Clinical trial results:
A Randomized, Open-Label, Parallel-Arm Study Comparing the Effect of Once-Weekly Dulaglutide with Once-Daily Liraglutide in Patients with Type 2 Diabetes (AWARD-6: Assessment of Weekly AdministRation of LY2189265 in Diabetes-6)

Summary

EudraCT number	2011-003810-18
Trial protocol	CZ HU DE PL ES SK
Global end of trial date	25 November 2013

Results information

Result version number	v1 (current)
This version publication date	04 July 2016
First version publication date	02 August 2015

Trial information

Trial identification

Sponsor protocol code	H9X-MC-GBDE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01624259
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 11377, Trial Alias: H9X-MC-GBDE

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, 1 877-285-4559,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-CTLilly,

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	25 November 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the study is to assess the benefits and risks of once-weekly dulaglutide compared to once-daily liraglutide in participants with type 2 diabetes who have inadequate glycemic control on metformin.

Protection of trial subjects:

The study was conducted in accordance with International Conference on Harmonisation (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:

Metformin: at least 1500 mg/day, oral, for 26 weeks

Evidence for comparator: -

Actual start date of recruitment	20 June 2012
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	United States: 194
Country: Number of subjects enrolled	Czech Republic: 55
Country: Number of subjects enrolled	Hungary: 40
Country: Number of subjects enrolled	Mexico: 41
Country: Number of subjects enrolled	Slovakia: 42
Country: Number of subjects enrolled	Puerto Rico: 7
Country: Number of subjects enrolled	Poland: 81
Country: Number of subjects enrolled	Spain: 48
Country: Number of subjects enrolled	Romania: 37
Country: Number of subjects enrolled	Germany: 54
Worldwide total number of subjects	599
EEA total number of subjects	357

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)	488
From 65 to 84 years	111
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No text entered

Pre-assignment

Screening details:

No text entered

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	LY2189265

Arm description:

LY2189265 (Dulaglutide): 1.5 milligrams (mg), subcutaneous (SC), once weekly for 26 weeks

Metformin: at least 1500 mg/day, oral, for 26 weeks

Arm type	Experimental
Investigational medicinal product name	LY2189265
Investigational medicinal product code	
Other name	Dulaglutide
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

LY2189265 (Dulaglutide): 1.5 milligrams (mg), subcutaneous (SC), once weekly for 26 weeks

Arm title	Liraglutide

Arm description:

Liraglutide: 0.6 mg, SC, once daily for 7 days, then titrated up to 1.2 mg, SC, once daily for 7 days, then titrated up to 1.8 mg, SC, once daily for 24 weeks

Metformin: at least 1500 mg/day, oral, for 26 weeks

Arm type	Active comparator
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Liraglutide: 0.6 mg, SC, once daily for 7 days, then titrated up to 1.2 mg, SC, once daily for 7 days, then titrated up to 1.8 mg, SC, once daily for 24 weeks

Number of subjects in period 1	LY2189265	Liraglutide
Started	299	300
Received at Least One Dose of Study Drug	299	300
Completed	269	269
Not completed	30	31
Physician decision	1	1
Adverse event, non-fatal	18	18
Withdrawal by Subject	5	7
Lost to follow-up	2	3
Protocol deviation	1	2
Abnormal laboratory measure	3	-

Baseline characteristics

Reporting groups	
Reporting group title	LY2189265
Reporting group description:	
LY2189265 (Dulaglutide): 1.5 milligrams (mg), subcutaneous (SC), once weekly for 26 weeks Metformin: at least 1500 mg/day, oral, for 26 weeks	
Reporting group title	Liraglutide
Reporting group description:	
Liraglutide: 0.6 mg, SC, once daily for 7 days, then titrated up to 1.2 mg, SC, once daily for 7 days, then titrated up to 1.8 mg, SC, once daily for 24 weeks Metformin: at least 1500 mg/day, oral, for 26 weeks	

Reporting group values	LY2189265	Liraglutide	Total
Number of subjects	299	300	599
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	56.49	56.81	
standard deviation	± 9.34	± 9.91	-
Gender, Male/Female Units: participants			
Female	161	151	312
Male	138	149	287
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	75	72	147
Not Hispanic or Latino	221	223	444
Unknown or Not Reported	3	5	8
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	20	23	43
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	21	16	37
White	256	259	515
More than one race	1	2	3
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
United States	97	97	194
Czech Republic	27	28	55
Hungary	21	19	40
Mexico	20	21	41
Slovakia	20	22	42

Puerto Rico	3	4	7
Poland	39	42	81
Spain	24	24	48
Romania	20	17	37
Germany	28	26	54
Body Weight			
Units: kilograms (kg)			
arithmetic mean	93.82	94.35	
standard deviation	± 18.23	± 18.96	-
Body Mass Index (BMI)			
BMI is an estimate of body fat based on body weight divided by height squared			
Units: kilograms per meter squared (kg/m^2)			
arithmetic mean	33.5	33.62	
standard deviation	± 5.07	± 5.16	-
Glycosylated hemoglobin (HbA1c)			
Units: percentage of glycosylated hemoglobin			
arithmetic mean	8.06	8.05	
standard deviation	± 0.81	± 0.79	-
Duration of diabetes			
Units: years			
arithmetic mean	7.13	7.28	
standard deviation	± 5.41	± 5.41	-

End points

End points reporting groups

Reporting group title	LY2189265

Reporting group description:

LY2189265 (Dulaglutide): 1.5 milligrams (mg), subcutaneous (SC), once weekly for 26 weeks

Metformin: at least 1500 mg/day, oral, for 26 weeks

Reporting group title	Liraglutide

Reporting group description:

Liraglutide: 0.6 mg, SC, once daily for 7 days, then titrated up to 1.2 mg, SC, once daily for 7 days, then titrated up to 1.8 mg, SC, once daily for 24 weeks

Metformin: at least 1500 mg/day, oral, for 26 weeks

Primary: 1: Change from Baseline to 26 Weeks Endpoint in Glycosylated Hemoglobin (HbA1c)

End point title	1: Change from Baseline to 26 Weeks Endpoint in Glycosylated Hemoglobin (HbA1c)

End point description:

Least Squares (LS) means of the glycosylated hemoglobin A1c (HbA1c) change from baseline to the primary endpoint at Week 26 was adjusted by fixed effects of treatment, country, visit, treatment-by-visit interaction, participant as random effect, and baseline HbA1c as covariates, via a mixed-effects model for repeated measures (MMRM) analysis using restricted maximum likelihood (REML).

End point type	Primary

End point timeframe:

Baseline, 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279[1]	272[2]		
Units: percentage of glycosylated hemoglobin				
least squares mean (standard error)	-1.42 (± 0.05)	-1.36 (± 0.05)		

Notes:

[1] - Received at least 1 dose of LY2189265 with evaluable HbA1c data.

[2] - Received at least 1 dose of Liraglutide with evaluable HbA1c data.

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for End Point 1

Statistical analysis description:

To show noninferiority of 1.5 mg LY2189265 relative to 1.8 mg liraglutide with 90% power, 222 completers (444 total) at 26 weeks were required. Noninferiority of 1.5 mg LY2189265 relative to 1.8 mg liraglutide was demonstrated if the upper bound of the twosided 95% Confidence Interval (CI) for the difference in mean change in HbA1c between the 1.5 mg LY2189265 arm and 1.8 mg liraglutide arm was below 0.4%.

Comparison groups	Liraglutide v LY2189265

Number of subjects included in analysis	551
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.07

Notes:

[3] - Family-wise Type I error rate was controlled by applying a serial gatekeeping strategy.
This calculation assumed a 0 difference in HbA1c between the 1.5 mg LY2189265 1.5-mg arm and 1.8 mg liraglutide, 0.4% margin of noninferiority, common Standard Deviation (SD) of 1.3% for change from baseline in HbA1c, 0.05 two-sided significance level, and 25% dropout rate at 26 weeks.
1-sided raw p-value (no multiplicity adjustment).

Statistical analysis title	Statistical Analysis 2 for End Point 1

Statistical analysis description:

Superiority analysis

Comparison groups	LY2189265 v Liraglutide
Number of subjects included in analysis	551
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.186 [4]
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.07

Notes:

[4] - 1-sided raw p-value (no multiplicity adjustment)

Secondary: 2: Change from Baseline in Body Weight at 26 Weeks

End point title	2: Change from Baseline in Body Weight at 26 Weeks

End point description:

LS means of the weight change from baseline to primary endpoint at Week 26 were calculated using analysis of covariance (ANCOVA) with HbA1c Strata, country, and treatment as fixed effects and baseline body weight as a covariate.

End point type	Secondary

End point timeframe:

Baseline, Up to 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299[5]	299[6]		
Units: kilograms (kg)				
least squares mean (standard error)	-2.9 (± 0.22)	-3.61 (± 0.22)		

Notes:

[5] - Received at least 1 dose of LY2189265 with evaluable body weight data.

[6] - Received at least 1 dose of Liraglutide with evaluable body weight data.

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for End Point 2

Statistical analysis description:

Treatment comparison from ANCOVA model at 26 weeks.

Comparison groups	LY2189265 v Liraglutide
Number of subjects included in analysis	598
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.01 [8]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	1.26
Variability estimate	Standard error of the mean
Dispersion value	0.28

Notes:

[7] - Analysis type other: Test for Difference

[8] - No adjustment for multiplicity.

Secondary: 3: Change from Baseline in Body Mass Index (BMI) at 26 Weeks

End point title	3: Change from Baseline in Body Mass Index (BMI) at 26 Weeks

End point description:

BMI is an estimate of body fat based on body weight divided by height squared. LS means of the BMI change from baseline to primary endpoint at Week 26 were calculated using ANCOVA with HbA1c Strata, country, and treatment as fixed effects and baseline BMI as a covariate.

End point type	Secondary

End point timeframe:

Baseline, Up to 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299[9]	299[10]		
Units: kilograms/square meter (kg/m^2)				
least squares mean (standard error)	-1.05 (± 0.08)	-1.3 (± 0.08)		

Notes:

[9] - Received at least 1 dose of LY2189265 with evaluable BMI data.

[10] - Received at least 1 dose of liraglutide with evaluable BMI data.

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for End Point 3

Statistical analysis description:

Treatment comparison from ANCOVA model.

Comparison groups	LY2189265 v Liraglutide
Number of subjects included in analysis	598
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	= 0.013 [12]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.45
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[11] - Analysis type other: Test for Difference

[12] - No adjustment for multiplicity.

Secondary: 4: Change from Baseline in Fasting Plasma Glucose (FPG) at 26 Weeks

End point title	4: Change from Baseline in Fasting Plasma Glucose (FPG) at 26 Weeks

End point description:

LS means of the FPG from baseline to primary endpoint at Week 26 were adjusted by fixed effects of treatment, country, baseline HbA1c strata, and baseline FPG as covariates, via ANCOVA with LOCF.

End point type	Secondary

End point timeframe:

Baseline, Up to 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	281[13]	277[14]		
Units: milligrams/deciliter (mg/dL)				
least squares mean (standard error)	-34.81 (± 2.13)	-34.25 (± 2.11)		

Notes:

[13] - Received at least 1 dose of LY2189265 with evaluable FPG data.

[14] - Received at least 1 dose of liraglutide with evaluable FPG data.

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for End Point 4

Statistical analysis description:

Treatment comparison from ANCOVA model.

Comparison groups	LY2189265 v Liraglutide
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other[15]
P-value	= 0.828 [16]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.69
upper limit	4.56
Variability estimate	Standard error of the mean
Dispersion value	2.61

Notes:

[15] - Analysis type other: Test for Difference

[16] - No adjustment for multiplicity.

Secondary: 5: Change from Baseline Daily Mean in 7-Point Self Monitored Plasma Glucose (SMPG) at 26 Weeks

End point title	5: Change from Baseline Daily Mean in 7-Point Self Monitored Plasma Glucose (SMPG) at 26 Weeks

End point description:

The SMPG data were collected at the following 7 time points: pre-morning meal; 2 hours post-morning meal; pre-midday meal; 2 hours post-midday meal; pre-evening meal; 2 hours post-evening meal; and bedtime. The mean of the 7 time points (Daily Mean) was also calculated.
LS means of the SMPG change from baseline to primary endpoint at Week 26 were adjusted by fixed effects of treatment, HbA1c strata, country, visit, treatment-by-visit interaction, participant as random effect and baseline SMPG as a covariate, via a MMRM analysis using REML.

End point type	Secondary

End point timeframe:

Baseline, 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	248[17]	256[18]		
Units: mg/dL				
least squares mean (standard error)	-40.76 (± 1.5)	-38.51 (± 1.45)		

Notes:

[17] - Received at least 1 dose of LY2189265 with evaluable 7-Point SMPG data.

[18] - Received at least 1 dose of liraglutide with evaluable 7-Point SMPG data.

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for End Point 5
Comparison groups	LY2189265 v Liraglutide
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[19]
P-value	= 0.228 [20]
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-2.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.91
upper limit	1.41
Variability estimate	Standard error of the mean
Dispersion value	1.86

Notes:

[19] - P-value from pairwise comparison of LS means at 26 weeks from REML-based MMRM.

Analysis type other: Test for Difference

[20] - No adjustment for multiplicity.

Secondary: 6: Percentage of Participants Achieving a Glycosylated Hemoglobin (HbA1c) ≤6.5% or <7% at 26 Weeks

End point title	6: Percentage of Participants Achieving a Glycosylated Hemoglobin (HbA1c) ≤6.5% or <7% at 26 Weeks

End point description:

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

End point type	Secondary

End point timeframe:

Up to 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293[21]	293[22]		
Units: percentage of participants				
HbA1c levels ≤6.5%	55	51		
HbA1c levels <7.0%	68	68		

Notes:

[21] - Received at least 1 dose of LY2189265 with evaluable HbA1c data.

[22] - Received at least 1 dose of Liraglutide with evaluable HbA1c data.

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for End Point 6
Statistical analysis description:	
Treatment comparison for HbA1c levels ≤6.5%	
Comparison groups	LY2189265 v Liraglutide
Number of subjects included in analysis	586
Analysis specification	Pre-specified
Analysis type	other[23]
P-value	= 0.322 [24]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.86

Notes:

[23] - No adjustment for multiplicity.

Analysis type other: Test for Difference

[24] - P-value of treatment comparison at Week 26 is from repeated generalized linear mixed model (GLM model).

Statistical analysis title	Statistical Analysis 2 for End Point 6
Statistical analysis description:	
Treatment comparison for HbA1c levels <7.0%.	
Comparison groups	LY2189265 v Liraglutide
Number of subjects included in analysis	586
Analysis specification	Pre-specified
Analysis type	other[25]
P-value	= 0.925 [26]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.63

Notes:

[25] - P-value of treatment comparison at Week 26 is from repeated generalized linear mixed model (GLM model).

Analysis type other: Test for Difference

[26] - No adjustment for multiplicity.

Secondary: 7: Change from Baseline in Homeostasis Model Assessment 2 steady-state Beta (β)- cell function (HOMA2-%B) at 26 Weeks

End point title	7: Change from Baseline in Homeostasis Model Assessment 2 steady-state Beta (β)- cell function (HOMA2-%B) at 26 Weeks

End point description:

The homeostatic model assessment (HOMA) quantifies insulin resistance and beta-cell function. HOMA2-%B is a computer model that uses fasting plasma insulin and glucose concentrations to estimate steady-state beta cell function (%B) as a percentage of a normal reference population (normal young adults). The normal reference population was set at 100%.
LS means of the HOMA2-%B change from baseline to primary endpoint at Week 26 was adjusted by fixed effects of treatment, country, baseline HbA1c strata, and baseline HOMA2-%B value as covariate, via an ANCOVA analysis using LOCF.

End point type	Secondary

End point timeframe:

Baseline, Up to 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275[27]	265[28]		
Units: percentage of HOMA2-%B				
least squares mean (standard error)	37.03 (± 2.26)	35.59 (± 2.27)		

Notes:

[27] - Received at least 1 dose of LY2189265 with evaluable HOMA2-%B data.

[28] - Received at least 1 dose of liraglutide with evaluable HOMA2-%B data.

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for End Point 7
Comparison groups	LY2189265 v Liraglutide
Number of subjects included in analysis	540
Analysis specification	Pre-specified
Analysis type	other[29]
P-value	= 0.608
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.06
upper limit	6.92
Variability estimate	Standard error of the mean
Dispersion value	2.79

Notes:

[29] - No adjustment for multiplicity.

Analysis type other: Test for Difference

Secondary: 9: Change From Baseline in Electrocardiogram (ECG) Parameters, Heart Rate (HR) at 26 Weeks

End point title	9: Change From Baseline in Electrocardiogram (ECG) Parameters, Heart Rate (HR) at 26 Weeks

End point description:

ECG HR was measured. LS means of change from baseline were analyzed using ANCOVA with HbA1c strata, country, and treatment as fixed effects and baseline HR as a covariate.

End point type	Secondary

End point timeframe:

Baseline, Up to 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	273[30]	284[31]		
Units: beats per minute (bpm)				
least squares mean (standard error)	1.9 (± 0.55)	4.1 (± 0.54)		

Notes:

[30] - Received at least 1 dose of LY2189265 with evaluable ECG heart rate data.

[31] - Received at least 1 dose of liraglutide with evaluable ECG heart rate data.

Statistical analyses

No statistical analyses for this end point

Secondary: 10: Change from Baseline in Electrocardiogram (ECG) Parameters PR and QTcF (Fridericia's) intervals at 26 Weeks

End point title	10: Change from Baseline in Electrocardiogram (ECG) Parameters PR and QTcF (Fridericia's) intervals at 26 Weeks

End point description:

The QT interval is a measure of the time between the start of the Q wave and the end of the T wave. QTcF is the measure of the time between the start of the Q wave and the end of the T wave adjusted using Fridericia's formula. PR is the interval between the P wave and the QRS complex. These parameters were calculated from electrocardiogram (ECG) data. LS means of change from baseline for the PR and QTcF intervals will be analyzed using the MMRM similar to MMRM model for primary outcome, using corresponding baseline and HbA1c strata. Only ECGs obtained at scheduled visits will be used in these summaries and analyses.

End point type	Secondary

End point timeframe:

Baseline, 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	273[32]	284[33]		
Units: milliseconds (msec)				
least squares mean (standard error)				
PR interval (n=270, 278)	3.8 (± 0.81)	3.3 (± 0.8)		
QTcF interval (n=273, 284)	0.39 (± 0.9)	-0.72 (± 0.89)		

Notes:

[32] - Received at least 1 dose of LY2189265 with evaluable ECG PR or QTcF interval data.

[33] - Received at least 1 dose of Liraglutide with evaluable ECG PR or QTcF interval data.

Statistical analyses

No statistical analyses for this end point

Secondary: 11: Change from Baseline in Heart Rate (HR) at 26 Weeks

End point title	11: Change from Baseline in Heart Rate (HR) at 26 Weeks

End point description:

Descriptive statistics for the actual measurements and LS means of change from baseline for HR (sitting) by treatment arm were analyzed using the MMRM model with treatment, country, visit, and treatment-by-visit interaction as fixed effects, baseline rate as a covariate, and participant as a random effect.

End point type	Secondary

End point timeframe:

Baseline, 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288[34]	288[35]		
Units: bpm				
least squares mean (standard error)	2.37 (± 0.4)	3.12 (± 0.4)		

Notes:

[34] - Received at least 1 dose of LY2189265 with evaluable heart rate data.

[35] - Received at least 1 dose of liraglutide with evaluable heart rate data.

Statistical analyses

No statistical analyses for this end point

Secondary: 12: Change from Baseline in Blood Pressure (BP) at 26 Weeks

End point title	12: Change from Baseline in Blood Pressure (BP) at 26 Weeks

End point description:

Descriptive statistics for the actual measurements and change from baseline for sitting systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured. LS means of change from baseline were calculated using MMRM with treatment, country, visit, and treatment-by-visit interaction as fixed effects, baseline BP as a covariate, and participant as a random effect.

End point type	Secondary

End point timeframe:

Baseline, 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278[36]	281[37]		
Units: milliliters of mercury (mmHg)				
least squares mean (standard error)				
Sitting DBP	-0.22 (± 0.4)	-0.31 (± 0.4)		
Sitting SBP	-3.36 (± 0.7)	-2.82 (± 0.7)		

Notes:

[36] - Received at least 1 dose of LY2189265 with evaluable BP data.

[37] - Received at least 1 dose of liraglutide with evaluable BP data.

Statistical analyses

No statistical analyses for this end point

Secondary: 13: Number of Participants with Adjudicated Acute Pancreatitis Events

End point title	13: Number of Participants with Adjudicated Acute Pancreatitis Events

End point description:

The number of participants with events of pancreatitis confirmed by adjudication were summarized cumulatively at 26 weeks (including a 30-day follow up). Pancreatitis events were adjudicated by a committee of physicians external to the Sponsor.
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 up to 30 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299[38]	300[39]		
Units: participants				
number (not applicable)	0	0		

Notes:

[38] - Received at least 1 dose of LY2189265 with evaluable adverse event data.

[39] - Received at least 1 dose of Liraglutide with evaluable adverse event data.

Statistical analyses

No statistical analyses for this end point

Secondary: 14: Change from Baseline in Calcitonin at 26 Weeks

End point title	14: Change from Baseline in Calcitonin at 26 Weeks

End point description:

A summary of participants having changes in calcitonin values from baseline to primary endpoint of 26 weeks is presented.

End point type	Secondary

End point timeframe:

Baseline, Up to 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292[40]	294[41]		
Units: picograms/milliliter (pcg/mL)				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)		

Notes:

[40] - Received at least 1 dose of LY2189265 with evaluable calcitonin laboratory data.

[41] - Received at least 1 dose of liraglutide with evaluable calcitonin laboratory data.

Statistical analyses

No statistical analyses for this end point

Secondary: 15: Change from Baseline in Lipase at 26 Weeks

End point title	15: Change from Baseline in Lipase at 26 Weeks

End point description:

A summary of participants having changes in lipase evaluation from baseline to primary endpoint of 26 weeks is presented.

End point type	Secondary

End point timeframe:

Baseline, Up to 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288[42]	289[43]		
Units: units/liter (U/L)				
median (inter-quartile range (Q1-Q3))	7 (0.5 to 17.5)	11 (2 to 23)		

Notes:

[42] - Received at least 1 dose of LY2189265 with evaluable lipase laboratory data.

[43] - Received at least 1 dose of liraglutide with evaluable lipase laboratory data.

Statistical analyses

No statistical analyses for this end point

Secondary: 16: Change from Baseline in Amylase at 26 Weeks

End point title	16: Change from Baseline in Amylase at 26 Weeks

End point description:

A summary of participants having changes in amylase evaluation from baseline to primary endpoint of 26 weeks is presented.

End point type	Secondary

End point timeframe:

Baseline, Up to 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287[44]	289[45]		
Units: U/L				
median (inter-quartile range (Q1-Q3))	7 (0 to 14)	6 (0 to 13)		

Notes:

[44] - Received at least 1 dose of LY2189265 with evaluable amylase laboratory data.

[45] - Received at least 1 dose of liraglutide with evaluable amylase laboratory data.

Statistical analyses

No statistical analyses for this end point

Secondary: 17: Percentage of Participants with Self-Reported Hypoglycemia Events

End point title	17: Percentage of Participants with Self-Reported Hypoglycemia Events

End point description:

Hypoglycemic events (HE) were classified as severe (episodes requiring the assistance of another person to actively administer resuscitative actions), documented symptomatic (any time a participant felt that he/she was experiencing symptoms and/or signs associated with hypoglycemia and had a plasma glucose [PG] concentration of ≤70 mg/dL), asymptomatic (events not accompanied by typical symptoms of hypoglycemia but with a measured PG of ≤ 70 mg/dL), nocturnal (events that occurred between bedtime and waking), or probable symptomatic (events during which symptoms of hypoglycemia were not accompanied by a PG determination but that was presumably caused by a PG of ≤70 mg/dL).

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 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299[46]	300[47]		
Units: percentage of participants				
number (not applicable)				
Documented symptomatic HE	2.7	2.7		
Asymptomatic HE	6.7	3.3		
Severe HE	0	0		
Nocturnal HE	1.3	2		
Probable symptomatic HE	1	1		

Notes:

[46] - Received at least 1 dose of LY2189265 with evaluable hypoglycemia event data

[47] - Received at least 1 dose of liraglutide with evaluable hypoglycemia event data

Statistical analyses

No statistical analyses for this end point

Secondary: 18: Percentage of Participants Requiring Additional Intervention for Severe, Persistent Hyperglycemia

End point title	18: Percentage of Participants Requiring 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.

End point type	Secondary

End point timeframe:

Baseline through 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299[48]	300[49]		
Units: percentage of participants				
number (not applicable)	0.3	1		

Notes:

[48] - Received at least 1 dose of LY2189265 with evaluable concomitant medication data.

[49] - Received at least 1 dose of liraglutide with evaluable concomitant medication data.

Statistical analyses

No statistical analyses for this end point

Secondary: 19: Rate of Hypoglycemic Events Adjusted per 30 Days

End point title	19: Rate of Hypoglycemic Events Adjusted per 30 Days

End point description:

HE were classified as severe (episodes requiring the assistance of another person to actively administer resuscitative actions), documented symptomatic (any time a participant felt that he/she was experiencing symptoms and/or signs associated with hypoglycemia and had a PG concentration of ≤70 mg/dL), asymptomatic (events not accompanied by typical symptoms of hypoglycemia but with a measured PG of ≤ 70 mg/dL), nocturnal (events that occurred between bedtime and waking), or probable symptomatic (events during which symptoms of hypoglycemia were not accompanied by a PG determination but that was presumably caused by a PG of ≤70 mg/dL). The hypoglycemia rate per 30 days was calculated by the number of hypoglycemia events within the period/number of days participant at risk within the period*30 days. 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 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299[50]	300[51]		
Units: number of events/participant/30 days				
arithmetic mean (standard deviation)				
Total HE	0.03 (± 0.12)	0.04 (± 0.25)		
Documented symptomatic HE	0.01 (± 0.08)	0.02 (± 0.17)		
Asymptomatic HE	0.02 (± 0.07)	0.01 (± 0.08)		
Severe HE	0 (± 0)	0 (± 0)		
Nocturnal HE	0.01 (± 0.05)	0.01 (± 0.1)		
Probable symptomatic HE	0 (± 0.02)	0.01 (± 1.12)		

Notes:

[50] - Received at least 1 dose of LY2189265 with evaluable hypoglycemic episode data.

[51] - Received at least 1 dose of liraglutide with evaluable hypoglycemic episode data.

Statistical analyses

No statistical analyses for this end point

Secondary: 20: Time to Initiation of Additional Intervention for Severe, Persistent Hyperglycemia

End point title	20: 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.

A median time to initiation of additional intervention could not be calculated due to the small number of events requiring rescue therapy. Value 999999 represents NA.

End point type	Secondary

End point timeframe:

Baseline through 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299[52]	300[53]		
Units: weeks				
median (confidence interval 95%)	999999 (999999 to 9999999)	999999 (999999 to 9999999)		

Notes:

[52] - 999999 represents NA. A small number of events requiring rescue therapy, therefore no evaluation.

[53] - 999999 represents NA. A small number of events requiring rescue therapy, therefore no evaluation.

Statistical analyses

No statistical analyses for this end point

Secondary: 21: Number of Participants with Allergic or Hypersensitivity Reactions

End point title	21: Number of Participants with Allergic or Hypersensitivity Reactions

End point description:

Allergic and hypersensitivity reactions that were considered possibly related to study drug by the investigator are presented. 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 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	300		
Units: Participants	1	5		

Statistical analyses

No statistical analyses for this end point

Secondary: 22: Number of Participants With Treatment Emergent LY2189265 Antibodies up to 26 Weeks and 4 Weeks After Last Dose

End point title	22: Number of Participants With Treatment Emergent LY2189265 Antibodies up to 26 Weeks and 4 Weeks After Last Dose

End point description:

LY2189265 (dulaglutide) anti-drug antibodies (ADA) were assessed at baseline, 26 weeks, and at the safety follow-up visit 4 weeks after study drug discontinuation in dulaglutide-treated participants. A participant was considered to have treatment emergent LY2189265 ADA if the participant had at least 1 titer that was treatment-emergent relative to baseline, defined as a 4-fold or greater increase in titer from baseline measurement. The number of participants with treatment-emergent LY2189265 ADA from postbaseline to follow up were summarized.

End point type	Secondary

End point timeframe:

Baseline up to 4 Weeks Post Last Dose of Study Drug

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290[54]	0[55]		
Units: Participants	3			

Notes:

[54] - Subject received at least 1 dose of LY2189265 with evaluable LY2189265 ADA data.

[55] - 99999 represents not applicable values

Statistical analyses

No statistical analyses for this end point

Secondary: 23: Percent Change from Baseline in Lipid Parameters at 26 Weeks

End point title	23: Percent Change from Baseline in Lipid Parameters at 26 Weeks

End point description:

A summary of percent change in lipid parameters (total cholesterol, high-density lipoprotein cholesterol [HDL-C], low density lipoprotein cholesterol [LDL-C], very low-density lipoprotein cholesterol [VLDL], and triglycerides) from baseline to primary endpoint of 26 weeks is presented. LS means of the lipid parameter from baseline to primary endpoint at Week 26 were adjusted by fixed effects of treatment, country, baseline HbA1c strata, and lipid parameter baseline as covariates, via ANCOVA with LOCF.

End point type	Secondary

End point timeframe:

Baseline, Up to 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	284		
Units: percent				
least squares mean (standard error)				
Total cholesterol (n=286, 284)	-1.64 (± 1.18)	0.67 (± 1.18)		
HDL-C (n=286, 284)	6.21 (± 1.02)	6.46 (± 1.02)		
LDL-C (n=276, 276)	-1.09 (± 2.17)	3.2 (± 2.15)		
VLDL (n=276, 276)	1.56 (± 2.63)	2.92 (± 2.6)		
Triglycerides (n=286, 284)	0.59 (± 2.76)	1.35 (± 2.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: 8: Number of Participants With Reported and Adjudicated Cardiovascular Events [Time Frame: Baseline up to 26 Weeks]

End point title	8: Number of Participants With Reported and Adjudicated Cardiovascular Events [Time Frame: Baseline up to 26 Weeks]

End point description:

Deaths and nonfatal cardiovascular (CV) adverse events (AEs) were adjudicated by a committee of physicians with cardiology expertise external to the Sponsor. The nonfatal CV AEs to be adjudicated include myocardial infarction, hospitalization for unstable angina, hospitalization for heart failure, coronary interventions (such as coronary artery bypass graft or percutaneous coronary intervention), and cerebrovascular events including cerebrovascular accident (stroke) and transient ischemic attack.

The number of participants with reported CV events, number of participants with nonfatal CV events confirmed by adjudication, and number of deaths confirmed by adjudication are 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.

End point type	Secondary

End point timeframe:

Baseline up to 26 Weeks

End point values	LY2189265	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299[56]	300[57]		
Units: Participants				
Any reported CV events	0	3		
Any adjudicated nonfatal CV events	0	1		
Any confirmed adjudicated deaths	0	0		

Notes:

[56] - Received at least 1 dose of LY2189265 with evaluable adjudicated CV event data.

[57] - Received at least 1 dose of liraglutide with evaluable adjudicated CV event data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Core Study

Adverse event reporting additional description:

H9X-MC-GBDE

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Liraglutide
Reporting group description: -	
Reporting group title	LY2189265
Reporting group description: -	

Serious adverse events	Liraglutide	LY2189265	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 300 (3.67%)	5 / 299 (1.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
lipase increased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
papillary thyroid cancer			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
meningioma			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 300 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
prostate cancer			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed[1]	0 / 149 (0.00%)	1 / 138 (0.72%)	
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			
ankle fracture			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 300 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
fall			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 300 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
angina pectoris			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
tachyarrhythmia			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
epilepsy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 300 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
polyneuropathy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
cholelithiasis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 300 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
hydronephrosis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal failure acute			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
schizophrenia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 300 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
bronchopneumonia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 300 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia influenzal			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory tract infection			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
vestibular neuronitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

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

Non-serious adverse events	Liraglutide	LY2189265	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	116 / 300 (38.67%)	113 / 299 (37.79%)	
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	25 / 300 (8.33%)	22 / 299 (7.36%)	
occurrences (all)	35	36	
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	17 / 300 (5.67%)	11 / 299 (3.68%)	
occurrences (all)	20	16	
diarrhoea			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	36 / 300 (12.00%)	36 / 299 (12.04%)	
occurrences (all)	51	56	
nausea			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	54 / 300 (18.00%)	61 / 299 (20.40%)	
occurrences (all)	77	108	
vomiting			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	25 / 300 (8.33%)	21 / 299 (7.02%)	
occurrences (all)	36	24	
dyspepsia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	18 / 300 (6.00%)	24 / 299 (8.03%)	
occurrences (all)	22	36	
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	21 / 300 (7.00%)	23 / 299 (7.69%)	
occurrences (all)	24	30	
Metabolism and nutrition disorders			

decreased appetite			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	20 / 300 (6.67%)	16 / 299 (5.35%)	
occurrences (all)	20	16	

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