14
Reproductive system and breast disorders			
dysmenorrhoea			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed[1]	1 / 41 (2.44%)	1 / 35 (2.86%)	2 / 34 (5.88%)
occurrences (all)	1	1	4
heavy menstrual bleeding			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed[2]	0 / 41 (0.00%)	0 / 35 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
epistaxis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
gastroenteritis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	2 / 51 (3.92%)	1 / 51 (1.96%)	3 / 52 (5.77%)
occurrences (all)	3	1	3
nasopharyngitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	3 / 51 (5.88%)	5 / 51 (9.80%)	2 / 52 (3.85%)
occurrences (all)	4	6	2
upper respiratory tract infection			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	4 / 51 (7.84%)	2 / 51 (3.92%)	6 / 52 (11.54%)
occurrences (all)	6	3	7
urinary tract infection			
alternative dictionary used: MedDRA 24.1			

subjects affected / exposed	3 / 51 (5.88%)	2 / 51 (3.92%)	0 / 52 (0.00%)
occurrences (all)	3	3	0

Non-serious adverse events	Placebo/0.75 mg Dulaglutide: OLE	0.75 mg Dulaglutide: OLE	1.5 mg Dulaglutide: OLE
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 47 (38.30%)	16 / 49 (32.65%)	20 / 50 (40.00%)
Injury, poisoning and procedural complications			
accidental overdose			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 47 (0.00%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 47 (2.13%)	1 / 49 (2.04%)	1 / 50 (2.00%)
occurrences (all)	1	1	1
headache			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	2 / 47 (4.26%)	5 / 49 (10.20%)	5 / 50 (10.00%)
occurrences (all)	2	6	6
General disorders and administration site conditions			
pyrexia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	2 / 47 (4.26%)	3 / 49 (6.12%)	1 / 50 (2.00%)
occurrences (all)	3	3	1
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 47 (0.00%)	3 / 49 (6.12%)	3 / 50 (6.00%)
occurrences (all)	0	5	3
abdominal pain upper			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	2 / 47 (4.26%)	0 / 49 (0.00%)	5 / 50 (10.00%)
occurrences (all)	2	0	21
diarrhoea			

alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 47 (0.00%)	1 / 49 (2.04%)	6 / 50 (12.00%)
occurrences (all)	0	1	21
nausea			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	1 / 47 (2.13%)	3 / 49 (6.12%)	6 / 50 (12.00%)
occurrences (all)	2	10	12
vomiting			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	4 / 47 (8.51%)	4 / 49 (8.16%)	5 / 50 (10.00%)
occurrences (all)	6	4	8
Reproductive system and breast disorders			
dysmenorrhoea			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed[1]	0 / 38 (0.00%)	0 / 34 (0.00%)	3 / 34 (8.82%)
occurrences (all)	0	0	3
heavy menstrual bleeding			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed[2]	0 / 38 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
epistaxis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	3 / 47 (6.38%)	0 / 49 (0.00%)	0 / 50 (0.00%)
occurrences (all)	3	0	0
Infections and infestations			
gastroenteritis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	4 / 47 (8.51%)	0 / 49 (0.00%)	3 / 50 (6.00%)
occurrences (all)	5	0	4
nasopharyngitis			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	4 / 47 (8.51%)	1 / 49 (2.04%)	3 / 50 (6.00%)
occurrences (all)	4	1	3

upper respiratory tract infection			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	3 / 47 (6.38%)	0 / 49 (0.00%)	1 / 50 (2.00%)
occurrences (all)	4	0	1
urinary tract infection			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	2 / 47 (4.26%)	1 / 49 (2.04%)	0 / 50 (0.00%)
occurrences (all)	2	1	0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants were adjusted accordingly.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender specific events only occurring in male or female participants were adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 February 2019	Exclusion criteria were modified as follows: -To exclude participants with a history of hyperglycemic hyperosmolar syndrome after initial diagnosis of type 2 diabetes mellitus (T2DM). - Clarified that use of bolus insulin at screening is excluded, shortened the exclusion period of bolus insulin to 6 weeks prior to screening, and added exception for short-term use of insulin for medical management of acute conditions. - Specified exclusion of only chronic [greater than (>)14 consecutive days] use of oral steroids. This revision prevents the unnecessary exclusion of participants who may have received short-term steroid therapy to treat an acute condition within 60 days of screening.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 March 2020	Global enrollment hold due to Covid-19.	27 May 2020

Notes:

Limitations and caveats

None reported