Clinical trial results:
Comparison of the Oxyntomodulin Analog, LY2944876, to Once-Weekly Exenatide and to Placebo in Patients with Type 2 Diabetes.

Summary

EudraCT number	2013-003552-21
Trial protocol	GR PL RO
Global end of trial date	25 August 2015

Results information

Result version number	v2 (current)
This version publication date	06 May 2021
First version publication date	04 April 2021
Version creation reason	• Correction of full data set Adjust to align with other database.

Trial information

Trial identification

Sponsor protocol code	I7I-MC-XNAA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02119819
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 15062

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)	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 August 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to compare the safety and effectiveness of the study drug known as LY2944876 to exenatide extended-release and placebo in participants with type 2 diabetes mellitus. All drugs will be given by an injection under the skin. Participants remain on stable doses of metformin, as prescribed by their personal investigator if they were on metformin at study entry. Participants' involvement in the study is expected to last about 30 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:

Metformin

Evidence for comparator: -

Actual start date of recruitment	14 May 2014
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: 193
Country: Number of subjects enrolled	Greece: 32
Country: Number of subjects enrolled	Mexico: 60
Country: Number of subjects enrolled	Poland: 66
Country: Number of subjects enrolled	Puerto Rico: 12
Country: Number of subjects enrolled	Romania: 57
Worldwide total number of subjects	420
EEA total number of subjects	155

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)	333
From 65 to 84 years	87
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

No Text Available

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

Arms

Are arms mutually exclusive?	Yes
Arm title	10 mg LY2944876

Arm description:

10 milligrams (mg) LY2944876 given subcutaneously (SC) once weekly for 24 weeks, plus background PO metformin.

Arm type	Experimental
Investigational medicinal product name	LY2944876
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

10 mg of LY2944876 administered subcutaneously.

Arm title	15 mg LY2944876

Arm description:

15 mg LY2944876 given SC once weekly for 24 weeks, plus background PO metformin..

Arm type	Experimental
Investigational medicinal product name	LY2944876
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

15 mg of LY2944876 administered Subcutaneously.

Arm title	30 mg LY2944876

Arm description:

30 mg LY2944876 given SC once weekly for 24 weeks, plus background PO metformin..

Arm type	Experimental
Investigational medicinal product name	LY2944876
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

30 mg of LY2944876 administered Subcutaneously.

Arm title	50 mg LY2944876

Arm description:

50 mg LY2944876 given SC once weekly for 24 weeks, plus background PO metformin..

Arm type	Experimental
Investigational medicinal product name	LY2944876
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

50 mg of LY2944876 administered Subcutaneously.

Arm title	Exenatide extended-release

Arm description:

2 mg exenatide extended-release given SC once weekly for 24 weeks, plus background PO metformin..

Arm type	Experimental
Investigational medicinal product name	Exenatide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

2 mg of exenatide administered Subcutaneously.

Arm title	Placebo

Arm description:

Placebo for LY2944876 and Exenatide given SC once weekly for 12 weeks,plus background PO metformin. Participants assigned to placebo will have no injections during the second 12 weeks of the study.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for LY2944876 and Exenatide administered Subcutaneously.

Number of subjects in period 1	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876
Started	66	71	73
Completed	57	66	69
Not completed	9	5	4
Physician decision	1	1	-

Consent withdrawn by subject	5	3	-
Adverse event, non-fatal	3	1	2
Jury Duty	-	-	1
Lost to follow-up	-	-	1
Left the city to get a job	-	-	-
Protocol deviation	-	-	-
Lack of efficacy	-	-	-

Number of subjects in period 1	50 mg LY2944876	Exenatide extended-release	Placebo
Started	70	69	71
Completed	63	62	56
Not completed	7	7	15
Physician decision	-	-	1
Consent withdrawn by subject	-	6	10
Adverse event, non-fatal	3	-	1
Jury Duty	-	-	-
Lost to follow-up	2	1	2
Left the city to get a job	1	-	-
Protocol deviation	1	-	-
Lack of efficacy	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	10 mg LY2944876
Reporting group description:	
10 milligrams (mg) LY2944876 given subcutaneously (SC) once weekly for 24 weeks, plus background PO metformin.	
Reporting group title	15 mg LY2944876
Reporting group description:	
15 mg LY2944876 given SC once weekly for 24 weeks, plus background PO metformin..	
Reporting group title	30 mg LY2944876
Reporting group description:	
30 mg LY2944876 given SC once weekly for 24 weeks, plus background PO metformin..	
Reporting group title	50 mg LY2944876
Reporting group description:	
50 mg LY2944876 given SC once weekly for 24 weeks, plus background PO metformin..	
Reporting group title	Exenatide extended-release
Reporting group description:	
2 mg exenatide extended-release given SC once weekly for 24 weeks, plus background PO metformin..	
Reporting group title	Placebo
Reporting group description:	
Placebo for LY2944876 and Exenatide given SC once weekly for 12 weeks,plus background PO metformin. Participants assigned to placebo will have no injections during the second 12 weeks of the study.	

Reporting group values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876
Number of subjects	66	71	73
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	58.1	59.0	56.1
standard deviation	± 9.4	± 8.5	± 8.3
Gender categorical Units: Subjects			
Female	33	40	26
Male	33	31	47

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	19	21	26
Not Hispanic or Latino	42	42	42
Unknown or Not Reported	5	8	5
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	2	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	4	3	5
White	55	59	59
More than one race	6	6	8
Unknown or Not Reported	0	1	0
Region of Enrollment Units: Subjects			
Greece	6	6	5
Puerto Rico	1	2	2
Romania	9	10	10
United States	32	33	33
Poland	9	10	12
Mexico	9	10	11

Reporting group values	50 mg LY2944876	Exenatide extended-release	Placebo
Number of subjects	70	69	71
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	55.6	57.6	56.5
standard deviation	± 8.4	± 9.1	± 9.7
Gender categorical Units: Subjects			
Female	33	32	35
Male	37	37	36
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	19	22	22
Not Hispanic or Latino	47	44	47
Unknown or Not Reported	4	3	2

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	2	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	5	2	6
White	58	59	58
More than one race	6	6	6
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Greece	4	5	6
Puerto Rico	1	3	3
Romania	9	9	10
United States	34	31	30
Poland	12	12	11
Mexico	10	9	11

Reporting group values	Total		
Number of subjects	420		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	199		
Male	221		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	129		
Not Hispanic or Latino	264		
Unknown or Not Reported	27		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	8		
Native Hawaiian or Other Pacific Islander	0		

Black or African American	25		
White	348		
More than one race	38		
Unknown or Not Reported	1		
Region of Enrollment Units: Subjects			
Greece	32		
Puerto Rico	12		
Romania	57		
United States	193		
Poland	66		
Mexico	60		

End points

End points reporting groups

Reporting group title	10 mg LY2944876
Reporting group description:	
10 milligrams (mg) LY2944876 given subcutaneously (SC) once weekly for 24 weeks, plus background PO metformin.	
Reporting group title	15 mg LY2944876
Reporting group description:	
15 mg LY2944876 given SC once weekly for 24 weeks, plus background PO metformin..	
Reporting group title	30 mg LY2944876
Reporting group description:	
30 mg LY2944876 given SC once weekly for 24 weeks, plus background PO metformin..	
Reporting group title	50 mg LY2944876
Reporting group description:	
50 mg LY2944876 given SC once weekly for 24 weeks, plus background PO metformin..	
Reporting group title	Exenatide extended-release
Reporting group description:	
2 mg exenatide extended-release given SC once weekly for 24 weeks, plus background PO metformin..	
Reporting group title	Placebo
Reporting group description:	
Placebo for LY2944876 and Exenatide given SC once weekly for 12 weeks,plus background PO metformin. Participants assigned to placebo will have no injections during the second 12 weeks of the study.	

Primary: Change from Baseline in Hemoglobin A1c (HbA1c) at Week 12

End point title	Change from Baseline in Hemoglobin A1c (HbA1c) at Week 12
End point description:	
HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time. Analysis Population Description (APD): All randomized participants with at least 1 post-baseline measurement and evaluable data. Missing observations are imputed using the Bayesian simple linear regression longitudinal model.	
End point type	Primary
End point timeframe:	
Baseline, Week 12	

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	68	68	65
Units: percentage of HbA1c				
least squares mean (standard error)	-1.080 (± 0.108)	-1.119 (± 0.103)	-1.429 (± 0.102)	-1.361 (± 0.105)

End point values	Exenatide extended-release	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	62		
Units: percentage of HbA1c				
least squares mean (standard error)	-1.428 (± 0.105)	-0.283 (± 0.104)		

Statistical analyses

Statistical analysis title	Hemoglobin A1c (HbA1c) at Week 12
Comparison groups	10 mg LY2944876 v Placebo
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.459
Method	Bayesian
Parameter estimate	Posterior Mean Difference
Point estimate	-0.78
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.05
upper limit	-0.52
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Hemoglobin A1c (HbA1c) at Week 12
Comparison groups	Placebo v 15 mg LY2944876
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.511
Method	Bayesian
Parameter estimate	Posterior Mean Difference
Point estimate	-0.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.07
upper limit	0.54
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Hemoglobin A1c (HbA1c) at Week 12
Comparison groups	Placebo v 30 mg LY2944876
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.988
Method	Bayesian
Parameter estimate	Posterior Mean Difference
Point estimate	-1.15
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.41
upper limit	-0.89
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Hemoglobin A1c (HbA1c) at Week 12
Comparison groups	50 mg LY2944876 v Placebo
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.934
Method	Bayesian
Parameter estimate	Posterior Mean Difference
Point estimate	-1.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.3
upper limit	-0.78
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Hemoglobin A1c (HbA1c) at Week 12
Comparison groups	Exenatide extended-release v 10 mg LY2944876
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.373
Method	Bayesian
Parameter estimate	Posterior Mean Difference
Point estimate	0.35

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.08
upper limit	0.61
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Hemoglobin A1c (HbA1c) at Week 12
Comparison groups	Exenatide extended-release v 15 mg LY2944876
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.433
Method	Bayesian
Parameter estimate	Posterior Mean Difference
Point estimate	0.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.07
upper limit	0.59
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Hemoglobin A1c (HbA1c) at Week 12
Comparison groups	Exenatide extended-release v 30 mg LY2944876
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.978
Method	Bayesian
Parameter estimate	Posterior Mean Difference
Point estimate	-0.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.28
upper limit	0.24
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Hemoglobin A1c (HbA1c) at Week 12
Comparison groups	Exenatide extended-release v 50 mg LY2944876

Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.904
Method	Bayesian
Parameter estimate	Posterior Mean Difference
Point estimate	0.09
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.17
upper limit	0.35
Variability estimate	Standard error of the mean
Dispersion value	0.16

Secondary: Change from Baseline in HbA1c at Week 24

End point title	Change from Baseline in HbA1c at Week 24

End point description:

HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time.

APD: All randomized participants with baseline and at least one post-baseline HbA1c data. Missing observations are imputed using the Bayesian simple linear regression longitudinal model.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	66	68	62
Units: percentage of HbA1c				
least squares mean (standard error)	-0.859 (± 0.128)	-1.162 (± 0.121)	-1.359 (± 0.119)	-1.318 (± 0.123)

End point values	Exenatide extended-release	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	51		
Units: percentage of HbA1c				
least squares mean (standard error)	-1.486 (± 0.123)	-0.357 (± 0.126)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Body Weight

End point title	Percent Change from Baseline in Body Weight

End point description:

APD: All randomized participants with baseline and at least one post-baseline data for body weight. Missing observations are imputed using the Bayesian simple linear regression longitudinal model.

End point type	Secondary

End point timeframe:

Baseline, Week 12; Baseline, Week 24

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57[1]	68[2]	68[3]	65[4]
Units: Percentage change				
least squares mean (standard error)				
Week 12	-1.255 (± 0.371)	-2.004 (± 0.352)	-2.074 (± 0.348)	-3.397 (± 0.357)
Week 24	-1.708 (± 0.496)	-2.269 (± 0.465)	-2.147 (± 0.460)	-3.572 (± 0.475)

Notes:

[1] - Week 12-n=57
Week 24-n= 55

[2] - Week 12-n=68
Week 24-n= 67

[3] - Week 12-n=67
Week 24-n= 68

[4] - Week 12-n=65
Week 24-n= 62

End point values	Exenatide extended-release	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63[5]	63[6]		
Units: Percentage change				
least squares mean (standard error)				
Week 12	-2.183 (± 0.358)	-1.331 (± 0.356)		
Week 24	-2.293 (± 0.477)	-1.777 (± 0.491)		

Notes:

[5] - Week 12-n=63
Week 24-n= 60
[6] - Week 12-n=63
Week 24-n= 51

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fasting Blood Glucose

End point title	Change from Baseline in Fasting Blood Glucose

End point description:

Least square means (LSM) was calculated from mixed-effects model with repeated measures (MMRM) analysis using restricted
maximum likelihood (REML) with metformin use, baseline body mass index (BMI) category, baseline HbA1c category, country, treatment, visit, and treatment-by-visit interaction as fixed effects, baseline fasting blood glucose as a covariate, and participant as a random effect.

APD: All randomized participants with baseline and at least one post-baseline data for fasting blood glucose. Missing observations are imputed using last observation carried forward (LOCF).

End point type	Secondary

End point timeframe:

Baseline, Week 12; Baseline, Week 24

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55[7]	68[8]	67	62[9]
Units: milligrams per deciliter (mg/dL)				
least squares mean (standard error)				
Week 12	-20.881 (± 4.618)	-21.991 (± 4.371)	-31.309 (± 4.305)	-28.405 (± 4.506)
Week 24	-21.497 (± 4.919)	-30.186 (± 4.639)	-29.875 (± 4.548)	-31.390 (± 4.785)

Notes:

[7] - Week 12: 55
Week 24: 54
[8] - Week 12: 68
Week 24: 66
[9] - Week 12: 62
Week 24: 60

End point values	Exenatide extended-release	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62[10]	58[11]		
Units: milligrams per deciliter (mg/dL)				
least squares mean (standard error)				
Week 12	-39.074 (± 4.419)	-1.588 (± 4.519)		

Week 24	-40.328 (± 4.726)	0.124 (± 4.973)		

Notes:

[10] - Week 12: 62
Week 24: 59
[11] - Week 12: 58
Week 24: 49

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in 7-point Self-Monitored Blood Glucose (SMBG) Values

End point title	Change from Baseline in 7-point Self-Monitored Blood Glucose (SMBG) Values

End point description:

SMBG 7-point profiles were measured at morning pre-meal, morning 2 hours post-meal, mid-day pre-meal, mid-day 2 hours post-meal, evening pre-meal, evening 2 hours post-meal, and at bedtime. LSM were calculated from MMRM analysis using REML with metformin use, baseline BMI category, baseline HbA1c category, country, treatment, visit, and treatment-by-visit interaction as fixed effects, baseline fasting blood glucose as a covariate, and participant as a random effect. LSM were calculated from MMRM analysis using REML with metformin use, baseline BMI category, baseline HbA1c category, country, treatment, visit, and treatment-by-visit interaction as fixed effects, baseline fasting blood glucose as a covariate, and participant as a random effect.

APD: All randomized participants with baseline and at least one post-baseline data for SMBG. Missing observations are imputed using last observation carried forward (LOCF).

End point type	Secondary

End point timeframe:

Baseline, Week (Wk) 12; Baseline, Week 24

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	64	66	60
Units: mg/dL				
least squares mean (standard error)				
Pre-Morning Meal (Week 12)	-26.8 (± 3.9)	-28.4 (± 3.8)	-34.3 (± 3.7)	-34.8 (± 3.8)
Pre-Morning Meal (Week 24)	-23.5 (± 4.7)	-29.1 (± 4.5)	-29.6 (± 4.3)	-34.2 (± 4.5)
Morning Meal 2hr (Week 12)	-27.9 (± 6.7)	-34.2 (± 6.8)	-36.0 (± 6.3)	-26.4 (± 6.6)
Morning Meal 2 hr (Week 24)	-29.9 (± 6.5)	-35.9 (± 6.5)	-37.1 (± 6.1)	-42.8 (± 6.4)
Pre-Midday Meal (Week 12)	-17.1 (± 5.1)	-19.6 (± 5.1)	-26.1 (± 4.8)	-24.2 (± 5.0)
Pre-Midday Meal (Week 24)	-16.3 (± 5.6)	-23.4 (± 5.6)	-22.4 (± 5.3)	-23.5 (± 5.4)
Midday Meal 2hr (Week 12)	-17.1 (± 6.4)	-20.7 (± 6.3)	-24.6 (± 6.0)	-22.2 (± 6.2)
Midday Meal 2hr (Week 24)	-12.2 (± 6.1)	-26.6 (± 5.9)	-21.9 (± 5.7)	-33.4 (± 5.9)
Pre-Evening Meal (Week 12)	-24.1 (± 5.3)	-24.8 (± 5.2)	-28.5 (± 4.9)	-30.1 (± 5.1)
Pre-Evening Meal (Week 24)	-24.9 (± 5.7)	-24.3 (± 5.6)	-33.0 (± 5.3)	-29.6 (± 5.4)
Evening Meal (Week 12)	-25.1 (± 5.9)	-26.5 (± 5.7)	-33.4 (± 5.4)	-32.8 (± 5.7)
Evening Meal 2hr (Week 24)	-30.2 (± 5.9)	-27.9 (± 5.8)	-26.0 (± 5.5)	-37.2 (± 5.8)
Bedtime (Week 12)	-19.3 (± 5.7)	-33.5 (± 5.8)	-33.2 (± 5.8)	-36.2 (± 5.6)
Bedtime (Week 24)	-28.9 (± 6.0)	-25.4 (± 6.0)	-32.3 (± 5.7)	-38.5 (± 5.9)

End point values	Exenatide extended-release	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	62		
Units: mg/dL				
least squares mean (standard error)				
Pre-Morning Meal (Week 12)	-38.7 (± 3.8)	-7.4 (± 3.8)		
Pre-Morning Meal (Week 24)	-36.8 (± 4.5)	-14.4 (± 4.9)		
Morning Meal 2hr (Week 12)	-43.5 (± 6.5)	-1.5 (± 6.5)		
Morning Meal 2 hr (Week 24)	-42.7 (± 6.4)	-6.3 (± 6.8)		
Pre-Midday Meal (Week 12)	-23.5 (± 5.0)	-2.3 (± 5.0)		
Pre-Midday Meal (Week 24)	-23.9 (± 5.5)	-4.0 (± 6.0)		
Midday Meal 2hr (Week 12)	-27.4 (± 6.2)	-8.9 (± 6.1)		
Midday Meal 2hr (Week 24)	-37.2 (± 5.9)	-8.5 (± 6.4)		
Pre-Evening Meal (Week 12)	-24.7 (± 5.1)	-1.5 (± 5.1)		
Pre-Evening Meal (Week 24)	-36.4 (± 5.6)	-5.7 (± 6.0)		
Evening Meal (Week 12)	-33.5 (± 5.7)	4.0 (± 5.6)		
Evening Meal 2hr (Week 24)	-36.9 (± 5.8)	1.1 (± 6.2)		
Bedtime (Week 12)	-41.6 (± 5.7)	5.6 (± 5.7)		
Bedtime (Week 24)	-42.9 (± 6.0)	-6.9 (± 6.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Lipids

End point title	Change from Baseline in Lipids

End point description:

Change from baseline in high-density lipoprotein cholesterol (HDL-C), total cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-C). LSM was calculated from MMRM analysis using REML with metformin use, baseline BMI category, baseline HbA1c category, country, treatment, visit, and treatment-by-visit interaction as fixed effects, baseline parameter result as a covariate, and participant an a random effect.

APD: All randomized participants with baseline and at least one post-baseline data for lipids. Missing observations are imputed using last observation carried forward (LOCF).

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	66	68	61
Units: mg/dL				
least squares mean (standard error)				
HDL-C	1.56 (± 1.03)	0.92 (± 0.98)	0.90 (± 0.96)	1.04 (± 1.01)
Total Cholesterol	-1.26 (± 4.37)	-1.12 (± 4.16)	-1.46 (± 4.09)	-5.11 (± 4.24)
Triglycerides	-14.63 (± 11.49)	-13.32 (± 10.93)	-15.40 (± 10.59)	-20.96 (± 11.16)
LDL-C	-1.37 (± 3.75)	-0.40 (± 3.57)	-0.24 (± 3.56)	-0.04 (± 3.72)

End point values	Exenatide extended-release	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	53		
Units: mg/dL				
least squares mean (standard error)				
HDL-C	2.35 (± 0.990)	2.17 (± 1.04)		
Total Cholesterol	-0.12 (± 4.22)	7.32 (± 4.40)		
Triglycerides	-11.83 (± 11.01)	10.61 (± 11.58)		
LDL-C	0.37 (± 3.65)	4.55 (± 3.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fasting Fibroblast Growth Factor 21

End point title	Change from Baseline in Fasting Fibroblast Growth Factor 21

End point description:

LSM was calculated from MMRM analysis using REML with metformin use, baseline BMI category, baseline HbA1c category, country, treatment, visit, and treatment-by-visit interaction as fixed effects, baseline parameter result as a covariate, and participant as a random effect.

APD: All randomized participants with baseline and at least one post-baseline data for fasting fibroblast growth factor 21. Missing observations are imputed using last observation carried forward (LOCF).

End point type	Secondary

End point timeframe:

Baseline, Week 12; Baseline, Week 24

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	68	65	64
Units: microgram per liter (µg/L)				
least squares mean (standard error)				
Week 12	-0.07 (± 0.071)	0.06 (± 0.068)	-0.03 (± 0.068)	-0.14 (± 0.069)
Week 24	0.06 (± 0.071)	-0.04 (± 0.068)	-0.07 (± 0.067)	-0.12 (± 0.070)

End point values	Exenatide extended-release	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	58		
Units: microgram per liter (µg/L)				
least squares mean (standard error)				
Week 12	-0.09 (± 0.069)	-0.11 (± 0.071)		
Week 24	-0.06 (± 0.069)	-0.09 (± 0.073)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Requiring Rescue Therapy

End point title	Percentage of Participants Requiring Rescue Therapy

End point description:

Participants who received rescue medication with non-study antihyperglycemic medications or change their stable dose of metformin.

APD: All randomized participants with baseline and at least one post-baseline data for participants requiring rescue therapy.

End point type	Secondary

End point timeframe:

Baseline through Therapy Completion (Week 24)

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	71	73	69
Units: percentage of participants				
number (not applicable)	6.1	2.8	2.7	4.3

End point values	Exenatide extended-release	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	71		
Units: percentage of participants				
number (not applicable)	2.9	11.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Developing Anti-Drug Antibodies to LY2944876 or Polyethylene Glycol

End point title	Percentage of Participants Developing Anti-Drug Antibodies to LY2944876 or Polyethylene Glycol

End point description:

Participants with a four-fold change in antibody titers from baseline

APD: All randomized participants who received study drug and had evaluable immunogenicity.

End point type	Secondary

End point timeframe:

Week 12 and Week 24

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	71	73	70
Units: percentage of participants				
number (not applicable)				
Week 12	1.7	1.4	1.5	0
Week 24	1.8	0	1.5	0

End point values	Exenatide extended-release	Placebo		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	71		
Units: percentage of participants				
number (not applicable)				
Week 12	1.6	0		
Week 24	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Maximum Concentration (Cmax) of LY2944876

End point title	Pharmacokinetics (PK): Maximum Concentration (Cmax) of LY2944876[12]

End point description:

Evaluable pharmacokinetic concentrations from the specified timepoints were combined and utilized in a population approach to determine the population mean estimate and standard deviation at steady-state.
APD: All randomized participants who received study drug LY2944876 and had evaluable PK data.

End point type	Secondary

End point timeframe:

Baseline, Week 8, Week 12, Week 16, Week 20, Week 24

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: No inferential statistics were planned for this endpoint.

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	71	73	70
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	607 (± 282)	799 (± 368)	1690 (± 732)	2570 (± 1240)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Adiponectin Levels

End point title	Change from Baseline in Adiponectin Levels

End point description:

LSM are calculated from MMRM analysis using REML with metformin use, baseline BMI category, baseline HbA1c category, country, treatment, visit, and treatment-by-visit interaction as fixed effects, baseline parameter result as a covariate, and participant as a random effect.
APD: All randomized participants with baseline and at least one post-baseline data for adiponectin levels. Missing observations are imputed using last observation carried forward (LOCF).

End point type	Secondary

End point timeframe:

Baseline, Week 12; Baseline, Week 24

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	71	73	69
Units: µg/L				
least squares mean (standard error)				
Week 12	0.14 (± 0.168)	0.03 (± 0.160)	-0.10 (± 0.157)	0.12 (± 0.161)
Week 24	0.03 (± 0.245)	0.30 (± 0.226)	0.28 (± 0.221)	0.58 (± 0.235)

End point values	Exenatide extended-release	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	71		
Units: µg/L				
least squares mean (standard error)				
Week 12	0.04 (± 0.160)	0.03 (± 0.164)		
Week 24	0.14 (± 0.231)	0.25 (± 0.250)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Beta-Hydroxy Butyrate Levels

End point title	Change from Baseline in Beta-Hydroxy Butyrate Levels

End point description:

LSM are calculated from MMRM analysis using REML with metformin use, baseline BMI category, baseline HbA1c category, country, treatment, visit, and treatment-by-visit interaction as fixed effects, baseline parameter result as a covariate, and participant as a random effect.
APD: All randomized participants with baseline and at least one post-baseline data for beta-hydroxy butyrate levels. Missing observations are imputed using last observation carried forward (LOCF).

End point type	Secondary

End point timeframe:

Baseline, Week 12; Baseline, Week 24

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	67	64	63
Units: mg/dL				
least squares mean (standard error)				
Week 12	-0.27 (± 0.13)	-0.28 (± 0.12)	-0.13 (± 0.12)	-0.31 (± 0.12)
Week 24	-0.33 (± 0.11)	-0.39 (± 0.10)	-0.34 (± 0.10)	-0.33 (± 0.10)

End point values	Exenatide extended-release	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	58		
Units: mg/dL				
least squares mean (standard error)				
Week 12	-0.29 (± 0.12)	-0.23 (± 0.13)		
Week 24	-0.19 (± 0.10)	-0.37 (± 0.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Glucagon Levels

End point title	Change from Baseline in Glucagon Levels

End point description:

LSM are calculated from MMRM analysis using REML with metformin use, baseline BMI category, baseline HbA1c category, country, treatment, visit, and treatment-by-visit interaction as fixed effects, baseline parameter result as a covariate, and participant as a random effect.
APD: All randomized participants with baseline and at least one post-baseline data for glucagon levels. Missing observations are imputed using last observation carried forward (LOCF).

End point type	Secondary

End point timeframe:

Baseline, Week 12; Baseline, Week 24

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	66	64	60
Units: picomol per liter (pmol/L)				
least squares mean (standard error)				
Week 12	-1.26 (± 0.82)	-2.65 (± 0.79)	-5.14 (± 0.79)	-6.21 (± 0.81)
Week 24	-2.30 (± 1.15)	-2.25 (± 1.05)	-4.40 (± 1.05)	-4.93 (± 1.11)

End point values	Exenatide extended-release	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	54		
Units: picomol per liter (pmol/L)				
least squares mean (standard error)				
Week 12	-1.58 (± 0.79)	-0.04 (± 0.84)		
Week 24	-0.19 (± 1.08)	0.66 (± 1.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Insulin Levels

End point title	Change from Baseline in Insulin Levels

End point description:

LSM are calculated from MMRM analysis using REML with metformin use, baseline BMI category, baseline HbA1c category, country, treatment, visit, and treatment-by-visit interaction as fixed effects, baseline parameter result as a covariate, and participant as a random effect.
APD: All randomized participants with baseline and at least one post-baseline data for insulin levels. Missing observations are imputed using last observation carried forward (LOCF).

End point type	Secondary

End point timeframe:

Baseline, Week 12; Baseline, Week 24

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	64	62	59
Units: micro-international units/milliliter				
least squares mean (standard error)				
Week 12	0.30 (± 1.21)	0.97 (± 1.13)	0.03 (± 1.14)	0.96 (± 1.17)
Week 24	-1.44 (± 1.51)	0.68 (± 1.39)	0.58 (± 1.40)	0.34 (± 1.48)

End point values	Exenatide extended-release	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: micro-international units/milliliter				

least squares mean (standard error)				
Week 12	2.78 (± 1.14)	-0.85 (± 1.16)		
Week 24	1.97 (± 1.40)	1.45 (± 1.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Area Under the Concentration Curve (AUC) of LY2944876

End point title	Pharmacokinetics: Area Under the Concentration Curve (AUC) of LY2944876[13]

End point description:

Evaluable pharmacokinetic concentrations from the specified timepoints were combined and utilized in a population approach to determine the population mean estimate and standard deviation at steady-state.

APD: All randomized participants who received study drug LY2944876 and had evaluable PK data.

End point type	Secondary

End point timeframe:

Baseline, Week 8, Week 12, Week 16, Week 20, Week 24

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: No inferential statistics were planned for this endpoint.

End point values	10 mg LY2944876	15 mg LY2944876	30 mg LY2944876	50 mg LY2944876
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	71	73	70
Units: nanograms*hour per milliliter (ng*h/mL)				
arithmetic mean (standard deviation)	88100 (± 40600)	117000 (± 50800)	247000 (± 106000)	381000 (± 187000)

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:	
I7I-MC-XNAA	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	LY2944876 10mg
Reporting group description:	
10 milligrams (mg) LY2944876 given subcutaneously (SC) once weekly for 24 weeks.	
Reporting group title	LY2944876 15mg
Reporting group description:	
15 mg LY2944876 given SC once weekly for 24 weeks.	
Reporting group title	LY2944876 30mg
Reporting group description:	
30 mg LY2944876 given SC once weekly for 24 weeks.	
Reporting group title	LY2944876 50mg
Reporting group description:	
50 mg LY2944876 given SC once weekly for 24 weeks.	
Reporting group title	Exenatide 2mg
Reporting group description:	
2 mg exenatide extended-release given SC once weekly for 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
Placebo for LY2944876 and Exenatide given SC once weekly for 12 weeks. Participants assigned to placebo will have no injections during the second 12 weeks of the study.	

Serious adverse events	LY2944876 10mg	LY2944876 15mg	LY2944876 30mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 66 (0.00%)	2 / 71 (2.82%)	2 / 73 (2.74%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
endometrial adenocarcinoma			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

endometrial cancer			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	1 / 71 (1.41%)	0 / 73 (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
Congenital, familial and genetic disorders			
branchial cyst			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
vessel perforation			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	0 / 73 (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			
acute myocardial infarction			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	1 / 71 (1.41%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
angina unstable			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	0 / 73 (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
Surgical and medical procedures			
cataract operation			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Eye disorders			
cataract			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal pain lower			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	0 / 73 (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
pancreatitis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
blood blister			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	0 / 73 (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
Renal and urinary disorders			
nephrolithiasis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
abscess limb			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	0 / 73 (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

urinary tract infection			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	LY2944876 50mg	Exenatide 2mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 70 (4.29%)	3 / 69 (4.35%)	2 / 71 (2.82%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
endometrial adenocarcinoma			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 70 (0.00%)	1 / 69 (1.45%)	0 / 71 (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
endometrial cancer			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 70 (0.00%)	0 / 69 (0.00%)	0 / 71 (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
Congenital, familial and genetic disorders			
branchial cyst			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 70 (1.43%)	0 / 69 (0.00%)	0 / 71 (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
Vascular disorders			
vessel perforation			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 70 (0.00%)	0 / 69 (0.00%)	1 / 71 (1.41%)
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			
acute myocardial infarction			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 70 (0.00%)	0 / 69 (0.00%)	0 / 71 (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
angina unstable			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 70 (0.00%)	1 / 69 (1.45%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
cataract operation			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 70 (0.00%)	1 / 69 (1.45%)	0 / 71 (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
Eye disorders			
cataract			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 70 (0.00%)	1 / 69 (1.45%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal pain lower			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 70 (1.43%)	0 / 69 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 70 (0.00%)	0 / 69 (0.00%)	0 / 71 (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

Skin and subcutaneous tissue disorders			
blood blister			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 70 (1.43%)	0 / 69 (0.00%)	0 / 71 (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
Renal and urinary disorders			
nephrolithiasis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 70 (0.00%)	0 / 69 (0.00%)	0 / 71 (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			
abscess limb			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 70 (0.00%)	0 / 69 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 70 (0.00%)	0 / 69 (0.00%)	0 / 71 (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	LY2944876 10mg	LY2944876 15mg	LY2944876 30mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 66 (51.52%)	47 / 71 (66.20%)	39 / 73 (53.42%)
Investigations			
lipase increased			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	4 / 66 (6.06%)	2 / 71 (2.82%)	2 / 73 (2.74%)
occurrences (all)	4	2	2
Injury, poisoning and procedural complications			

muscle strain			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	4 / 71 (5.63%)	1 / 73 (1.37%)
occurrences (all)	0	4	1
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	4 / 66 (6.06%)	2 / 71 (2.82%)	1 / 73 (1.37%)
occurrences (all)	4	2	1
headache			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	5 / 66 (7.58%)	9 / 71 (12.68%)	5 / 73 (6.85%)
occurrences (all)	7	13	5
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 66 (1.52%)	1 / 71 (1.41%)	2 / 73 (2.74%)
occurrences (all)	1	1	7
constipation			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	3 / 66 (4.55%)	4 / 71 (5.63%)	4 / 73 (5.48%)
occurrences (all)	3	4	4
diarrhoea			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	7 / 66 (10.61%)	15 / 71 (21.13%)	13 / 73 (17.81%)
occurrences (all)	35	24	45
dyspepsia			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	1 / 71 (1.41%)	2 / 73 (2.74%)
occurrences (all)	0	1	3
flatulence			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 66 (1.52%)	1 / 71 (1.41%)	4 / 73 (5.48%)
occurrences (all)	1	1	4
gastrooesophageal reflux disease			

alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 66 (1.52%)	1 / 71 (1.41%)	1 / 73 (1.37%)
occurrences (all)	1	1	1
nausea			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	11 / 66 (16.67%)	21 / 71 (29.58%)	20 / 73 (27.40%)
occurrences (all)	28	33	53
vomiting			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	8 / 66 (12.12%)	6 / 71 (8.45%)	10 / 73 (13.70%)
occurrences (all)	9	6	21
Respiratory, thoracic and mediastinal disorders			
oropharyngeal pain			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	3 / 66 (4.55%)	3 / 71 (4.23%)	1 / 73 (1.37%)
occurrences (all)	3	3	1
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	2 / 71 (2.82%)	0 / 73 (0.00%)
occurrences (all)	0	2	0
back pain			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	4 / 66 (6.06%)	6 / 71 (8.45%)	1 / 73 (1.37%)
occurrences (all)	4	7	1
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	4 / 66 (6.06%)	1 / 71 (1.41%)	3 / 73 (4.11%)
occurrences (all)	4	1	3
influenza			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 66 (1.52%)	4 / 71 (5.63%)	1 / 73 (1.37%)
occurrences (all)	1	5	3

nasopharyngitis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	8 / 66 (12.12%)	9 / 71 (12.68%)	5 / 73 (6.85%)
occurrences (all)	8	11	5
sinusitis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 66 (1.52%)	5 / 71 (7.04%)	2 / 73 (2.74%)
occurrences (all)	1	6	2
upper respiratory tract infection			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 66 (3.03%)	10 / 71 (14.08%)	5 / 73 (6.85%)
occurrences (all)	3	12	5
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 66 (0.00%)	0 / 71 (0.00%)	4 / 73 (5.48%)
occurrences (all)	0	0	6
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	3 / 66 (4.55%)	6 / 71 (8.45%)	6 / 73 (8.22%)
occurrences (all)	3	6	6

Non-serious adverse events	LY2944876 50mg	Exenatide 2mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 70 (65.71%)	38 / 69 (55.07%)	16 / 71 (22.54%)
Investigations			
lipase increased			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	5 / 70 (7.14%)	0 / 69 (0.00%)	0 / 71 (0.00%)
occurrences (all)	9	0	0
Injury, poisoning and procedural complications			
muscle strain			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 70 (1.43%)	0 / 69 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

dizziness			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 70 (2.86%)	1 / 69 (1.45%)	1 / 71 (1.41%)
occurrences (all)	2	1	1
headache			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	6 / 70 (8.57%)	9 / 69 (13.04%)	4 / 71 (5.63%)
occurrences (all)	11	14	4
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	3 / 70 (4.29%)	4 / 69 (5.80%)	1 / 71 (1.41%)
occurrences (all)	3	5	2
constipation			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	5 / 70 (7.14%)	2 / 69 (2.90%)	1 / 71 (1.41%)
occurrences (all)	8	2	1
diarrhoea			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	12 / 70 (17.14%)	18 / 69 (26.09%)	4 / 71 (5.63%)
occurrences (all)	25	52	16
dyspepsia			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	5 / 70 (7.14%)	1 / 69 (1.45%)	0 / 71 (0.00%)
occurrences (all)	8	2	0
flatulence			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 70 (2.86%)	1 / 69 (1.45%)	0 / 71 (0.00%)
occurrences (all)	2	1	0
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	4 / 70 (5.71%)	2 / 69 (2.90%)	0 / 71 (0.00%)
occurrences (all)	4	2	0
nausea			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	32 / 70 (45.71%)	17 / 69 (24.64%)	4 / 71 (5.63%)
occurrences (all)	90	55	4
vomiting			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	22 / 70 (31.43%)	6 / 69 (8.70%)	2 / 71 (2.82%)
occurrences (all)	37	12	3
Respiratory, thoracic and mediastinal disorders			
oropharyngeal pain			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 70 (2.86%)	4 / 69 (5.80%)	1 / 71 (1.41%)
occurrences (all)	2	4	1
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	5 / 70 (7.14%)	1 / 69 (1.45%)	0 / 71 (0.00%)
occurrences (all)	5	1	0
back pain			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 70 (2.86%)	2 / 69 (2.90%)	2 / 71 (2.82%)
occurrences (all)	2	3	3
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 70 (2.86%)	0 / 69 (0.00%)	0 / 71 (0.00%)
occurrences (all)	2	0	0
influenza			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 70 (2.86%)	1 / 69 (1.45%)	2 / 71 (2.82%)
occurrences (all)	2	1	3
nasopharyngitis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	4 / 70 (5.71%)	6 / 69 (8.70%)	2 / 71 (2.82%)
occurrences (all)	4	7	3
sinusitis			
alternative dictionary used:			

MedDRA 18.1			
subjects affected / exposed	0 / 70 (0.00%)	2 / 69 (2.90%)	2 / 71 (2.82%)
occurrences (all)	0	2	2
upper respiratory tract infection			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	3 / 70 (4.29%)	4 / 69 (5.80%)	1 / 71 (1.41%)
occurrences (all)	3	4	1
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 70 (1.43%)	0 / 69 (0.00%)	0 / 71 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	8 / 70 (11.43%)	2 / 69 (2.90%)	1 / 71 (1.41%)
occurrences (all)	9	2	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 July 2014	Added Safety and tolerability to secondary outcomes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported