Clinical trial results:
A Randomized, Parallel-Arm, Double-Blinded Study Comparing the Effect of Once-Weekly Dulaglutide with Placebo in Patients with Type 2 Diabetes Mellitus on Sulfonylurea Therapy (AWARD-8: Assessment of Weekly AdministRation of LY2189265 in Diabetes – 8)

Summary

EudraCT number	2012-002911-24
Trial protocol	AT SI
Global end of trial date	02 December 2014

Results information

Result version number	v1 (current)
This version publication date	29 July 2016
First version publication date	29 July 2016

Trial information

Trial identification

Sponsor protocol code	13193

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01769378
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Alias: H9X-MC-GBDG , Trial Number: 13193

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Mon - Fri 9 AM - 5 PM Eastern time (UTC/GMT - 5 hours, EST), Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Mon - Fri 9 AM - 5 PM Eastern time (UTC/GMT - 5 hours, EST), Eli Lilly and Company, 1 877-285-4559,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 December 2014
Global end of trial reached?	Yes
Global end of trial date	02 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the efficacy and safety of once-weekly dulaglutide compared to placebo in participants with type 2 diabetes who have inadequate glycemic control with sulfonylurea monotherapy.

Protection of trial subjects:

This study was conducted in accordance with 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: -

Evidence for comparator: -

Actual start date of recruitment	25 January 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 37
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Romania: 96
Country: Number of subjects enrolled	United States: 71
Country: Number of subjects enrolled	South Africa: 10
Country: Number of subjects enrolled	Mexico: 50
Country: Number of subjects enrolled	Slovenia: 16
Country: Number of subjects enrolled	Croatia: 12
Country: Number of subjects enrolled	Puerto Rico: 3
Worldwide total number of subjects	300
EEA total number of subjects	129

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)	232
From 65 to 84 years	68
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

not applicable

Pre-assignment

Screening details:

All randomized participants, except for 1, in the dulaglutide group, were treated with at least 1 dose of study drug and comprised the ITT population. One participant did not receive study drug because after randomization the physician determined that the participant would be unable to successfully comply with the protocol.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dulaglutide

Arm description:

Dulaglutide 1.5 milligram (mg) administered subcutaneously (SQ) once weekly for 24 weeks added to the participant's prescribed glimepiride dose.

Arm type	Experimental
Investigational medicinal product name	Dulaglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Cutaneous use

Dosage and administration details:

Dulaglutide 1.5 milligram (mg) administered subcutaneously (SQ) once weekly for 24 weeks added to the participant's prescribed glimepiride dose.

Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Cutaneous use

Dosage and administration details:

Participants meeting the eligibility criteria on glimeperide will continue glimepiride at their prestudy dose.

Arm title	Placebo

Arm description:

Placebo administered SQ once weekly for 24 weeks added to the participant's prescribed glimepiride dose.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Cutaneous use

Dosage and administration details:	
Placebo administered SQ once weekly for 24 weeks added to the participant's prescribed glimepiride dose.	
Investigational medicinal product name	Glimeperide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Cutaneous use
Dosage and administration details:	
Participants who met eligibility criteria on glimeperide will continue glimepiride at their prestudy dose.	

Number of subjects in period 1	Dulaglutide	Placebo
Started	240	60
Received at least 1 dose of study drug	239	60
Completed	215	56
Not completed	25	4
Consent withdrawn by subject	10	3
Adverse event, non-fatal	10	-
Sponsor Decision	1	-
Lost to follow-up	2	-
Entry criteria not met	1	-
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Dulaglutide
Reporting group description:	
Dulaglutide 1.5 milligram (mg) administered subcutaneously (SQ) once weekly for 24 weeks added to the participant's prescribed glimepiride dose.	
Reporting group title	Placebo
Reporting group description:	
Placebo administered SQ once weekly for 24 weeks added to the participant's prescribed glimepiride dose.	

Reporting group values	Dulaglutide	Placebo	Total
Number of subjects	240	60	300
Age Categorical Units: participants			
<=18 years	0	0	0
Between 18 and 65 years	183	49	232
>=65 years	57	11	68
Gender, Male/Female Units: participants			
Female	135	32	167
Male	105	28	133
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	112	27	139
Not Hispanic or Latino	128	33	161
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	21	5	26
Asian	3	2	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	7	4	11
White	203	47	250
More than one race	6	2	8
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Argentina	29	8	37
Austria	4	1	5
Romania	78	18	96
United States	57	14	71
South Africa	7	3	10
Mexico	40	10	50
Slovenia	13	3	16
Croatia	10	2	12
Puerto Rico	2	1	3

End points

End points reporting groups

Reporting group title	Dulaglutide
Reporting group description:	
Dulaglutide 1.5 milligram (mg) administered subcutaneously (SQ) once weekly for 24 weeks added to the participant's prescribed glimepiride dose.	
Reporting group title	Placebo
Reporting group description:	
Placebo administered SQ once weekly for 24 weeks added to the participant's prescribed glimepiride dose.	

Primary: Change from Baseline in Glycosylated Hemoglobin A1c (HbA1c) at 24 Weeks

End point title	Change from Baseline in Glycosylated Hemoglobin A1c (HbA1c) at 24 Weeks
End point description:	
Least Squares Means (LS Means) of the HbA1c change from baseline to primary endpoint was adjusted by fixed effects of treatment, country, visit, treatment-by-visit interaction, participant as random effect and baseline HbA1c as covariate, via a Mixed-effects model for repeated measures (MMRM) analysis using restricted maximum likelihood (REML).	
End point type	Primary
End point timeframe:	
Baseline, 24 Weeks	

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215[1]	53[2]		
Units: percent change of HbA1c				
least squares mean (standard error)	-1.38 (± 0.08)	-0.11 (± 0.14)		

Notes:

[1] - All randomized participants who received ≥1 dose of study drug and had evaluable HbA1c data.

[2] - All randomized participants who received ≥1 dose of study drug and had evaluable HbA1c data.

Statistical analyses

Statistical analysis title	Statistical Analysis for Primary Endpoint
Comparison groups	Dulaglutide v Placebo
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Squares Mean Difference
Point estimate	-1.27

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.57
upper limit	-0.97
Variability estimate	Standard error of the mean
Dispersion value	0.15

Secondary: Percentage of Participants Who Achieve HbA1c <7.0% and ≤6.5% at 24 Weeks

End point title	Percentage of Participants Who Achieve HbA1c <7.0% and ≤6.5% at 24 Weeks

End point description:

The percentage of participants who achieved the target HbA1c values at endpoint will be analyzed with a repeated logistic regression model (the generalized estimation equation [GEE] model). The model includes country, treatment, visit and treatment interaction and baseline HbA1c as a continuous covariate.

End point type	Secondary

End point timeframe:

24 Weeks

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215[3]	53[4]		
Units: percentage of participants				
number (not applicable)				
Percent Achieved <7.0 HbA1c Level	55.3	18.9		
Percent Achieved ≤6.5 HbA1c Level	40	9.4		

Notes:

[3] - All randomized participants who received ≥1 dose of study drug and had evaluable HbA1c data.

[4] - All randomized participants who received ≥1 dose of study drug and had evaluable HbA1c data.

Statistical analyses

Statistical analysis title	Statistical Analysis for <7.0% HbA1c

Statistical analysis description:

<7.0% HbA1c

Comparison groups	Dulaglutide v Placebo
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11.37

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.82
upper limit	33.84

Statistical analysis title	Statistical Analysis for ≤6.5% HbA1c
Statistical analysis description: ≤6.5% HbA1c	
Comparison groups	Dulaglutide v Placebo
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.71
upper limit	35.34

Secondary: Change from Baseline in Fasting Serum Glucose (FSG) at 24 Weeks

End point title	Change from Baseline in Fasting Serum Glucose (FSG) at 24 Weeks

End point description:

LS Means of the FSG from baseline to primary endpoint was adjusted by fixed effects of treatment, country, baseline HbA1c strata, and baseline FSG as covariate, via Analysis of Covariance Model (ANCOVA) with Last Observation Carried Forward (LOCF).

End point type	Secondary

End point timeframe:

Baseline, 24 Weeks

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	218[5]	51[6]		
Units: milligrams per deciliter (mg/dL)				
least squares mean (standard error)	-30.6 (± 4.46)	2.93 (± 6.76)		

Notes:

[5] - Participants received ≥1 dose of study drug and had evaluable FSG data at baseline, post baseline.

[6] - Participants received ≥1 dose of study drug and had evaluable FSG data at baseline, post baseline.

Statistical analyses

Statistical analysis title	Statistical Analysis for Change from Baseline FSG
Comparison groups	Dulaglutide v Placebo
Number of subjects included in analysis	269
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Squares Mean Difference
Point estimate	-33.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.55
upper limit	-20.53
Variability estimate	Standard error of the mean
Dispersion value	6.6

Secondary: Change from Baseline in Body Weight at 24 Weeks

End point title	Change from Baseline in Body Weight at 24 Weeks

End point description:

LS Means of the body weight change from baseline to primary endpoint was adjusted by fixed effects of treatment, country, visit, treatment-by-visit interaction, participant as random effect and baseline body weight as covariate, via a MMRM analysis using REML.

End point type	Secondary

End point timeframe:

Baseline, 24 Weeks

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212[7]	53[8]		
Units: kilograms (kg)				
least squares mean (standard error)	-0.91 (± 0.21)	-0.24 (± 0.4)		

Notes:

[7] - Participants received ≥1 dose of study drug and had evaluable body weight data.

[8] - Participants received ≥1 dose of study drug and had evaluable body weight data.

Statistical analyses

Statistical analysis title	Statistical Analysis for Body Weight
Comparison groups	Dulaglutide v Placebo

Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.53
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	0.43

Secondary: Change from Baseline in Body Mass Index (BMI) at 24 Weeks

End point title	Change from Baseline in Body Mass Index (BMI) at 24 Weeks

End point description:

LS Means of the BMI change from baseline to primary endpoint was adjusted by fixed effects of treatment, country, visit, treatment-by-visit interaction, participant as random effect and baseline BMI as covariate, via a MMRM analysis using REML.

End point type	Secondary

End point timeframe:

Baseline, 24 Weeks

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212[9]	53[10]		
Units: kilograms per/square meter kg/m^2				
least squares mean (standard error)	-0.32 (± 0.08)	-0.1 (± 0.15)		

Notes:

[9] - Participants who received ≥1 dose of study drug and evaluable BMI at baseline and post-baseline.

[10] - Participants who received ≥1 dose of study drug and evaluable BMI at baseline and post-baseline.

Statistical analyses

Statistical analysis title	Statistical Analysis for Body Mass Index
Comparison groups	Dulaglutide v Placebo
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.161 [11]
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.23

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.16

Notes:

[11] - No adjustment for multiplicity

Secondary: Change from Baseline in Mean of all 7-Point Self Monitored Plasma Glucose (SMPG) at 24 Weeks

End point title	Change from Baseline in Mean of all 7-Point Self Monitored Plasma Glucose (SMPG) at 24 Weeks

End point description:

LS Means of the SMPG change from baseline to primary endpoint at week 24 was adjusted by fixed effects of treatment, country, visit, treatment-by-visit interaction, participant as random effect and baseline SMPG value as covariate, via a MMRM analysis using REML.

End point type	Secondary

End point timeframe:

Baseline, 24 Weeks

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203[12]	49[13]		
Units: mg/dL				
least squares mean (standard error)	-37.22 (± 3.1)	-8.27 (± 4.77)		

Notes:

[12] - Participants who received ≥1 dose of study drug and had evaluable SMPG data.

[13] - Participants who received ≥1 dose of study drug and had evaluable SMPG data.

Statistical analyses

Statistical analysis title	Statistical Analysis for 7-Point SMPG
Comparison groups	Dulaglutide v Placebo
Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-28.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.49
upper limit	-19.4
Variability estimate	Standard error of the mean
Dispersion value	4.85

Secondary: Number of Participants with Reported and Adjudicated Cardiovascular Events

End point title	Number of Participants with Reported and Adjudicated Cardiovascular Events

End point description:

Information on cardiovascular (CV) risk factors was collected at baseline. Deaths and nonfatal cardiovascular adverse events (AEs) were adjudicated by an external committee of physicians with cardiology expertise. Nonfatal cardiovascular AEs to be adjudicated included myocardial infarction, hospitalization for unstable angina, hospitalization for heart failure, coronary interventions, and cerebrovascular events, including cerebrovascular accident (stroke) and transient ischemic attack. The number of participants with CV events confirmed by adjudication is summarized cumulatively at 24 weeks plus 30-day follow up. Serious and all other non-serious adverse events regardless of causality are summarized in the Reported Adverse Events module.

End point type	Secondary

End point timeframe:

Baseline through 24 Weeks, 30-day Follow Up

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	60		
Units: participants				
number (not applicable)				
Any reported CV events	2	0		
Any adjudicated nonfatal CV events	2	0		
Any confirmed adjudicated CV deaths	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adjudicated Acute Pancreatitis Events

End point title	Number of Participants with Adjudicated Acute Pancreatitis Events

End point description:

The number of participants with pancreatitis confirmed by adjudication is summarized cumulatively at 24 weeks plus 30-day follow up. A summary of serious and other non-serious adverse events regardless of causality is located in the Reported Adverse Events module.

End point type	Secondary

End point timeframe:

Baseline through 24 Weeks, 30-day Follow Up

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	60		
Units: participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Calcitonin at 24 Weeks

End point title	Change from Baseline in Calcitonin at 24 Weeks

End point description:

End point type	Secondary

End point timeframe:

Baseline, 24 Weeks

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215[14]	59[15]		
Units: picogram per milliliter (pg/ml)				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)		

Notes:

[14] - Participants who received at least one dose of study drug and evaluable calcitonin data.

[15] - Participants who received at least one dose of study drug and evaluable calcitonin data.

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Hypoglycemic events (HE) were classified as severe (defined as episodes requiring the assistance of another person to actively administer resuscitative actions), documented symptomatic (defined as any time a participant feels that he/she is experiencing symptoms and/or signs associated with hypoglycemia, and has a plasma glucose level of =<3.9 mmol/L), asymptomatic (defined as events not accompanied by typical symptoms of hypoglycemia but with a measured plasma glucose of =<3.9 mmol/L), nocturnal (defined as any hypoglycemic event that occurred between bedtime and waking), or probable symptomatic (defined as events during which symptoms of hypoglycemia were not accompanied by a plasma glucose determination). Percentage is calculated as the number of participants reporting HE each visit/ the total number of participants reporting HE during the entire study treatment period.

End point type	Secondary

End point timeframe:

Baseline through 24 Weeks

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239[16]	60[17]		
Units: percentage of participants				
number (not applicable)				
Symptomatic	11.3	1.7		
Asymptomatic	13.4	1.7		
Probable	2.5	0		
Severe	0	0		
Nocturnal	6.7	1.7		

Notes:

[16] - All randomized participants who received at least one dose of study drug.

[17] - All randomized participants who received at least one dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of HE Adjusted Per 30 Days

End point title	Rate of HE Adjusted Per 30 Days

End point description:

The hypoglycemia rate per 30 days during defined period is calculated by the number of hypoglycemia events within the period/number of days participant at risk within the period*30 days.

End point type	Secondary

End point timeframe:

Baseline through 24 weeks

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	60		
Units: number of events/participants/30 days				
arithmetic mean (standard deviation)				
Total HE	0.19 (± 0.59)	0.01 (± 0.03)		
Documented symptomatic HE	0.07 (± 0.33)	0 (± 0.02)		
Asymptomatic HE	0.11 (± 0.45)	0 (± 0.02)		
Severe HE	0 (± 0)	0 (± 0)		
Nocturnal HE	0.02 (± 0.16)	0 (± 0.02)		
Probable symptomatic HE	0.01 (± 0.04)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Requiring Additional Intervention for Severe, Persistent Hyperglycemia

End point title	Percentage of Participants Requiring Additional Intervention for Severe, Persistent Hyperglycemia

End point description:

Additional Intervention: any additional therapeutic intervention in participants who developed persistent, severe hyperglycemia despite full compliance with the assigned therapeutic regimen, or initiation of an alternative antihyperglycemic medication following study drug discontinuation.

End point type	Secondary

End point timeframe:

Baseline through 24 Weeks

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	60		
Units: percentage of participants				
number (not applicable)	2.1	11.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Initiation of Additional Intervention for Severe, Persistent Hyperglycemia

End point title	Time to Initiation of Additional Intervention for Severe, Persistent Hyperglycemia

End point description:

An additional intervention (rescue therapy) was defined as any additional therapeutic intervention in participants who developed persistent, severe hyperglycemia despite full compliance with the assigned therapeutic regimen, or initiation of an alternative antihyperglycemic medication following study drug discontinuation. Participants who had no rescue therapy within specified study period were considered as censored observations at the last available contact date up to specified study period.

End point type	Secondary

End point timeframe:

Baseline through 24 Weeks

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	60		
Units: weeks				
arithmetic mean (standard error)	22.59 (± 0.36)	22.47 (± 0.66)		

Statistical analyses

No statistical analyses for this end point

Secondary: Dulaglutide Anti-Drug Antibodies (ADA)

End point title	Dulaglutide Anti-Drug Antibodies (ADA)[18]

End point description:

Number of participants with treatment emergent (TE) dulaglutide anti-drug antibodies from postbaseline to follow up were summarized. A participant is considered to have TE dulaglutide ADA if the participant has at least one titer that is treatment-emergent relative to baseline, defined as a 4-fold or greater increase in titer from baseline measurement.

End point type	Secondary

End point timeframe:

Baseline up to 4 Weeks Post-Last Dose of Study Drug

Notes:

[18] - 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: The study was double-blinded and samples were collected from all participants. Those participants in the dulaglutide treatment group were tested for anti-drug antibody positive samples; placebo participants were not tested for ADA's.

End point values	Dulaglutide			
Subject group type	Reporting group			
Number of subjects analysed	239			
Units: participants				
number (not applicable)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Lipase

End point title	Change from Baseline in Lipase

End point description:

A summary of changes in lipase evaluation from baseline to endpoint.

End point type	Secondary

End point timeframe:

Baseline, 24 Weeks

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	233[19]	60[20]		
Units: Units/Liter				
median (inter-quartile range (Q1-Q3))	8 (1 to 18)	4.5 (-2.5 to 15.5)		

Notes:

[19] - All participants who received at least one dose of study drug and had evaluable lipase data.

[20] - All participants who received at least one dose of study drug and had evaluable lipase data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Amylase

End point title	Change from Baseline in Amylase

End point description:

A summary of changes in amylase evaluation from baseline to endpoint.

End point type	Secondary

End point timeframe:

Baseline, 24 Weeks

End point values	Dulaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	233[21]	60[22]		
Units: Units/Liter				
median (inter-quartile range (Q1-Q3))	8 (1 to 18)	2 (-5 to 11)		

Notes:

[21] - Participants who received at least one dose of study drug and had evaluable amylase data.

[22] - Participants who received at least one dose of study drug and had evaluable amylase data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
H9X-MC-GBDG	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Dula 1.5
Reporting group description: -	

Serious adverse events	Placebo	Dula 1.5	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)	9 / 239 (3.77%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
anaplastic astrocytoma			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 60 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
ulna fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 60 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
angina pectoris			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 60 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
cerebrovascular accident			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 60 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
rheumatoid arthritis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 60 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
osteomyelitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 60 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
otitis media			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 60 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary tuberculosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 60 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
hypoglycaemia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	0 / 60 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Dula 1.5	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 60 (5.00%)	44 / 239 (18.41%)	
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 60 (0.00%)	20 / 239 (8.37%)	
occurrences (all)	0	30	
eructation			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 60 (0.00%)	14 / 239 (5.86%)	
occurrences (all)	0	24	
nausea			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 60 (0.00%)	25 / 239 (10.46%)	
occurrences (all)	0	31	
Metabolism and nutrition disorders			
hyperglycaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 60 (5.00%)	1 / 239 (0.42%)	
occurrences (all)	3	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported